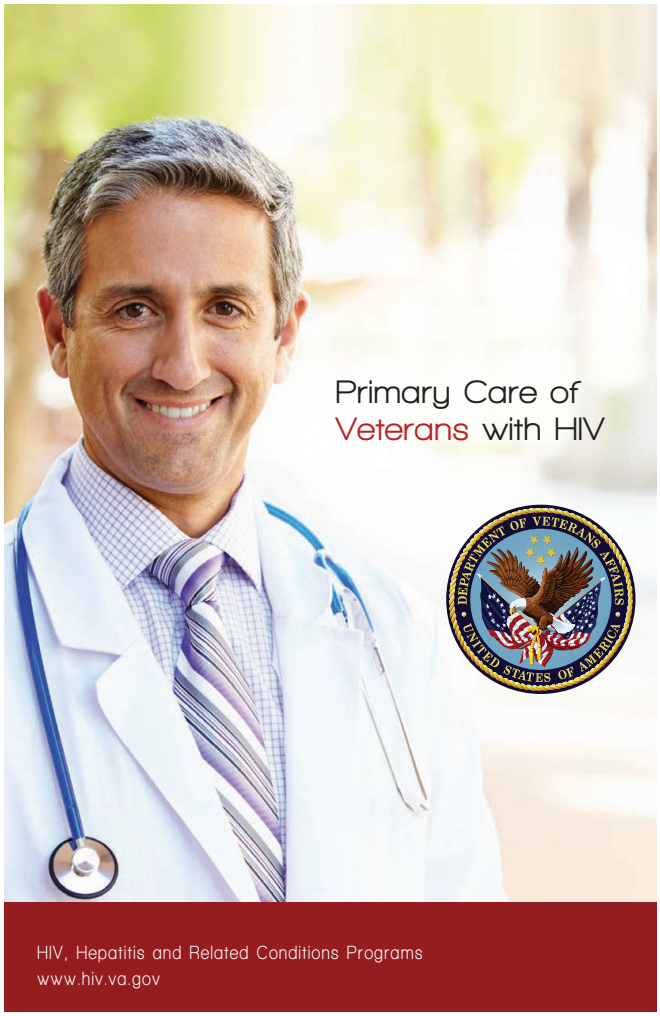

Primary Care of Veterans with HIV

HIV, Hepatitis and Related Conditions Programs (HHRC)
in the Office of Specialty Care Services
Veterans Health Administration
U.S. Department of Veterans Affairs

January 2019

IMPORTANT NOTICE

The editors of this manual are committed to providing accurate information on HIV-related care. However, please be aware that therapy options and protocols continue to change. Readers are invited to check for updates to drug information at Drugs@FDA (**http://www.accessdata.fda.gov/scripts/cder/drugsatfda/**) and to treatment guidelines at AIDS Info (**http://aidsinfo.nih.gov/**).

We hope that you will send feedback and suggestions for future editions to: **VHAHHRC@va.gov**

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Introduction

In 2009, the first edition of Primary Care of Veterans with HIV was released, quickly becoming an important resource for providers delivering high-quality primary care to Veterans living with HIV. Over the past decade, as more Veterans with HIV infection in care in facilities operated by the U.S. Department of Veterans Affairs (VA) have been diagnosed, linked to care, and started on highly active antiretroviral therapy (HAART), the role of primary care has grown, with much of this care provided not only through HIV specialty care clinics but also via Infectious Disease-Patient Aligned Care Teams. Much of this is provided not only through HIV specialty care clinics but also via infectious Disease-Patient Aligned Care Teams. The phenomenal benefits of HAART are perhaps best illustrated by survival of these Veterans into their eighth decade of life. Over the last decade, the proportion of Veterans in VA care with HIV aged 70 years and up has increased from 5% to 15%. The aging of this population has made management of conditions traditionally associated with other individuals, such as cardiovascular disease, diabetes, and malignancy, even more important.

Recognizing a continued need to focus on age-related comorbid illnesses, substance use, and other critical issues for Veterans living with HIV, we have updated and added to this original resource. This manual serves as a point-of-care reference for HIV clinicians providing HIV and primary care to their HIV patients. We hope it will also be of use to non-VA providers who care for Veterans with HIV outside of the VA healthcare system. This manual is meant to be a practical guide to screening and treatment of many of the most common and serious comorbid conditions among people living with HIV.

The HIV, Hepatitis, and Related Conditions Programs in the VA Office of Specialty Care Services would like to thank all the VA subject matter experts who contributed to the update of this manual. We gratefully acknowledge their expertise, enthusiasm, and the countless hours they dedicated to revising a resource aimed at improving the care and well-being of our Veterans. We also extend our thanks to members of the VA HIV Technical Advisory Group for their advice and guidance.

Comments and suggestions regarding this manual are welcome, and can be e-mailed to hivhhrc@va.gov.

This manual is dedicated to all the providers across the VA system who strive to provide excellent HIV care to our Veterans, and to the Veterans who have entrusted the VA with their care.

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Abbreviations for Antiretroviral Drugs and Dosing Instructions Commonly Used in This Manual

DOSING TERMINOLOGY

BID = twice daily
IM = intramuscular
IV = intravenous
PO = orally
PRN = as needed
Q2H, Q4H, etc = every 2 hours, every 4 hours, etc
QAM = every morning
QD = once daily
QH = every hour
QHS = every night at bedtime
QID = 4 times per day
QOD = every other day
TID = 3 times per day
TIW = 3 times per week

ANTIRETROVIRAL TERMINOLOGY

ART = antiretroviral therapy
ARV = antiretroviral
FI = fusion inhibitor
NNRTI = nonnucleoside reverse transcriptase inhibitor
NRTI = nucleoside (or nucleotide) reverse transcriptase inhibitor
PI = protease inhibitor

ANTIRETROVIRAL DRUGS

3TC = lamivudine
ABC = abacavir
APV = amprenavir
ATV = atazanavir
d4T = stavudine
ddC = zalcitabine
ddI = didanosine
DLV = delavirdine
DRV = darunavir
EFV = efavirenz
ENF = enfuvirtide
ETR = etravirine
FPV = fosamprenavir
FTC = emtricitabine
IDV = indinavir
LPV/r = lopinavir/ritonavir
MVC = maraviroc
NFV = nelfinavir
NVP = nevirapine
RAL = raltegravir
RTV = ritonavir
/r = ritonavir, low dose
SQV = saquinavir
TDF = tenofovir
TPV = tipranavir
ZDV = zidovudine

Interactions Tables

Common Medications: ARV Interactions

For information on potential ARV interactions with the following medications, see the specified chapters:

Acid-lowering medications (See **Gastroesophageal Reflux Disease (GERD)**, p. 431)

Hormonal contraceptives (See **Women's Health**, p. 283)

Lipid-lowering medications (See **Lipid-Lowering Medications**, p. 25)

Psychoactive medications: antidepressants, sedatives, antipsychotics (See **Psychoactive Medications**, p. 41)

St. John's wort (See **Food and Supplements**, p. 23)

Antiepileptic Medications

Carbamazepine, phenytoin, and phenobarbital may ↓ PI and NNRTI levels substantially.

Medication	ARV Interactions	Comments
Carbamazepine CYP450 inducer	**PIs:** may ↓ PI levels • ATV: ↑ carbamazepine levels • DRV: ↑ carbamazepine AUC 45% • RTV: ↑ carbamazepine levels • LPV/r: ↑ carbamazepine levels • Other PIs: may also ↑ carbamazepine levels • COBI: ↓ COBI levels	Should not be used; use alternative antiepileptics. • Contraindicated with ATV/c or DRV/c DRV: no significant change DRV/r: Monitor anticonvulsant level and adjust dose accordingly. ATV/r, LPV/r: Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. **Do not coadminister with LPV/r QDay**. Two-way interactions also affect PI and NNRTI levels.
	NNRTIs: may ↓ levels of all NNRTIs • EFV: ↓ carbamazepine AUC 27%; ↓ EFV levels	Monitor carbamazepine and EFV/NVP levels, if possible; use alternative antiepileptics. ETR and RPV should not

Note: Some medications mentioned in this chapter may not be available on the VHA National Formulary (https://www.pbm.va.gov/NationalFormulary.asp). Consult VA pharmacists for alternatives.

Medication	ARV Interactions	Comments
-	36% • ETR and NVP: ↓ carbamazepine and NNRTI levels • RPV: expect ↓ RPV levels	be coadministered.
	NRTIs **TAF**: ↓TAF possible	Consider alternative anticonvulsant.
	INSTIs • DTG:↓ DTG levels possible • EVG/c: carbamazepine AUC ↑ 43% EVG AUC ↓ 69% and C_{min} ↓ >99% ↓COBI expected • EVG plus PI/r: ↓ EVG	DTG: Consider alternative anticonvulsant. EVG/c: **Contraindicated. Do not coadminister.** EVG plus PI/r: Consider alternative anticonvulsant.
	MVC: ↓ MVC levels	If used concurrently without a strong CYP 3A4 inhibitor, give MVC 600 mg BID or alternative antiepileptic agent.
Phenobarbital CYP450 inducer	**PIs**: may ↓ PI levels • DRV: ↓ phenobarbital levels • RTV: ↓ phenobarbital levels • COBI: ↓ COBI levels	Should not be used; use alternative antiepileptics. • Contraindicated with ATV/c or DRV/c. Avoid concomitant use if possible; use alternative antiepileptics. Do not coadminister with LPV/r once daily or unboosted ATV. Two-way interactions also affect PI and NNRTI levels.
	NNRTIs: may ↓ NNRTI levels • EFV and NVP: ↓ phenobarbital levels • ETR: ↓ ETR levels • RPV: expect ↓ RPV levels	Monitor phenobarbital and EFV/NVP levels, if possible; use alternative antiepileptics. ETR and RPV should not be coadministered.
	NRTIs **TAF**: ↓ TAF possible	Consider alternative anticonvulsant.

Medication	ARV Interactions	Comments
-	**INSTIs** • DTG: ↓ DTG levels possible EVG/c: carbamazepine AUC ↑ 43% EVG AUC ↓ 69% and C_{min} ↓ >99% ↓ COBI expected EVG plus PI/r: ↓ EVG	DTG: Consider alternative anticonvulsant. EVG/c: **Contraindicated. Do not coadminister**. EVG plus PI/r: Consider alternative anticonvulsant.
	MVC: ↓ MVC levels	If used concurrently without a strong CYP 3A4 inhibitor, give MVC 600 mg BID or alternative antiepileptic agent.
Phenytoin CYP450 inducer	**PIs**: may ↓ PI levels • DRV: ↓ phenytoin levels • ATV: ↓ phenytoin levels • LPV/r: ↓ LPV/r AUC 33%, ↓ ↓ phenytoin AUC 31% • RTV: anticipate ↓ phenytoin levels • COBI: ↓ COBI levels	Contraindicated with COBI Avoid if possible; use alternative antiepileptics. Two-way interactions also affect PI and NNRTI levels. Do not co-administer with ATV, LPV/r QDay.
	NNRTIs: may ↓ NNRTI levels • EFV: ↓ phenytoin levels, ↓ EFV levels • ETR: ↓ ETR and phenytoin levels • NVP: ↓ phenytoin and NVP levels • RPV: ↓ RPV expected	Monitor phenytoin and EFV/NVP levels, if possible; use alternative antiepileptics. ETR and RPV should not be coadministered.
	NRTIs **TAF**: ↓ TAF possible **INSTIs** • DTG: ↓ DTG levels possible EVG/c: carbamazepine AUC ↑ 43% EVG AUC ↓ 69%	Consider alternative anticonvulsant. DTG: Consider alternative anticonvulsant. EVG/c: **Contraindicated. Do not coadminister.** EVG plus PI/r: Consider alternative anticonvulsant.

Medication	ARV Interactions	Comments
-	and C_{min} ↓ >99% ↓ COBI expected EVG plus PI/r: ↓ EVG	-
	MVC: ↓ MVC levels	If used concurrently without a strong CYP 3A4 inhibitor, give MVC 600 mg BID or alternative antiepileptic agent.
Valproate	**PIs** • LPV /r: ↑ LPV AUC 75%, may ↓ valproate levels	Monitor VPA levels and virologic response. Monitor for LPV-related toxicities.
	NNRTIs: no significant changes in NNRTI or valproate levels	-
Lamotrigine	**PIs** • ATV/r: ↓ lamotrigine levels 32% • LPV/r: ↓ lamotrigine levels 50% • RTV: ↓ lamotrigine levels	Dose increase of lamotrigine may be needed; consider TDM or an alternative. No data when used with COBI.

Antifungal Medications

Medication	ARV Interactions	Comments
Fluconazole Inhibitor of CYP 2C9	**PIs** • ATV/r or ATV/c: no significant change	No dosage adjustment necessary.
	NNRTIs • NVP: 110% ↑ in NVP levels • EFV: no significant change • ETR, RPV: potential ↑ in • NNRTI levels	Avoid use with NVP. EFV, ETR: dosage adjustment not required. RPV: no dose adjustment needed. Monitor for breakthrough fungal infection.

Psychoactive Medications: ARV Interactions

Antidepressants

Class of Medication	Considerations
SSRI	
Citalopram, escitalopram	• RTV causes no change in levels
Fluoxetine	• RTV: ↑ RTV AUC 19%, no change in C_{max}
Paroxetine	• DRV/r: paroxetine AUC 39%
Sertraline	• DRV/r: sertraline AUC and Cmin ↓ 49% • EFV: ↓ sertraline by 39% based on clinical response
	• In general, when used with PIs, SSRIs should be titrated based on clinical response. • SSRI interactions with ATV/c or DRV/c are unknown, thus it is recommended to titrate SSRI dose using the lowest available dose. • SSRI with COBI: possible increase in SSRI level; initiate with low dose SSRI and titrate based on SSRI response.
SNRI	
Venlafaxine, duloxetine	• PIs may increase SNRI level. It is recommended to start at lowest effective dosage; monitor for adverse effects.
Tricyclic (TCA)	• All PIs (including ATV/c and DrV/c) may decrease TCA levels. It is recommended to start at low dosage, use lowest effective dosage; monitor for adverse effects. • EVG/c: use lowest dose of TCA and titrate carefully.
Other Antidepressants	
Bupropion	• EFV: ↓ bupropion AUC 55%, based on clinical response • LPV: ↓ bupropion AUC 57% • EVG/c: ↑ or ↓ bupropion possible
Buspirone	• All PIs or COBI-boosted agents: ↑buspirone levels expected • Use a low dose of buspirone with caution and and titrate buspirone dose based on clinical response.

Note: Some medications mentioned in this chapter may not be available on the VHA National Formulary (https://www.pbm.va.gov/NationalFormulary.asp). Consult VA pharmacists for alternatives.

Class of Medication	Considerations
Mirtazapine	• No data; RTV may ↑ mirtazapine levels • Start at low dosage, use lowest effective dosage; monitor for adverse effects.
Nefazodone	• RTV may ↑ nefazodone levels • Nefazodone may ↑ MVC • Start at low dosage, use lowest effective dosage; monitor for adverse effects. • MVC dosage: 150 mg BID
Trazodone	• RTV: ↑ trazodone AUC >200% • DRV, LPV/r: ↑ trazodone AUC EVG/c or boosted PI: ↑ trazodone possible • EVG/c or boosted PI: ↑ trazodone possible • Start at low dosage, use lowest effective dosage; monitor for CNS and cardiovascular effect.
St. John's wort	• Substantial ↓ in levels of most PIs, NNRTIs, and MVC • Do not coadminister.

Sedatives, Hypnotics

Class of Medication	Considerations
Benzodiazepine	
Midazolam and Triazolam	• Do not coadminister with PIs, COBI, or EFV due to expected significant increases in midazolam and triazolam concentration. • **Higher risk of benzodiazepine adverse effects in elderly patients; avoid if possible.** • For procedures, may consider single-dose IV midazolam with close monitoring.
Alprazolam, Clonazepam and Diazepam	• Consider alternative BZP due to possible increased concentrations.
Alprazolam and NNRTIs	• Monitor for alprazolam therapeutic effectiveness.
Diazepam and ETR	• Decreased dose of diazepam may be required; monitor for adverse effects.

Lorazepam, Temazepam, and Oxazepam	• Where BZD are indicated, consider using these agents. • These benzodiazepines are, in part, metabolized via non-CYP450 pathways; lower potential for interactions). • Start at low dosage, use lowest effective dosage; monitor for adverse effects.
Other Sedatives, Hypnotics	
Suvorexant	• Monitor for adverse effects and reduce dose if necessary. • All PIs or COBI: ↑ suvorexant expected
Zolpidem	• COBI: ↑ zolpidem expected • RTV: ↑ zolpidem AUC 27%

Antipsychotics

Few data on interactions between ARVs and antipsychotics

Class of Medication	Considerations
Olanzapine	• RTV: ↓ olanzapine AUC 53%, half-life ↓ 50% • Start at low dosage, use lowest effective dosage; monitor for adverse effects.
Quetiapine	• PIs or COBI-boosted agents: ↑quetiapine expected Starting quetiapine in a patient receiving a PI or COBI: • Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine effectiveness and adverse effects. Starting a PI in a patient receiving a stable dose of quetiapine: • Reduce quetiapine dose to 1/6 of the original dose. Closely monitor for quetiapine effectiveness and adverse effects.
Other Antipsychotics	
Perphenazine, Risperidone, Thioridazine	• All PIs, ATV/c, and DRV/c: ↑ antipsychotic possible • Titrate antipsychotic dose using the lowest initial dose, or adjust maintenance dose accordingly. Monitor for toxicities.

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Behavioral Health

Mental Health

Depression

KEY POINTS

- Depression can be a life-threatening disorder.
- Depression among people with HIV is common and is associated with increased high-risk behavior, decreased physical activity, nonadherence to antiretroviral therapy (ARV), and progression of immunodeficiency.
- Depression can be diagnosed and treatment can be initiated in the primary care setting.
- Tools such as the Patient Health Questionnaire (PHQ) can be used for screening and for ongoing monitoring of patients identified as depressed.
- Potentially treatable causes of secondary depressive symptoms in HIV-infected persons should be investigated and treated.
- Antidepressant medication and psychotherapy both have a role in treatment of HIV-infected persons with depression.

Linking Primary Care and Mental Health Care Services in the Treatment of Depression

VA medical centers and community-based outpatient clinics integrate mental health services into primary care settings. Clinic structures and services vary from one facility to another. Primary care providers should be familiar with local practices on referring patients for mental health consultation.

WHEN TO REFER

Indications for referring depressed patients to a mental health care provider:

- Disabling symptoms - Presence of functional impairment at work/school, in social relationships, or self-care
- Suicidal thought with plan or intent
- Severe hopelessness or negativism
- Persistent agitation
- Psychotic symptoms
- Pronounced affective instability
- Suspected bipolar disorder
- Three or more ineffective therapeutic trials of antidepressant medication
- Complicated psychopharmacologic regimens requiring medications which the provider is not experienced in prescribing
- Need for tricyclic antidepressants (TCAs)

Note: Some medications mentioned in this chapter may not be available on the VHA National Formulary (https://www.pbm.va.gov/NationalFormulary.asp). Consult VA pharmacists for alternatives.

BACKGROUND

- Lifetime prevalence of depression among HIV-infected persons in the United States is 20-40%, up to 2-fold higher than it is among HIV-uninfected persons. Among Veterans, this percentage may even be higher.
- The risk of suicide mortality in HIV-infected persons is 3-5 times higher than in HIV-uninfected counterparts, despite the availability of ARV therapy.
- Depression increases the risk of acquiring HIV infection and the likelihood of high-risk sexual behavior among persons already infected with HIV.
- Depression is associated with nonadherence to ARV therapy, progression of HIV disease, and decline in CD4 cell count.
- Treatment of depression improves adherence to ARV therapy.

Veterans with HIV

In fiscal year 2015, among Veterans served by the Veterans Health Administration (VHA), the documented prevalence of any depression (including depression not otherwise specified) was 19.8% while the documented prevalence of major depressive disorder (MDD) only was 6.5%. Of Veterans admitted to the hospital in 2011 with serious illnesses including HIV/AIDS, 11.4% were diagnosed with depression.

EVALUATION

Note: The VA has published guidelines for evaluation and treatment of depression. See **References**.

SCREENING

Recommended Screening for Depression in Primary Care Settings

The VA recommends using the PHQ-2 and PHQ-9 instruments to screen for depression in the primary care setting, a use for which they are validated. The VA also recommends that the result of screens be entered in the chart on the day the screens are administered. Telephone screening is acceptable, provided that positive screening results are addressed by appropriate risk assessments and interventions.

PHQ-2 and PHQ-9

The PHQ-2 is a two-question screen. The maximum score is 6, and a positive score is 3. If the PHQ-2 result is negative, further screening is unnecessary. If the PHQ-2 result is positive, further screening becomes necessary. In most VAs, a positive PHQ-2 automatically triggers the VHA Pocket Card Suicide Risk Questions, a three-item screening (see below for the Pocket Card items). The patient must be screened on the same day. A PHQ-9 is also used, with responses to all questions and the summary score to be recorded in the patient's chart. Alternatively, the patient can be screened with the PHQ-9 alone, with responses to all questions and the summary score to be recorded in the patient's chart.

Patients who screen positive for depression should be evaluated for risk factors that indicate a need for urgent intervention. Foremost in this process is an explicit assessment for the presence of suicidal ideation. After an evaluation of screening results and a discussion with the patient, the provider can decide whether the patient may benefit from urgent intervention or further specialized mental health evaluations.

Note: The CPRS Clinical Reminder supporting the standard PHQ-2 and PHQ-9 tools will display the questions comprising these instruments when the "Perform PHQ-2" and "Perform PHQ-9" buttons are selected, and it allows for documentation of depression screen results. Figure 1 is an example:

Figure 1. CPRS Clinical Reminder, Depression Screening

Acceptable screening is summarized as follows:

Screening Tool Used	PHQ-2 Result	PHQ-9 Result
PHQ-2	Negative	Not required
PHQ-2	Positive	Required on same day
PHQ-9	Not required	NA

The Patient Health Questionnaire – 2 (PHQ-2)

Patient Name: _____ Date of Visit: _____

Over the past two 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
			Total point score: _____	

Scoring the PHQ-2

PHQ-2 Score	Positive Predictive Value Probability of Major Depressive Disorder (%)	Positive Predictive Value Probability of Any Depressive Disorder (%)
1	15.4	36.9
2	21.1	48.3
3	38.4	75.0
4	45.5	81.2
5	56.4	84.6
6	78.6	92.9

The Patient Health Questionnaire – 9 (PHQ-9)

Over the last 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

The Patient Health Questionnaire – 9 (PHQ-9)				
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 television	0	1	2	3
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	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3
Add columns:				
	0	+_____	+_____	+_____
	= 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**	
☐	☐	☐	☐	

Scoring the PHQ-9	
1-4	Minimal depression
5-9	Mild depression
10-14	Moderate depression
15-19	Moderately severe depression
20-27	Severe depression
Clinicians should be particularly alert to patients' responses to question 9, "Thoughts that you would be better off dead, or of hurting yourself in some way." **Any** affirmative response to question 9, or a PHQ-9 score of >9, requires that a suicide risk assessment be completed within 24 hours. See below.	

The PHQ-9 is validated for use only with English-speaking persons of European origin; some experts feel it is less sensitive for depression in many patients with Asian or Latino backgrounds. As with all symptom questionnaires, assessment results should be interpreted and guided by clinical experience.

Suicide Risk Screen Pocket Card

Are you feeling hopeless about the present or future?
Have you had recent thoughts about taking your life?
Do you have a plan to take your life?
Have you ever had a suicide attempt?

Clinical Interpretation of Preliminary Suicide Risk Screen

If positive: A comprehensive suicide risk assessment should be completed immediately and documented in CPRS.

If negative: No further action is needed at this time.

Assessment of Suicide Risk

Veteran suicide is a serious public health issue, and HIV infection also puts patients at risk of suicidality. Primary care providers are on the front line in identifying Veterans with risk factors for suicide and ensuring they receive appropriate interventions. An affirmative response to questions about suicidality on screening instruments, such as the PHQ-9, should prompt further investigation. When the PHQ-9 is used, a score of >9 or any affirmative response to question 9 suggests that a suicide risk screening (e.g., the VHA Pocket Card Suicide Risk Questions screening or the local facility's Comprehensive Suicide Risk Assessment) should be performed within 24 hours; ideally, this risk assessment should immediately follow a positive screening result for depression.

Such assessments may be performed by telephone, provided that the assessment is made by an acceptable provider, and that the results are appropriately documented. An acceptable provider is an MD, NP, DO, PsyD or PhD Psychologist, LCSW, APN, PA (or a trainee with appropriate co-signature), or other allied health care professional who, by virtue of educational background *and* approved credentialing, privileging, or scope of practice, has been determined by the facility to be capable of diagnosing and treating mental illness.

All VA medical centers have a designated suicide prevention coordinator, whose role includes providing general consultation to clinicians concerning risk assessment, providing resources for suicidal individuals, and ensuring that high risk patients receive education and support about approaches to reduce risks.

The CPRS contains a detailed suicide risk assessment template; however, at this time, there is no unified national template for comprehensive screening, thus providers should utilize their local version. To assess patients for suicide risk:

- **Look** for warning signs
- **Assess** for risk and protective factors
- **Ask** the questions

1. Look for warning signs

- Threatening to hurt or kill self
- Looking for ways to kill self; seeking access to pills, weapons, or other means
- Talking or writing about death, dying, or suicide

Any of the above warning signs requires immediate attention and referral. Consider hospitalization for safety until complete assessment may be made.

Additional warning signs include:

- Hopelessness
- Rage, anger, seeking revenge
- Acting reckless or engaging in risky activities, seemingly without thinking
- Feeling trapped – like there's no way out
- Increasing alcohol or drug abuse
- Withdrawing from friends, family, or society
- Anxiety, agitation, unable to sleep or sleeping all the time
- Dramatic changes in mood
- No reason for living, no sense of purpose in life

2. Assess for risk and protective factors

Factors that may increase risk for suicide

- Current ideation, intent, plan, access to means (e.g., weapons or drugs that may be lethal)
- Previous suicide attempt or attempts

- Alcohol/substance abuse
- Previous history of psychiatric diagnosis
- Impulsivity and poor self-control
- Hopelessness – presence, duration, severity
- Recent losses – physical, financial, personal
- Recent discharge from an inpatient unit
- Family history of suicide
- History of abuse (physical, sexual, or emotional)
- Comorbid health problems, especially a newly diagnosed problem or worsening symptoms
- Age, gender, race (elderly or young adult, unmarried, white, male, living alone)
- Same-sex sexual orientation
- Transgender identity

Factors that may decrease risk for suicide

- Positive social support
- Spirituality
- Sense of responsibility to family
- Children in the home, pregnancy
- Life satisfaction
- Reality-testing ability
- Positive coping skills
- Positive problem-solving skills
- Positive therapeutic relationship

3. Ask the questions

Note: Asking about suicide does not induce patients to contemplate killing themselves.

- Are you feeling hopeless about the present/future? If yes, ask …
- Have you had thoughts about taking your life? If yes, ask …
- When did you have these thoughts and do you have a plan to take your life?
- Have you ever had a suicide attempt?

Response to Suicide Risk

- **Assure the patient's immediate safety and determine the most appropriate treatment setting.**
- Refer for mental health treatment in a clinically indicated timeframe or assure that follow-up appointment is made.
- Consult with the facility suicide prevention coordinator.

- Inform and involve someone close to the patient with patient's consent.
- Limit access to means of suicide, including firearms. If the Veteran is unwilling to remove firearms (e.g., having a trusted friend hold them temporarily), consider offering a gun lock during the session or discussing other ways of securing all weapons (e.g., lock firearm and store ammunition separately).
- Increase contact and make a commitment to help the patient through the crisis.
- Provide number of ER or urgent care center to the patient and significant others.
- Veteran's Crisis Line (formerly the National Suicide Prevention Lifeline): 800-273-TALK (800-273-8255, press 1). Offer the Veteran and their family/caregiver information about the Veteran's Crisis line, which is available 24 hours a day, 7 days a week, 365 days a year.

Depressive Symptoms Associated with Illnesses Other than Major Depression

Given the overlap between symptoms of depression and symptoms of other illnesses and medication side effects common among persons infected with HIV, all potentially treatable or reversible causes of depression should be considered when persons infected with HIV present with depressive symptoms. The reciprocal relationship between symptoms and depression may be a recurring cycle. Early detection and treatment of depressive symptoms is an important part of proper management of both HIV-related symptoms and medication adherence.

Screening	• PHQ-2 • PHQ-9
History	• Relationship between onset of depression symptoms and major life stressors • Concurrent chronic disease • Medication history, including recent changes • Use of alcohol or other psychoactive drugs, whether legal or illegal • Past history of depression • Suicidal thoughts • Family history of mental illness
Physical examination	• Mini mental status • Neurologic screening • Signs of hypogonadism • Signs of hypothyroidism

Laboratory studies	• Low serum zinc concentration • Serum electrolytes • BUN/creatinine • Calcium (for hypercalcemia) • Complete Blood Count (CBC) (for anemia) • Thyroid Stimulating Hormone (TSH) • Serum testosterone • Hepatitis serologies • Rapid Plasma Regain (RPR)
Differential diagnosis	• Mood disorders • Major depression • Bipolar affective disorder • Dysthymia (minor depression) • Demoralization • Drug use • Alcohol use/abuse • Anemia • HIV-associated dementia, other dementia • Hypercalcemia • Renal failure • Hepatitis • Hypothyroidism • Hypogonadism • Drug effects or side effects (e.g., EFV*, anabolic steroids, corticosteroids, sedative-hypnotics, beta-blockers, interferon-containing hepatitis C therapy, alcohol, methamphetamine withdrawal) • CNS infections • CNS neoplasms

* EFV is associated with CNS side effects, anxiety, and disturbed sleep (these usually resolve with time), but it has not been shown to convey a higher risk of depressive disorders.

℞ MANAGEMENT

Patients with depressive symptoms who do not require referral to a mental health provider may be managed safely in the primary care setting. There is evidence that treatment with selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), or tricyclic antidepressants (TCAs) is superior to placebo in relieving symptoms of depression in HIV-infected patients. However, a surprisingly high proportion of placebo recipients in clinical studies also experience symptom relief.

Psychotherapy of many kinds, including cognitive behavioral therapy, acceptance and commitment therapy, social support counseling, and individual psychodynamic therapy, is also effective in treating depression in HIV-infected patients. Comparison of methods is complicated by differences in definitions of depression used in various studies and by the heterogeneity of various scoring instruments.

Interestingly, a study of the effect of treatment of depression on adherence to ARV therapy found that participants treated with psychotherapy or psychotherapy plus medication were more adherent to ARV therapy than those treated with medication alone, or with placebo.

Exercise, even in moderate amounts, may improve or help prevent depressive symptoms. Smoking cessation has also been found to reduce depressive symptoms.

SSRIs, rather than TCAs, are recommended for starting pharmacotherapy for depression, because of the superior safety profile of SSRIs. A patient requiring pharmacologic therapy with an agent other than an SSRI probably should be managed in collaboration with a psychiatrist. Of the SSRIs, citalopram and escitalopram have minimal interactions with ARVs and therefore are frequently chosen for patients on concomitant ARV therapy.

Response to Pharmacotherapy

- Patients typically start responding to SSRIs in 2-4 weeks.
- Patients who show no improvement on maximal-dose therapy after 8 weeks should be switched to another medication or be referred to a psychiatrist.
- Suicidality may remain or emerge during the first several weeks of pharmacologic therapy, even as depression seems to decrease; close follow-up is recommended, with screening for suicidality as needed.

SSRI Discontinuation Syndrome

SSRIs and SNRIs should be tapered slowly rather than discontinued abruptly. Side effects associated with abrupt discontinuation include dizziness, irritability, anxiety, chills, myalgias, and nausea. Symptoms typically occur one day after discontinuing and can last up to two weeks. They remit when the drug is restarted. The discontinuation syndrome is more likely with venlafaxine and shorter-acting SSRIs, such as paroxetine, than with longer-acting agents, such as fluoxetine.

Commonly Used Antidepressant Medications

SSRIs

- **Pros:** Favored by some experts because of low potential for fatal overdose
- **Cons:** Risk of **discontinuation symptoms** with certain agents if discontinued abruptly
- Increased risk of suicidality among children and young adults with depression during first month of taking SSRIs
- **Most common side effects:** sexual dysfunction, nausea, sweating, sleep disturbance
- Contraindicated for use with monoamine oxidase inhibitors (MAOIs) or triptans because of risk of serotonin syndrome
- Interactions with ARVs incompletely studied

Generic Drug Name	Usual Starting Dosage/Dosage Titration	Comments/Drug Interactions
Citalopram	Start at 20 mg QD; may increase daily dosage after 7 days, if no adverse effects; maximum dosage: 40 mg QD.	Metabolized by CYP 3A4; however, no significant change in citalopram levels when coadministered with RTV, and no dosage adjustment required.
Escitalopram	Start at 5-10 mg QD; may increase daily dosage after 7 days, but no evidence of increased efficacy; maximum dosage: 20 mg QD.	Metabolized by mixture of enzymes, including CYP 3A4; however, no significant change in citalopram levels when coadministered with RTV, and no dosage adjustment required.
Fluoxetine	Start at 20 mg QD; not to exceed 80 mg QD. Also available in weekly delayed release dose formulation: 90 mg once weekly commence 7 days after last daily dose of daily 20 mg formulation.	Metabolized by CYP 2D6; may increase RTV AUC by 20% but no adjustment required when coadministered with RTV.

Paroxetine	Start at 20 mg QD; may increase daily dosage by 10 mg every 7 days to maximum of 50 mg QD.	DRV and FPV decrease paroxetine levels; titrate paroxetine to effect. Must be tapered slowly when discontinuing to avoid rebound depression symptoms and discontinuation symptoms. Slightly more sedating than other SSRIs.
Sertraline	Start at 50 mg QD; may increase daily dosage by 25-50 mg every 7 days to maximum of 200 mg QD.	DRV decreases sertraline levels; titrate sertraline to effect.

SNRIs

- Increase presynaptic levels of serotonin and norepinephrine
- Also approved for treatment of neuropathic pain and peripheral neuropathy
- **Most common side effects:** GI events (nausea, diarrhea, constipation), dry mouth
- **Other side effects:** somnolence, insomnia, dizziness, nervousness, headache, sexual dysfunction can occur

Generic Drug Name	Usual Starting Dosage/Dosage Titration	Comments/Drug Interactions
Duloxetine	Start at 20 mg QD; may increase to BID, then to 60 mg QD or divided as 30 mg BID.	Hepatically metabolized; not recommended for use in patients with hepatic impairment. To discontinue, taper gradually.
Venlafaxine Formulations		
Venlafaxine immediate release	Start at daily dosage of 75 mg divided BID (i.e., 37.5 mg BID) or TID (i.e., 25 mg TID) with food; may increase total daily dosage by up to 25 mg per dose every 4 days;	Metabolized by CYP 2D6 When stopping venlafaxine, it is essential to taper slowly to avoid discontinuation symptoms. Postmarketing studies suggest that venlafaxine overdoses

	maximum daily dosage: 375 mg divided TID (i.e., 125 mg TID).	are more associated with fatal outcomes than are SSRI overdoses, but less than TCA overdoses; use lowest effective dosage of venlafaxine.

Other

Generic Drug Name	Usual Starting Dosage/Dosage Titration	Comments/Drug Interactions
Bupropion Formulations		
Bupropion	-	Inhibits CYP 2D6 EFV, LPV/r, and TPV decrease bupropion levels; titrate bupropion to effect. Side effects: restlessness, agitation, insomnia. Bupropion increases seizure incidence (0.4% at 300 mg/day or higher); contraindicated in patients with elevated risk of seizures. Sexual dysfunction unlikely.
Bupropion immediate release	Start at 75-100 mg BID for 3 days, increase to 100 mg TID on day 4; maximum daily dosage: 450 mg divided QID.	No single dose should exceed 150 mg, and doses should be taken at least 6 hours apart. Dosage escalation should be delayed for agitation, motor restlessness, or insomnia.
Bupropion SR	Start at 100-150 mg QAM; increase to usual dosage of 150 mg BID no earlier than day 4; maximum daily dosage: 400 mg divided BID (i.e., 200 mg BID).	Doses of bupropion SR should be taken at least 8 hours apart. Dosage escalation should be delayed for agitation, motor restlessness, or insomnia.

Other

Generic Drug Name	Usual Starting Dosage/Dosage Titration	Comments/Drug Interactions
Bupropion Formulations		
Bupropion XR	Start at 150 mg QAM; increase to usual dose of 300 mg QAM no earlier than day 4; maximum dosage: 450 mg QD.	Doses should be taken at least 24 hours apart. Dosage escalation should be delayed in the event of agitation, motor restlessness, or insomnia.

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PTSD and Trauma Informed HIV Care

KEY POINTS

- PTSD among people living with HIV (PLWH) is common and is associated with non-adherence to ARV and decreased virologic control.
- PTSD can result from HIV-related or unrelated trauma events.
- PTSD can be diagnosed and preliminarily treated in primary care.
- Psychotropic medications and psychotherapy are effective at treating PTSD in PLWH.
- VA has a PTSD Consultation Program for frontline VA providers working with a Veteran with PTSD, https://www.ptsd.va.gov/professional/consult/index.asp

BACKGROUND

- After a traumatic or life-threatening event (e.g., combat, assault, including child sexual assault, natural disaster), it is common to have reactions such as reliving the event (nightmares, intrusive memories); avoidance of situations that remind a person of the event; negative beliefs and feelings; and hypervigilance or increased startle response. However, if these symptoms do not remit or worsen after one month, a diagnosis of PTSD may be indicated per DSM-5 diagnostic criteria.
- Veterans are at increased risk for developing PTSD due to combat exposure. 11-30% of Veterans have combat-related PTSD depending on war era and deployment, with Vietnam War Veterans at highest risk for PTSD.
- Military sexual trauma is also linked to PTSD, with 55% of female and 38% of male Veterans reporting sexual harassment in the military. According to one study of female Veterans, those with MST had higher rates of PTSD compared to those with other trauma (60% versus 43%, respectively). MST was also a stronger predictor of PTSD than other traumas.
- Trauma exposure and PTSD are disproportionately higher for people living with HIV due to higher likelihood of trauma exposure in childhood (including physical and sexual abuse); repeated traumatization later in life; physical and sexual assault; and crime-related violence. Additionally, sexual and physical abuse are correlated with increased HIV risk behaviors (e.g., substance use, multiple sexual partners, commercial sex work, high risk sexual practices) and subsequent HIV infection.

Note: Some medications mentioned in this chapter may not be available on the VHA National Formulary (https://www.pbm.va.gov/NationalFormulary.asp). Consult VA pharmacists for alternatives.

- African Americans men who have sex with men (MSM) are disproportionately represented among new HIV infections and often experience racism-based trauma, which is also linked to greater HIV risk.
- Approximately 95% of PLWH report experiencing one lifetime trauma and 54% meet criteria for PTSD.
- Up to 40% of PLWH identify their HIV diagnosis as the traumatic event associated with the onset of their PTSD symptoms. Research has found that those with a history of PTSD are more likely to experience their HIV diagnosis as traumatic.
- Trauma exposure is associated with poorer health outcomes among PLWH, such as:
  - Higher rates of antiviral non-adherence, particularly if PTSD-related dissociative symptoms and substance use are present.
  - Decreased health-related quality of life for PLWH who reported greater HIV-related trauma symptoms.
  - Decreased virologic control (viral load >400 c/mL). One study found this was predicted by minority racial/ethnic membership, lower baseline CD4, more lifetime traumas, and more severe traumas.
  - Dysfunction and suppression of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in higher cortisol levels and chronic systemic inflammation.
  - Increased likelihood of Coronary Artery Disease (CAD) for those who experienced their HIV diagnosis as traumatic.
  - More chronic pain conditions in PLWH that reported multiple traumas.
- Per the Substance Abuse and Mental Health Services Administration (SAMHSA), a trauma-informed approach consists of:
  - Realizing the impact of trauma and the potential pathways to recovery.
  - Recognizing the signs and symptoms of trauma in Veterans, their families, staff, and others involved in the health care system.
  - Responding by integrating trauma knowledge into policies, procedures, and practices.
  - Anticipating and avoiding practices that may re-traumatize Veterans (e.g., being overly authoritative or confrontational, not respecting personal space, challenging or discounting reports of abuse/trauma, labeling and pathologizing Veteran's feelings and reactions).
- A trauma-informed approach involves key principles to promote recovery and resilience from trauma:
  - Safety
  - Trustworthiness and transparency
  - Peer support

- Collaboration and mutuality
- Empowerment, voice, and choice
- Cultural, historical, and gender issues

Veterans with HIV/AIDS

- To provide trauma-informed care, clinicians know and recognize the impact of trauma on mental health and health behavior; as such, clinicians understand and are able to identify the potential relationship between trauma, HIV risk behavior (e.g., substance use, high risk sexual practices), and HIV acquisition.
- 25% of Veterans with HIV are also diagnosed with PTSD.
- Among Veterans who do not have HIV, PTSD and substance use diagnoses increased their risk of HIV infection by 12 times compared to those without PTSD and substance use diagnoses.
- Among Vietnam War Veterans with PTSD, those who used intravenous drugs were more likely to be exposed to HIV.
- Among active duty personnel, positive screens for PTSD were correlated with HIV risk behavior (unprotected anal intercourse, treatment for sexually transmitted infections, and injection drug use); HIV risk behavior was even higher for those with PTSD and major depressive disorder. This study's findings were comparable to the prevalence of HIV risk behaviors found in other trauma populations.

EVALUATION

Acute Stress Disorder and PTSD are both disorders that can arise after exposure to a traumatic event. Both Acute Stress Disorder and PTSD have similar clinical symptoms; however, Acute Stress Disorder and PTSD differ regarding the required number of symptoms and duration of symptoms. A trauma-informed approach to evaluation includes universally screening for Acute Stress Disorder and PTSD. Unrecognized and unaddressed trauma symptoms can negatively affect medical and mental health outcomes and screening for trauma can prevent misdiagnosis and inappropriate treatment planning. Therefore, clinicians should:

1. Ask all Veterans about any history of trauma.
2. Only use validated instruments for screening and assessment.
3. Screen all Veterans who have histories of trauma for other mental health disorders (e.g., anxiety-related disorders, depressive disorders) and suicidal thoughts and behaviors.

4. Be aware that some Veterans will not connect their trauma history and current behavioral patterns (e.g., substance use, avoidance, high risk sexual behaviors).
5. Do not require Veterans to describe emotionally-overwhelming trauma events in detail.
6. Focus on how trauma symptoms affect the Veteran's current functioning.
7. Inform the Veteran how you will use screening results for treatment planning to promote shared decision-making.

Effective evaluation also involves clinicians knowing the impact of trauma on physical and mental health and recognizing clinical symptoms based on DSM-5 diagnostic criteria. Furthermore, to effectively assess for clinical symptoms, clinicians develop rapport and foster a relationship of mutual trust, safety, and collaboration. Clinicians also understand historical (e.g., past history of trauma) and cultural (e.g., racial, military, socio-economic status, gender, sexual identity) factors influence conceptualization of symptoms and diagnosis.

Pages 168-172 were removed due to copyright permissions. *See the printed manual or American Psychiatric Association Diagnostic and Statistical Manual Criteria for PTSD.* https://www.psychiatry.org/psychiatrists/practice/dsm

SCREENING

- Screening for PTSD in Primary Care is important since many people with PTSD and other mental health disorders (particularly those with stigma-related concerns) present initially in primary care settings versus specialty mental health.
- The VA recommends using the Primary Care PTSD Screen (PC-PTSD) or the PTSD Checklist (PCL) to screen for PTSD in the primary care and specialty care settings, and are validated in these contexts. The PC-PTSD and PCL are available in Mental Health Assistant in CPRS[1]

The PC-PTSD and the PCL1

The PC-PTSD is a 4-question screener. If 3 of 4 items are endorsed, the PC-PTSD is considered a positive screen. If the PC-PTSD result is negative, further screening is not necessary.

If the PC-PTSD result is positive, the patient should be screened on the same day with the PCL (a 20-item questionnaire that assesses the DSM-5 PTSD criteria) with all responses and the total score recorded in the patient's chart. As an alternative, the patient can be screened with the PCL with all responses and the total score recorded in the patient's chart. An overall cutoff score of 33 on the PCL is recommended for screening.

Patients who screen positive for PTSD should be evaluated for risk factors that indicate a need for immediate intervention. Specifically, patients should be assessed for the presence of suicidal ideation and suicide risk, since PTSD is associated with increased risk for self-harm and history of suicide attempts. Providers should assess for the patient's immediate safety and determine the most appropriate treatment plan. CPRS has a detailed suicide risk assessment template. See **Depression**, p. 149. Furthermore, for patients with suspected PTSD, we recommend an appropriate diagnostic evaluation including determination of DSM criteria via a structured diagnostic interview (i.e., Clinician-Administered PTSD Scale for DSM-5; CAPS-5), functional status, medical history, past treatment history, and relevant family history.

Acceptable screening is summarized as follows:

Screening Tool Used	PC-PTSD Result	PCL Result
If PC-PTSD initially used:	And result Negative, then:	Not required
If PC-PTSD initially used:	And result Positive, then:	Required on the same day
If PCL initially used:	Not required	N/A

1 There is a more recent version of the PC-PTSD, the PC-PTSD-5, which was updated in accordance with DSM-5 criteria. Compared to the PC-PTSD, the PC-PTSD-5 has 1 additional item ("In the past month, have you felt guilty or unable to stop blaming yourself or others for the event(s) or any problems the event(s) may have caused?") and is considered a positive screen if patient endorses 3 of 5 questions. At the time of this manual, the PC-PTSD-5 was not yet available in Mental Health Assistant. Also, VA and DoD are continuing to use the 4-question PC-PTSD, which is reasonable because the PC-PTSD performs well as a screen for PTSD diagnosed according to DSM-5. Research is underway to confirm the optimal cutoff point for the PC-PTSD-5.

The PC-PTSD

Have you ever had any experience that was so frightening, horrible or upsetting, that **in the past month**, you:

1. Have had any nightmares about it or thought about it when you did not want to?

   Yes / No
2. Tried hard not to think about it or went out of your way to avoid situations that remind you of it?

   Yes / No
3. Were constantly on guard, watchful, or easily startled?

   Yes / No
4. Felt numb or detached from others, activities, or your surroundings?

   Yes / No

Scoring the PC-PTSD

PC-PTSD Score	Probability of PTSD (%)
1	44
2	51
3	65
4	71

Prins et al. (2003). The primary care PTSD screen (PC-PTSD): Development and operating characteristics. Primary Care Psychiatry, 9(1), 9–14.

The PCL

Below is a list of problems and complaints that people sometimes have in response to stressful life experiences. Please read each one carefully, then select the appropriate number to indicate how much you have been bothered by that problem in the past month.

In the past month, how much were you bothered by:	0 Not at all	1 A little bit	2 Moderately	3 Quite a bit	4 Extremely
1. Repeated, disturbing, and unwanted memories of the stressful experience?	-	-	-	-	-
2. Repeated, disturbing dreams of the stressful experience?	-	-	-	-	-
3. Suddenly feeling or acting as if the stressful experience were actually happening again (as if you were actually back there reliving it)?	-	-	-	-	-
4. Feeling very upset when something reminded you of the stressful experience?	-	-	-	-	-
5. Having strong physical reactions when something reminded you of the stressful experience (for example, heart pounding, trouble breathing, sweating)?	-	-	-	-	-
6. Avoiding memories, thoughts, or feelings related to the stressful experience?	-	-	-	-	-
7. Avoiding external reminders of the stressful experience (for example, people, places, conversations, activities, objects, or situations)?	-	-	-	-	-
8. Trouble remembering important parts of the stressful experience?	-	-	-	-	-
9. as: I am bad, there is something seriously wrong with me, no one can be trusted, the world is completely dangerous)?	-	-	-	-	-
10. Blaming yourself or someone else for the stressful experience or what happened after it?	-	-	-	-	-

In the past month, how much were you both ered by:	0 Not at all	1 A little bit	2 Moderately	3 Quite a bit	4 Extremely
11. Having strong negative feelings such as fear, horror, anger, guilt, or shame?	-	-	-	-	-
12. Loss of interest in activities that you used to enjoy?	-	-	-	-	-
13. Feeling distant or cut off from other people?	-	-	-	-	-
14. Trouble experiencing positive feelings (for example, being unable to feel happiness or have loving feelings for people close to you)?	-	-	-	-	-
15. Irritable behavior, angry outbursts, or active aggressively?	-	-	-	-	-
16. Taking too many risks or doing things that could cause you harm?	-	-	-	-	-
17. Being "super alert" or watchful or on guard?	-	-	-	-	-
18. Feeling jumpy or easily startled?	-	-	-	-	-
19. Having difficulty concentrating?	-	-	-	-	-
20. Trouble falling or staying asleep?	-	-	-	-	-

Scoring the PCL

PCL Score	Qualitative Description
Lower than 33	Patient does not meet criteria for PTSD
33 or higher	Patient meets criteria for PTSD and may benefit additional assessment and treatment for PTSD

As with all self-report questionnaires, assessment results should be interpreted and guided by clinical experience.

PTSD Symptoms may be Associated with Conditions Other than PTSD

Given the overlap between PTSD symptoms and symptoms of other illnesses or disorders, the following should be considered when patients with HIV present with PTSD symptoms.

Screening	• PC-PTSD (see above) • PCL (see above)
History	• Relationship between the onset of PTSD symptoms and trauma/stressors • Differentiating between PTSD symptoms related to HIV or another trauma/stressor • Concurrent medical disease • Use of alcohol or illegal/legal substances • Past history of PTSD or trauma • Family history of mental illness
Differential Diagnosis	• Other Trauma- and Stressor-related Disorders (e.g., Acute Stress Disorder, Adjustment Disorder) • Obsessive-compulsive Disorder • Anxiety Disorders (e.g., Panic Disorder, Generalized Anxiety Disorder) • Mood Disorders (e.g., Major Depression, Bipolar Disorder) • Personality Disorders • Conversion Disorder • Psychotic Disorders • Traumatic Brain Injury and other Cognitive Disorders • Alcohol or Drug Use/abuse • Sleep Disturbance

Special Considerations for Veterans with HIV and PTSD

Veterans with HIV, whether they have been diagnosed with PTSD or not, have likely experienced trauma in their lives. As clinicians, caring for any Veteran in the VA healthcare system, trauma should be in the back of our minds. Veterans with HIV and comorbid PTSD and other mental health or substance use disorders often experience stigma and discrimination, which can sometimes be subtle. Stigma includes feeling that you will be judged, discriminated, or stereotyped because of a condition. As with many people, Veterans may want to avoid talking about PTSD, mental health, or substance use problems. For some Veterans, Primary Care may be the first place they disclose or share their trauma or PTSD symptoms.

Trauma Informed Care for Veterans with HIV

The following key principles clinicians are recommended to ensure a trauma-informed approach for Veterans who have a history of trauma and HIV.

Establish Safety:

- Demonstrate respect and professionalism.
- Review confidentiality, particularly regarding how information about trauma and HIV will be used.
- Establish specific routines, as a structured setting can provide a sense of safety and familiarity.
- Ask about trauma, HIV, and topics involving sex. Bringing up these issues may feel taboo or intrusive. However, asking in a supportive, caring way gives Veterans permission to talk about these issues that they may not feel comfortable with raising on their own. This helps promote safety and trust. It can also be helpful to inform Veterans that everyone is asked these questions. Also, provide Veterans with a rationale for why they are being asked.
- To minimize and prevent further stigmatization, clinicians should avoid labeling HIV-positive Veterans or assuming stereotypes (e.g., they are gay, MSM, sex workers, injection drug users, promiscuous) and should use person-first language (e.g., Veteran with HIV rather than an HIV/AIDS patient, Veteran with substance use disorder rather than substance user, lesbian/gay/bisexual/transgender Veteran rather than a gay, a lesbian, a bisexual, or a transgender.)

Prevent Re-traumatization:

- Be aware and sensitive to the needs of Veterans with trauma histories and HIV. Consider the behaviors or stimuli in the treatment setting that may trigger traumatic memories.
  - For example, the following may be triggering depending on the trauma: small enclosed spaces, abrupt loud noises, clinician demographics (e.g., race, ethnicity, age, gender, sexual orientation) if pertinent to the trauma (e.g., a female Veteran with a history of MST by male superiors may prefer female providers).
  - Some Veterans may find the word "HIV" triggering. As such, clinicians should find emotionally neutral terms to discuss HIV.
  - Clinicians should assist Veterans in finding a provider of their gender preference.
  - Routine gynecological/prostate exams may re-traumatize Veterans; thus, mental health can be involved for consultation as well as Veteran support or emotional assistance.
- Clinicians should also take symptoms and reports of trauma seriously. Ignoring, questioning, or challenging these may be invalidating and reinforce shame, avoidance, and helplessness, particularly if their reports previously went ignored.
- Veterans should not be required to describe trauma details that are emotionally-overwhelming.
- Trustworthiness and Transparency:
- Be clear and honest with treatment plans, boundaries, and obligations.
- Be dependable and consistent. Follow through with the treatment plan and the Veteran's requests.

Peer Support:

- Encourage Veterans to seek social support from family, friends, and other Veterans.
- Peer support and social interactions with similar others are particularly important since many Veterans with trauma and HIV often feel marginalized, stigmatized, and alone in their experience.
- Peer support allows Veterans to form mutual relationships, to move beyond trauma and HIV, and to mirror and to learn alternative, adaptive coping strategies and to promote resiliency to trauma and HIV.

Collaboration and Mutuality:

- Ask permission from the Veteran to talk about potentially sensitive or difficult topics.
- Use a patient-centered style of communication by asking open-ended questions with a focus on eliciting the Veteran's self-identified symptoms, problems, and treatment goals.
- Provide affirmations about progress made toward goals or overcoming barriers (e.g., behavior change, medication adherence, adaptive coping, decreasing avoidance).
- Reflect back to the Veteran what they are communicating to demonstrate active listening and to verify your understanding of what the Veteran is sharing.

Empowerment, Voice, and Choice:

- Provide Veterans with a sense of control and help them feel empowered to make their own decisions.
- Assist with basic and social needs by making referral to Social Work for resources such as housing, shelters (especially for female Veterans and their children), employment, transportation, etc.
- Educate about common symptoms, reactions, and consequences of trauma and HIV. Education can help normalize symptoms, correct misinformation and myths related to trauma and HIV, and provide relief to Veterans who feel they are alone in their struggle.
- Inform about resources (e.g., mental health treatment, educational hand
- outs, peer support groups, medications, medical treatment options).
- Build hope and resilience. Focus on the Veteran's strengths, positive attributes, and positive resources. Emphasize the Veteran's past ability to cope with hardship and to overcome adversity, also assure them that PTSD and HIV are both treatable and manageable conditions. Help the Veteran find meaning and recovery from their HIV narratives to work towards post-traumatic growth.

Cultural and Historical Issues:

- Determine if a Veteran has experienced multiple traumas or a single trauma, since research shows those with multiple traumas are most susceptible to severe traumatic responses.
- Determine the context of how the Veteran contracted and was diagnosed with, as these events may involve a traumatic event.
- Define how culture affects how a Veteran organizes information, interprets, and resolves their trauma and HIV status.
- Identify people who know about a specific cultural factor and can help interpret cultural patterns and serve as liaisons (e.g., if working with a gay or bisexual male Veteran, find a peer support specialist who is also a sexual minority and familiar with the military culture and history of oppression around LGBT issues).
- Determine how a Veteran's social support network views and reacts to the trauma and HIV.

Psychotherapy and Other PTSD Treatment Options

Evidence-based psychotherapy is the primary intervention for PTSD. Clinicians are encouraged to be familiar with these treatments to effectively educate patients about PTSD treatment options and to assist in shared decision-making regarding treatment options, all of which are principles of a trauma informed approach.

There are various trauma-focused psychotherapies that are evidence-based and help people make sense of the trauma; learn to better handle negative thoughts

and feelings; reconnect with loved ones; and set treatment goals. The psychotherapies with the strongest evidence from clinical trials include:

- Cognitive Processing Therapy (CPT) is an intervention whereby patients learn skills to understand how trauma has changed their thoughts and feelings. Changing how patients think about the trauma therefore helps change how patients feel about the trauma.
- Prolonged Exposure (PE) is an intervention whereby patients repeatedly talk about the trauma until the memories are no longer distressing. This helps the patient achieve a sense of control over their thoughts and feelings about trauma. PE also helps patients return to places or do things that are safe that they previously avoided because they reminded them of the trauma.
- Eye Movement Desensitization and Reprocessing (EMDR) is a trauma-focused psychotherapy that helps patients process upsetting memories, thoughts, and feelings related to trauma. Of note, EMDR is different than CPT and PE because it involves paying attention to back-and-forth movement or sound while recalling the upsetting memories with the aim of making memories less distressing.

Other treatment recommendations include:

- Psychotherapy for insomnia (Cognitive Behavior Therapy – Insomnia, or CBTi) is also recommended for managing sleep difficulties related to PTSD. Often, patients with PTSD experience PTSD-related nightmares.
- PTSD Recovery/Support Groups available in Primary Care
- To promote Veteran empowerment and choice, consistent with a trauma-informed approach, there are also self-help tools developed by the VA for Veterans, including the PTSD Coach Mobile App and the Mindfulness Coach App. These are apps that can be downloaded to a smartphone for Veterans to use.
  - The PTSD Coach app provides facts about PTSD and research-based self-help skills (for example, tools for screening and tracking symptoms, stress management skills). We recommend Veterans use the PTSD Coach app with professional medical treatment.
  - The Mindfulness Coach app provides education about mindfulness and its benefits for coping with negative thoughts and emotions. It also provides reminders and tools to practice and track progress.
- Consistent with the peer support principle of trauma informed care, most VAs offer peer support mentorship, often from another Veteran who is diagnosed with and treated for PTSD. This can help the Veteran with trust and potentially overcoming barriers of avoidance and stigma.

Trauma-focused psychotherapy for people living with or at risk for HIV:

- Trauma-focused psychotherapy decreases HIV risk behavior (i.e., unprotected sex).

- PTSD treatment in patients who are HIV-positive is associated with greater adaptive coping, decreased trauma-related symptoms (i.e., intrusive and avoidance symptom) and decreased substance use); however, findings are mixed and warrant additional future research on this topic.
- There is a paucity of research regarding the effects of PTSD treatment on HIV medical outcomes; however, studies find that cognitive behavioral therapy for people living with HIV was effective in enhancing adherence, increasing CD4-cell counts, and reducing depressive symptomatology.

WHEN TO REFER

Indications for referring patients with PTSD to a mental health provider:

- Suicidal thought with plan or intent.
- Symptoms that are disabling or significantly disrupting a patient's life (e.g., work, relationships, daily functioning).
- If symptoms persist after several months following the trauma or worsen over time.
- Pronounced affective instability.

MANAGEMENT

Patients diagnosed with PTSD who choose not to engage in, are unable to access trauma-focused psychotherapy, or require additional treatment may benefit from pharmacotherapy. Sertraline, paroxetine, fluoxetine, and venlafaxine are all appropriate agents to be used as monotherapy according to the most recent 2017 VA/DoD Clinical Practice Guidelines for the Management of Posttraumatic Stress Disorder (PTSD) and Acute Stress Disorder. The following medications (see below) used for PTSD are either "recommended for" or "suggested for" by the 2017 PTSD guidelines. All antidepressants have a Black Box Warning that warns of a possible increased risk of suicidal thoughts and behavior in children, adolescents, and young adults. These risks, however, are not increased beyond the age of 24 and may decrease in adults aged 65 and older.

Sertraline, paroxetine, and fluoxetine are in the antidepressant class of Selective Serotonin Reuptake Inhibitors (SSRIs). This class of medications, although relatively safe, may interact with antiretroviral medications. Because of the potential for interactions, careful dose titration of the SSRI to the desired effect is recommended using the lowest feasible SSRI dose and monitoring for antidepressant effect. Venlafaxine is in the antidepressant class of Serotonin Norepinephrine Reuptake Inhibitors (SNRIs). Venlafaxine is a substrate of CYP 3A4 and subject to many drug-drug interactions if co-administered with a strong CYP 3A4 inhibitor or inducer. Both fluoxetine and venlafaxine have QT-prolongation effects which may be worsened when used with other ARV therapies that increase the risk.

According to the VA/DoD PTSD guidelines, nefazodone, imipramine, and phenelzine are also recommended as monotherapy if recommended pharmacotherapy is ineffective, unavailable, or not in accordance with patient preference or tolerance. However, it is important to note that both nefazodone and phenelzine have serious potential toxicities, including hypertensive crisis for phenelzine and liver failure for nefazadone, which both may lead to death.

POTENTIAL ARV INTERACTIONS

PTSD and Associated Trauma

Medication	Antiretroviral	Interaction
Sertraline	• Darunavir/ritonavir • Darunavir/cobicistat • Lopinavir/ritonavir • Atazanair/cobicistat	Sertraline AUC decreased by 49% with darunavir/ritonavir; titrate sertraline dose to clinical response • SSRIs are CYP 2D6 inhibitors and may ↑ CYP 2D6 substrate exposure (i.e. ritonavir) and risk of toxicity • Careful dose titration of SSRI to desired effect using lowest feasible dose and monitoring for antidepressant effect
Paroxetine	• Darunavir/ritonavir • Darunavir/cobicistat • Atazanair/cobicistat • Tipranavir • Lopinavir/ritonavir	• Paroxetine AUC decreased by 39% with darunavir/ritonavir; titrate paroxetine dose to clinical response • Tipranavir and lopinavir/ritonavir may ↑ paroxetine levels • SSRIs are CYP 2D6 inhibitors and may ↑ CYP 2D6 substrate exposure (i.e. ritonavir) and risk of toxicity • Careful dose titration of SSRI to desired effect using lowest feasible dose and monitoring for antidepressant effect
Fluoxetine	• Atazanavir/cobicistat • Efavirenz • Atazanair/cobicistat • Darunavir/cobicistat	• The combination of the following medications with fluoxetine can potentially ↑ the risk of QT-interval prolongation; consider an alternative agent to avoid toxicity

Medication	Antiretroviral	Interaction
-	-	• SSRIs are CYP 2D6 inhibitors and may ↑CYP 2D6 substrate exposure (i.e. ritonavir) and risk of toxicity • Careful dose titration of SSRI to desired effect using lowest feasible dose and monitoring for antidepressant effect
Venlafaxine	• Atazanavir • Darunavir • Ritonavir	• These ARVs are CYP 3A4 inhibitors. Concomitant use with venlafaxine, a substrate of CYP 3A4, may result in ↑ venlafaxine plasma concentrations and toxicity; Consider therapy modification or carefully titrate dose of venlafaxine to desired effect using lowest feasible dose and monitoring for antidepressant effect
Nefazodone	• PIs • Ritonavir • Maraviroc	• Nefazodone, a strong CYP3A4 inhibitor, may ↑ exposure of maraviroc. Use is contraindicated in patients with severe renal impair • Consider alternatives to, or reduced doses of, nefazodone in patients treated with PIs • Nefazodone, a strong CYP3A4 inhibitor, may ↑ exposure of maraviroc. Use is contraindicated in patients with severe renal impairment
Imipramine	• Atazanavir • Ritonavir • Darunavir • Tipranavir	• The combination atazanavir with imipramine should be avoided due to the increased risk of QT-prolongation • Use with atazanavir or darunavir may increase plasma concentrations of imipramine leading to potential toxicity; Consider therapy modification
Phenelzine	No contraindications or major drug-drug interactions with antiretroviral agents	

Medication	Antiretroviral	Interaction
Prazosin	No contraindications or major drug-drug interactions with antiretroviral agents	

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Serious Mental Illness (Bipolar Disorder, Schizophrenia, etc.)

KEY POINTS

- Individuals with serious mental illness (SMI) are at increased risk of contracting and transmitting HIV.
- SMI among HIV-infected persons is associated with high-risk behavior, nonadherence to ARV therapy, and all-cause mortality.
- Psychotropic medication and psychotherapy are effective for treating SMI; treatment may reduce high-risk behavior and may improve adherence to ARV therapy in HIV-infected persons.
- Progression of HIV to AIDS can produce symptoms of mania and psychosis.

BACKGROUND

The category of SMI includes mood disorders, such as bipolar I and II, and psychotic disorders, such as schizophrenia, that significantly impair functioning.

Prevalence estimates of HIV within the SMI population are much higher (4-23%) than the general population (0.5%).

Individuals with SMI are more likely to engage in high-risk sexual behaviors, such as having unprotected sex, having multiple sex partners, and commercial sex work. They are also significantly more likely to be the victims of sexual violence and more likely to have sexually transmitted diseases (STDs).

Mental health symptoms in SMI such as impulsivity, hypersexuality, cognitive impairment, low self-esteem, and social skill deficits contribute to risky sexual behavior. Persons with SMI are also more likely to be of low socioeconomic status, live in ultra urban areas, and spend time in institutions (e.g., hospitals, jail). Consequently, they may not have access to condoms (e.g., due to cost or availability in institutions) and yet often live in urban cores that have high rates of STDs and HIV.

Co-occurrence of substance use disorders is common in persons with SMI. Dual diagnosis is linked to more sexual risk behavior, as well as increased risk of HIV infection and mortality.

Comorbidity of SMI and HIV is associated with poor adherence to ARV therapy and psychotropic medications, as well as poorer health outcomes in general.

Note: Some medications mentioned in this chapter may not be available on the VHA National Formulary (https://www.pbm.va.gov/NationalFormulary.asp). Consult VA pharmacists for alternatives.

Veterans with SMI

- Approximately 15% of Veterans have SMI, with schizophrenia occurring in about 3% and bipolar disorder in about 2% of Veterans.
- Veterans with SMI are up to 2 times more likely to have HIV than those without SMI.
- Veterans with SMI are more likely to develop chronic medical conditions and are at particularly high risk for cardiac disease.
- Veterans with SMI have 1.32 to 1.55 times greater risk of all-cause mortality.

WHEN TO REFER

SMI typically requires ongoing medication management by a mental health care provider. Indications for referral to address acute issues include:

- Suicidal thought with plan or intent
- Pronounced affective instability
- Active psychotic symptoms (e.g., hallucinations, delusions)
- Increased impulsive and risky behavior
- Significant functional impairment (e.g., in work, school, relationships, or self-care)

EVALUATION

Bipolar Disorder

Characterized by manic (bipolar I) or hypomanic (bipolar II) episodes and major depressive episodes

Manic Episode	Persistent elevated or irritable mood **and** increased activity or energy lasting at least *1 week* **and** at least 3 of the following during same period: 1. Inflated self-esteem or grandiosity 2. Decreased need for sleep 3. Hyper-talkative or pressured speech 4. Racing thoughts 5. Distractibility 6. Increased goal-directed activity (social, work, sexual) or psychomotor agitation 7. Increased risky behavior (e.g., buying sprees, foolish business investments, promiscuity unusual for the individual)
Hypomanic Episode	Criteria as in manic episode, lasting at least *4 days*

Schizophrenia

Characterized by positive symptoms, negative symptoms, and cognitive symptoms (e.g., working memory and attention problems)
Presence of symptoms for at least 6 months with at least 2 symptoms present for a significant portion of time in a 1-month period

Positive Symptoms	Must have at least 1 of the first 3 positive symptoms: 1. Delusions 2. Hallucinations 3. Disorganized speech 4. Disorganized behavior
Negative symptoms	1. Catatonic behavior (e.g., stupor, catalepsy, mutism, waxy flexibility, stereotypy, echolalia, echopraxia, negativism, posturing, grimacing) 2. Avolition 3. Flat affect

Other psychotic disorders include: *delusional disorder*, in which delusions are the most prominent symptom and other symptoms (including hallucinations) are typically absent; *schizoaffective disorder*, with concurrent positive symptoms of schizophrenia and a major mood episode; *brief psychotic disorder*, with schizophrenia symptoms lasting less than 1 month; and *schizophreniform disorder*, with schizophrenia symptoms lasting between 1 and 6 months.

Manic and psychotic symptoms may be associated with illnesses other than SMI

The onset of SMI typically occurs in late adolescence to early adulthood (16-35 years of age). First presentation of manic or psychotic symptoms in middle aged and older adults may be associated with an illness other than SMI. Potentially treatable or reversible causes of these symptoms (see list below) should be considered when persons with HIV present with manic or psychotic symptoms.

Factors to Consider	• Age of first symptom onset • Past history of depression and SMI • Concurrent chronic disease • Medication history, including recent changes • Use of alcohol or other psychoactive drugs, whether legal or illegal • Suicidal thoughts • Family history of mental illness
Laboratory studies	• RPR • TSH • ACTH (for Cushing's disease) • B12

	• PBG and ALA (for AIP)
Differential Diagnosis	• Acute intermittent porphyria (AIP) • CNS infections • CNS neoplasms • Cushing's disease • Delirium • Dementia • Drug use • Drug effects or side effects • HIV-related mania or psychosis (see section below) • Hyperthyroidism • Hypothyroidism

HIV-related Mania and Psychosis

Mania

Rates of manic episodes in early HIV infection are only slightly higher than the general population at 1-2%; however, 4-8% of individuals with AIDS exhibit mania. AIDS-related mania is secondary to HIV infection of the central nervous system and tends to be associated with dementia and cognitive slowing. It may occur in those without a personal or family history of mood disorders and differs from typical bipolar mania in that symptoms tend to be more severe and chronic in nature. Additionally, those with AIDS mania are more likely to experience irritability rather than euphoria, and are less likely to be hyper-talkative.

Psychosis

Prevalence estimates of new onset psychosis in persons with HIV range from 0.23-15.2%. New onset psychosis typically occurs in the context of AIDS or in later stages of HIV infection. AIDS-related dementia, opportunistic infection, substance dependence, and ARV therapy toxicity (especially with efavirenz, but also neviparine and zidovudine) have been implicated in new onset psychosis. Paranoid delusions and hallucinations are the most common symptoms, whereas bizarre delusions are less common than in schizophrenia. Psychosis in persons with HIV is more variable in course and more likely to remit fully over time. Importantly, lower dosage, shorter duration of antipsychotic medications is recommended for HIV-related psychosis than for schizophrenia.

Psychosocial Interventions

Psychosocial interventions for persons with SMI and HIV (or risk of HIV) address three main targets:

1) Behavioral risk reduction

These interventions decrease risk of infection (in uninfected persons) and transmission (in infected persons) by reducing risky sexual behavior. Effective interventions for persons with SMI provide information, increase motivation to engage in safe sex practices, and address skills for condom-use and communication. Interventions may also address risk due to injection drug use in a similar manner.

2) Increased medication adherence

Reasons for medication non-adherence vary by patient and a root cause analysis is important to understand why a patient is non-adherent to ARV therapy and/or psychotropic medication. Factors targeted to improve adherence include education, increased collaboration between clinician and patient, motivational interviewing to reduce ambivalence about taking medications, and reminders provided through environmental cues, social support, and/or technological support.

3) Reducing SMI symptoms and improving functioning

Managing symptoms of SMI may decrease risk behavior and improve medication adherence, in addition to improving quality of life. Monitoring and care coordination appear to be particularly important for SMI. Effective interventions for individuals with schizophrenia and bipolar disorder (see examples in table below) reduce relapse and re-hospitalization rates and improve psychosocial and occupational functioning.

Cognitive Behavioral Therapy	Identifies triggers of negative or delusional thoughts; challenges inaccurate beliefs; teaches more effective coping strategies
Family-focused interventions	Develop a collaborative relationship; provide psychoeducation, communication skills, and problem-solving skills to caregivers
Cognitive/Functional Remediation	Teach strategies that target attention, memory, organization, problem-solving, and reasoning; practice with various exercises
Social Skills Training	Involves role modeling and behavioral rehearsal, combined with positive reinforcement and corrective feedback
Interpersonal and Social Rhythm Therapy	Teaches problem-solving skills to help maintain daily routines and sleep-wake cycles

℞ MANAGEMENT

The treatment of Bipolar Disorder is directed to each subtype (type I vs. type II) for mood stabilization as well as targeted control of behavioral symptoms including reducing agitation, aggression, and impulsivity. The first line pharmacotherapy options for Bipolar Type I Disorder typically include lithium, valproate, or a second generation antipsychotic (SGA). Since lithium

is predominately metabolized by the kidneys and excreted unchanged in the urine, it is least likely to have specific cytochrome P450 (CYP) drug interactions with ARV therapy. Patients with manic and mixed episodes of depression may require treatment of valproic acid, carbamazepine, oxcarbazepine, or a SGA. Both carbamazepine and oxcarbazepine are potent CYP 3A4 inducers and interact with many ARV therapies that are metabolized through the CYP 3A4 pathway including protease inhibitors (PI) and Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI).

For those patients with acute depressive episodes in Bipolar Type II Disorder, first line pharmacotherapy options include lithium, lamotrigine, and SGAs. Patients with HIV and a comorbid psychiatric disorder are at an increased risk for suicide. All antiepileptic drugs (AED) used for bipolar disorder including carbamazepine, oxcarbazepine, lamotrigine, and valproic acid may potentially increase the risk of suicidal thoughts and behavior. Therefore, patients who are receiving any AEDs should be monitored for worsening of depression, suicidal thoughts or behaviors, and/or any unusual changes in mood or behavior.

Schizophrenia is a lifelong illness that routinely requires pharmacological intervention in addition to cognitive and behavioral care. Antipsychotics are first line agents used for acute and maintenance treatment for patients diagnosed with Schizophrenia and/or Psychosis. Antipsychotics are separated into first and second generations. Both classes are associated with a number of side-effects including anticholinergic side effects, extrapyramidal symptoms, alterations in plasma glucose, weight gain, dyslipidemia, sexual dysfunction, and the risk for neuroleptic malignant syndrome which although rare can be life threatening. The first generation antipsychotics have historically fallen out of favor as first line agents due to higher propensity for extrapyramidal symptoms (EPS), QT-interval prolongation, and tardive dyskinesia. Second generation antipsychotics are commonly used as first line agents for the treatment of Schizophrenia and Psychosis, however, these agents have a higher risk for metabolic related side-effects. Some second generation antipsychotics, are similar to first generation antipsychotics (i.e. thioridazine, chlorpromazine, haloperidol, fluphenazine, and perphenazine) in that some of the agents are associated with QT-interval prolongation. Individuals with a previous cardiac history should avoid combinations listed below.

! POTENTIAL ARV INTERACTIONS

Bipolar Disorder

Medication	Antiretroviral	Interaction
Valproic Acid	• Lopinavir/ritonavir • Tipranavir	• Concurrent use of valproic acid with medications may result in ↓ valproic acid serum concentrations and decreased efficacy • Consider an alternative mood stabilizer if antiretrovirals are indicated

Medication	Antiretroviral	Interaction
Carbamazepine	• NNRTI class • PI class • Dolutegravir • Elvitegravir • Cobicistat • Tenofovir • Maraviroc	• Carbamazepine is a strong CYP 3A4 inducer • Coadministration of carbamazepine with antiretrovirals metabolized by CYP 3A4 may ↓ the antiretroviral exposure and therapeutic effect which can lead to the development of antiretroviral resistance • Consider an alternative mood stabilizer if antiretrovirals are indicated
Oxcarbazepine	• Rilpivirine • Darunavir • Tenofovir • Dolutegravir • Elvitegravir • Cobicistat	• Oxcarbazepine is a CYP 3A4 inducer • Coadministration of oxcarbazepine with antiretrovirals that are metabolized by CYP 3A4 may ↓ the antiretroviral exposure and therapeutic effect which can lead to the development of antiret roviral resistance • Consider an alternative mood stabilizer if antiretrovirals are indicated
Lamotrigine	• Atazanavir • Lopinavir/ritonavir	• Coadministration of lamotrigine with agents may result in ↓ lamotrigine serum concentrations • Doses of lamotrigine may need to be increased if medications are indicated • Consider an alternative mood stabilizer if antiretrovirals are indicated
Lithium	No contraindications or major drug-drug interactions with ARV therapy	

Schizophrenia/Psychosis

Medication	Antiretroviral	Interaction
Clozapine	• Saquinavir • Nelfinavir • Atazanavir • Efavirenz • Lopinavir/ritonavir	• Clozapine may prolong the QT-interval and should be avoided with agents that also increase the risk • Consider alternative therapy

Medication	Antiretroviral	Interaction
Olanzapine	• Saquinavir • Fosamprenavir • Efavirenz • Lopinavir/ritonavir	• Olanzapine may prolong the QT-interval and should be avoided with agents that also increase the risk • Consider alternative therapy
Quetiapine	• Saquinavir • Atazanavir • Cobicistat • Darunavir • Efavirenz • Indinavir • Lopinavir/ritonavir • Nelfinavir	• Quetiapine may prolong the QT-interval and should be avoided with agents that also increase the risk • Quetiapine is a CYP3A4 substrate. Use with strong CYP3A4 inhibitors such as cobicistat, indinavir, or darunavir may result in ↑quetiapine exposure and toxicity • Consider alternative therapy
Lurasidone	• PI class • Cobicistat • Fosamprenavir • Delaviridine	• Lurasidone is a CYP3A4 substrate. Concurrent use with a strong CYP3A4 inhibitor may result in ↑ lurasidone exposure and toxicity • Use with PIs and cobicistat is contraindicated • Consider alternative therapy
Risperidone	• Saquinavir • Efavirenz	• Concurrent use of risperidone and agents may result in increased risk of QT-prolongation • Consider alternative therapy
Ziprasidone	• Atazanavir • Efavirenz • Lopinavir/ritonavir • Nelfinavir • Saquinavir	• Ziprasidone may prolong the QT interval and should be avoided with agents that also increase the risk • Consider alternative therapy
Aripiprazole	• Saquinavir • Efavirenz • Atazanavir • Indinavir • Lopinavir/ritonavir • Rilpivirine • Nelfinavir • Cobicistat	• Aripiprazole may prolong the QT interval and should be avoided with agents that also increase the risk • Concomitant use with agents is contraindicated • Consider alternative therapy

Medication	Antiretroviral	Interaction
First Generation Antipsychotics (thioridizane, chlorpromazine, haloperidol, etc.)	• PI class • Efavirenz	• All first generation antipsychotics have the risk of prolonging the QT-interval and should be avoided with antiretroviral medications that can also increase the risk • Consider alternative therapy

Condom Access

One step that all VA providers can take is prescribing condoms. As mentioned above, despite being at increased risk for HIV/AIDS, there are multiple specific factors that decrease the likelihood that these individuals will be able to use condoms. VA prescribers (e.g., physicians, nurse practitioners, physician assistants) can officially prescribe condoms through CPRS and these are filled at no cost to the Veteran through the VA pharmacy. They are ordered formally (just like an Rx; in many VAs, they are found here: Orders→Meds by Drug Name→condom, miscellaneous) as a means of helping the VA account for the demand and use of this resource. Taking this step not only provides free condoms to these Veterans, it also communicates to them the importance of using protection and offers a way for providers to bring up this topic at every encounter. Condoms can also be placed in restrooms, waiting rooms, and other areas to ensure that they are freely available to all individuals.

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