How Syndemic Mental Health Conditions Perpetuate HIV—and What You Can Do About It



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Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years

Dr Grelotti reported no relevant financial relationships with ineligible companies. (Updated October 18, 2026)

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Learning Objectives

After attending this presentation, learners will be able to:

- List psychosocial health conditions associated with HIV transmission and worse health outcomes among people with HIV
- Describe a tripartite approach to addressing mental health and substance use disorders in HIV primary care
- Identify medications that primary care practitioners can use to treat mental health and substance use disorders in people with HIV

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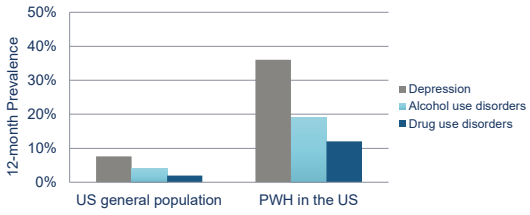
Outline

- How psychosocial syndemics affect HIV outcomes
- The three Rs in addressing mental health and substance use problems in primary care
  - Recognize
  - Respond
  - Refer
- Practical psychopharmacology in HIV primary care

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Higher prevalence of psychosocial conditions among people with HIV (PWH)

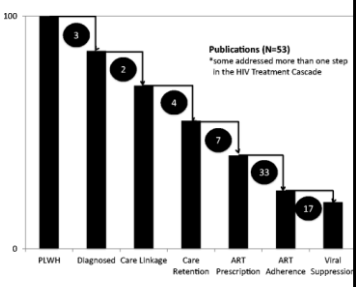


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Substance use, depression, and trauma are associated with HIV transmission and worse health outcomes among people with HIV

Among studies examining alcohol, 77% showed an association between alcohol and worse outcomes for at least one step in the HIV care cascade



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Depression, substance use, and trauma are considered psychosocial syndemic conditions

A syndemic is a set of intertwined and mutually enhancing epidemics involving disease interactions at the biological level that develop and are sustained in a community/ population because of harmful social conditions and injurious social connections.

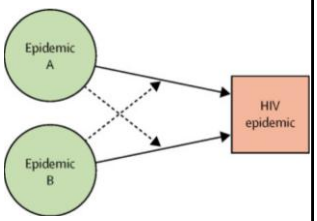
- Singer & Clair 2003

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What is syndemic theory?

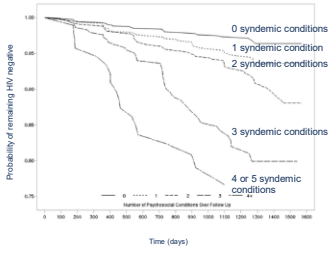
- **Harmful social conditions:** Political, economic, and cultural factors affecting communities leads to disease concentration
- **Disease concentration**: Diseases occurring at the same time and in the same location lead to disease interaction
- **Disease interaction**: Interactions of diseases lead to mutually reinforcing harmful effects on health



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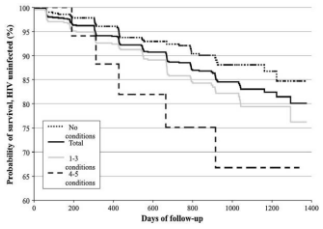
Stimulant use, polydrug use, hazardous alcohol use, depression, and childhood sexual abuse increase the risk of HIV acquisition: EXPLORE study



Mimiaga et al, 2015

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The number of psychosocial syndemics (history of forced sex, suicidal thoughts or actions, club drug use, alcohol intoxication, and/or selling sex) predicts HIV acquisition in the Bangkok MSM Cohort Study



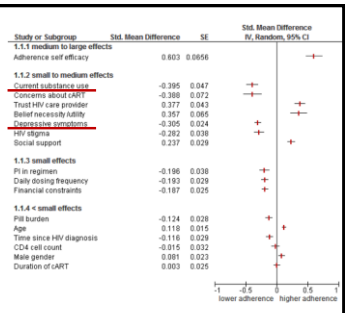
Guadamuz et al. 2014

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Current substance use and depressive symptoms are associated with poor adherence to oral ART among PWH

Meta-analysis of 207 studies with adherence measures.

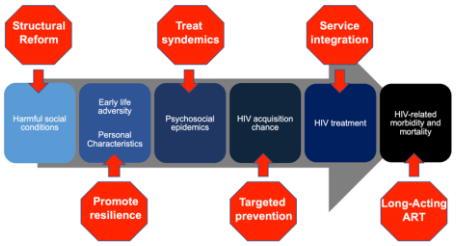


Langebeek et al. 2015

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Syndemic theory and its application to solving psychosocial health problems affecting PWH



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Treating syndemics can improve health behaviors

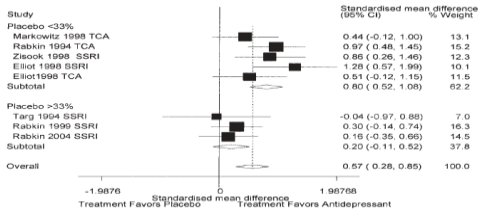
Meta-analysis of 44 randomized controlled trials targeting both syndemics (mental health symptoms, alcohol use, and drug use) and health behaviors (sexual risk behavior, antiretroviral adherence) show improvement in mental health, substance use, and sexual risk behavior

Outcomes	# of effects	*d*	Lower CI (95%)	Upper CI (95%)	*Z* score	*p* value for *Z* score	*Q* statistic	*p* value for *Q* statistic
Syndemics	29	0.20	0.12	0.29	4.71	<.001	73.47	<.001
Mental Health	16	0.23	0.12	0.34	4.06	<.001	28.67	0.018
Substance Use	13	0.17	0.05	0.30	2.67	.008	40.64	<.001
Health Behaviors	19	0.16	0.03	0.30	2.36	.018	58.17	<.001
Antiretroviral Adherence	7	0.17	−0.14	0.49	1.08	.282	26.66	<.001
Sexual Risk Behavior	12	0.17	0.02	0.32	2.29	.022	31.23	.001

Pantalone et al. 2020 Slide 15

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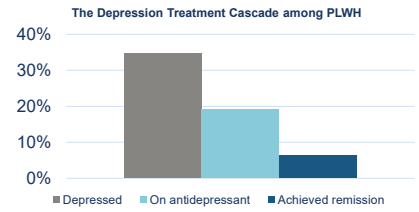
Treatment of depression with antidepressants improves depression and antiretroviral adherence



Himmerich & Mergl 2005, Sin & DiMatteo 2014 Slide 16

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Many PWH are not recognized as being depressed or do not have their depression treatment optimally managed



Dipreto et al. 2019 Slide 17

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Provider challenges to evidence-based antidepressant treatment

HIV provider routine practices and beliefs	%
Belief that treating depression is part of their role	77%
How depression is assessed:	
• Screening	32%
• Observation or patient discloses	61%
Confidence in prescribing:	
• Prescribing an initial antidepressant	59%
• Use of full dose ranges	45%
• Changing or augmenting antidepressants	14%
Follow up within 4 weeks	37%

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A tripartite approach to addressing mental health and substance use problems in HIV primary care: *Recognize, Respond, & Refer*



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Recognize: Ask about current and past mental health in your history

- Mental health history, current and past
- Previous or current psychotherapy and medication treatment
- Anxiety disorders, bipolar disorder, depression, violent behavior
- Suicidal, homicidal ideation; history of hospitalization due to mental health issues
- History of trauma, including sexual and physical abuse, intimate partner and other violence; post-traumatic stress disorder (with appreciation for the sensitive nature of these inquiries and the emotional responses they may elicit)
- History of substance use and treatments for substance use (if any, note which substances used)

Hochberg et al. 2024

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Recognize: Screen with validated screening instruments

Condition	Screening tool	Interpretation	Frequency
Depression	Patient Health Questionnaire-9 (PHQ-9) Patient Health Questionnaire-2 (PHQ-2)	PHQ-9 of 10 or higher PHQ-2 of 3 or higher	Annually
Anxiety	Generalized Anxiety Disorder 7-item (GAD-7) Generalized Anxiety Disorder 2-item (GAD-2)	GAD-7 of 8 or higher GAD-2 of 3 or higher	Annually
Nicotine use	Ask: Do you currently use tobacco or nicotine products?	A yes response	Every visit
Alcohol use	Alcohol Use Disorder Identification Test (AUDIT) Alcohol Use Disorder Identification Test Concise (AUDIT-C)	AUDIT of 8 or higher AUDIT-C of 4 or higher for men; 3 or higher for women	Annually
Drug use	Drug Abuse Screening Test (DAST)	DAST of 3 or higher	Annually

Horbreg et al. 2024

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Respond

- Talk: Provide empathic listening, validation
- Educate: About mental health and its treatment
- Evaluate:
  - For possible medical contributions to the condition
  - For possible medical sequelae of the problem
  - For interest in mental health treatments
- Treat: with medication, if appropriate
- Assess safety (e.g., suicidal ideation, withdrawal risk)

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Respond: Listening to patients and providing psychoeducation are important






- Depression never discriminates. It took me a long time to realize it but the key is to not be afraid to open up. – Dwayne "The Rock" Johnson
- And then I said those words, "I need help. I'll get help." And my life turned around. – Elton John
- I sought counseling after 20 years of not thinking about the death of my mother and two years of total chaos in my life. – Prince Harry
- I suffer from depression and PTSD. But the kindness of doctors, family, and my friends – it saved my life. – Lady Gaga

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Respond: Gaining confidence in prescribing medications for mental health and addiction

Familiarize yourself with prescribing a set of medications based on the following criteria:

- Availability (e.g., generic, available on most formularies, including the AIDS Drug Assistance Plan (ADAP) formularies)
- Safe (generally free of interactions)
- Ease of prescribing, minimizing need for titration

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Respond: Tailor choice of medication for major depressive disorder (MDD) to address multiple problems

- MDD **+/- anxiety disorder**
  - SSRI (selective serotonin reuptake inhibitor)
  - SNRI (serotonin and norepinephrine reuptake inhibitor), e.g. Desvenlafaxine
- MDD **+ prominent anhedonia**
  - Bupropion extended release
- MDD **+ nicotine use**
  - Bupropion extended release
- MDD **+ fatigue**
  - Bupropion extended release or SNRI
- MDD **+ insomnia or weight loss**
  - Mirtazapine
- MDD **+ cognitive concerns**
  - Vortioxetine
- MDD **+ pain**
  - Duloxetine (and likely other SNRIs)
- MDD **+ concern for sexual side effects**
  - Bupropion extended release, mirtazapine, vilazodone, or vortioxetine

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Respond: Desvenlafaxine

- **Mechanism:** Serotonin and Norepinephrine Reuptake Inhibitor
- **Indication:** Major Depressive Disorder, also commonly prescribed for anxiety disorders and may be helpful for neuropathic pain and vasomotor symptoms in menopause
- **Dose:** 50 mg by mouth daily - *Starting does is an effective dose; no titration required*
- **Interactions:** Few. Minimal CYP metabolism (primarily conjugated via UGT)
- **Caution:** Hypertension / dose-related increase in diastolic blood pressure (BP); check BP before starting and periodically
- **Common side effects:** Nausea, dizziness, insomnia, diaphoresis, constipation, dry mouth, somnolence, sexual dysfunction
- **Taper off to avoid discontinuation syndrome**

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Respond: Bupropion extended release

- **Mechanism:** Norepinephrine-dopamine reuptake inhibitor
- **Indication:** Major Depressive Disorder and smoking cessation
- **Dose:** Bupropion *extended release* 150 mg by mouth once daily. After one week may increase to 300 mg by mouth once daily. Max dose is 450 mg by mouth once daily.
  - *It is unlikely that you will prescribe the immediate release or sustained release formulations*
- **Interactions:** Few with modern antiretroviral therapy. Metabolized by CYP2B6 and may interact with protease inhibitors and efavirenz
- **Caution:** Lowers seizure threshold. Avoid in people with seizure, eating disorder
- **Common side effects:** Insomnia, dry mouth, anxiety, headache, nausea
  - Less likely than other antidepressants to cause sexual side effects and weight gain
- **Taper to avoid discontinuation syndrome** (irritability, fatigue, headache)

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Respond: Mirtazapine

- **Mechanism:** Alpha-2 antagonist (increasing norepinephrine and serotonin) and antihistaminergic
- **Indication:** Major Depressive Disorder
- **Dose:** 15 mg at bedtime
- **Interactions:** Few. Mostly a CYP3A4 substrate
- **Caution:** Anticholinergic effects (dry mouth, constipation), narrow-angle glaucoma
- **Common side effects:** Increased cholesterol, weight gain, increased appetite, drowsiness
- **Taper to avoid discontinuation syndrome**

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Respond: Other medications to familiarize yourself with

- **Avoid benzodiazepines, try these instead:**
  - **Trazodone**: An antidepressant often used for insomnia
  - **Hydroxyzine**: An antihistamine often used for anxiety or insomnia
- **Respond to psychosis**
  - **Olanzapine**: An antipsychotic that is can be used for substance-induced psychosis pending specialist evaluation and treatment

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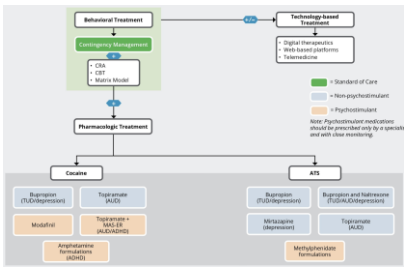
Respond: Medication for addiction treatment

- Nicotine use disorder
  - Nicotine replacement therapy, Bupropion, Varenicline
- Alcohol use disorder
  - Naltrexone*, Acamprosate, Disulfiram
    *If hepatic contraindications to naltrexone use, consider acamprosate for patients with creatinine clearance greater than 30 ml/minute
  - Not FDA approved: Topiramate, Gabapentin, Baclofen
- Opioid use disorder
  - Methadone (specialty clinic only), Buprenorphine, Naltrexone

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Respond: Treatment algorithm for stimulant use disorders



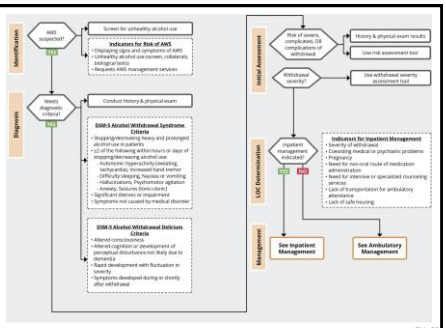
CRA: Community Reinforcement Approach; CBT: Cognitive Behavioral Therapy; TUD: Tobacco Use Disorder; AUD: Alcohol Use Disorder; ADHD: Attention Deficit/ Hyperactivity Disorder

ASAM/AAAP 2024

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Respond: Screen and assess for unhealthy alcohol use and risk for alcohol withdrawal syndrome (AWS)

Withdrawal management is a critical component of initiating treatment of alcohol use disorder (AUD). AUD treatment includes identification/screening separately for both unhealthy alcohol use and withdrawal symptoms, diagnosis, assessment of withdrawal and its treatment, supportive care (e.g., thiamine supplementation), and AUD treatment (e.g., behavioral, pharmacological). Withdrawal is increasingly managed in outpatient settings.



ASAM 2020

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Respond: Naltrexone

- **Mechanism**: Opioid receptor antagonist
- **Indication**: Moderate to severe alcohol use disorder (even with active drinking) and prevention of relapse in opioid use disorder
- **Dose**: 50mg Daily (oral) or 380mg IM Q28Days (injectable)
- **Side effects**: Nausea / vomiting, dizziness, headache, elevated LFTs, injection site reaction (injectable only), decreased appetite
- **Contraindications:** Acute hepatitis, liver enzymes ≥3 to 5 times normal, or liver failure; opioid use or risk of opioid withdrawal
- **Monitoring:** Periodic liver function tests
- **Other practical considerations:** Strong genetic component to response; some people report that they still drink but drink less

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Respond: Notable interactions with new long-acting antiretroviral medications

Medications to avoid with cabotegravir-rilpivirine (lower rilpivirine levels):	Medications to avoid with lenacapavir (lower lenacapvir levels):	Medications to use with caution with lenacapavir (increased medication levels up to one year after last administration):
• Phenobarbital • Phenytoin • Carbamazepine • Oxcarbazepine • Modafinil • Armodafinil	• Phenobarbital • Phenytoin • Carbamazepine • Oxcarbazepine • Modafinil • Armodafinil	• Midazolam • Triazolam • Diazepam • Alprazolam • Quetiapine • Lurasidone • Clozapine

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Refer: Reasons one might refer a patient for mental health or substance use care

- Safety and high-risk concerns
  - Suicidal ideation
  - Homicidal ideation
  - Inability to care for self
  - Withdrawal from alcohol or drugs
- Diagnostic complexity or severe symptoms
- Moderate- or high-risk substance use disorders
  - Multiple failed attempts to quit with your help
- Need for specialized treatment or additional treatment modalities
- Practice and resource limitations

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Refer: Access to different types of treatment

- Other medication treatments
  - Esketamine
  - Long-acting treatments
- Psychotherapy
- Somatic therapy
  - Electroconvulsive therapy
  - Transcranial Magnetic Stimulation

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Refer: Different levels of care

- Integrated behavioral health
- Outpatient mental health care (psychiatry and psychotherapy, individual and group)
- Intensive outpatient, partial hospitalization
- Residential substance use treatment programs
- Crisis stabilization, inpatient hospitalization

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Refer: Current investigational studies of depression in PWH

- SOOTHE (NCT05570812)
  - Intervention: Pregnenolone vs placebo
  - Mechanism: Neurosteroid / HPA axis / GABA
  - Population: PWH on ART with depression
- Inflammation & Depression in HIV (NCT05849038)
  - Intervention: Baricitinib vs placebo
  - Mechanism: JAK inhibition / anti-inflammatory
  - Population: PWH with depression + inflammation
- ACTG A5402 (NCT06705478)
  - Intervention: Pramipexole ER vs Escitalopram
  - Mechanism: Dopamine agonist vs SSRI
  - Population: PWH with MDD ± mild neurocognitive disorder



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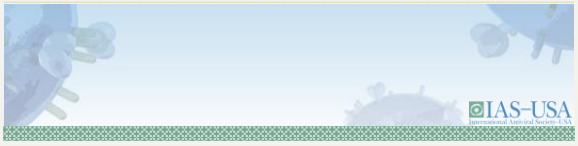
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Summary

- Mental health and substance use problems are more prevalent among PWH than in the general population and contribute to poor health outcomes
- Mental health and substance use problems are treatable, and treatment improves health outcomes
- Nonspecialist providers using the three Rs play an important role in the care of PWH and comorbid mental health and/or substance use problems

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Q and A Session



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