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Treatment Considerations for HIV-Infected Individuals with Severe Mental Illness

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Abstract

There has been a general recognition of a syndemic that includes HIV/AIDS and severe mental illnesses including schizophrenia, major depression, bipolar disorder, post-traumatic stress disorder, and others. The pathophysiology and direction of effects between severe mental illness and HIV infection is less clear however, and relatively little work has been done on prevention and treatment for people with these complex, co-occurring conditions. Here we present the most recent work that has been published on HIV and mental illness. Further, we describe the need for better treatments for “triple diagnosed persons”; those with HIV, mental illness, and substance abuse and dependence. Finally, we describe the potential drug-drug interactions between psychotropic medications and anti-retrovirals, and the need for better treatment guidelines in this area. We describe one example of an individually tailored intervention for persons with serious mental illness and HIV (PATH+) that shows that integrated community-based treatments using advanced practice nurses (APNs) as health navigators can be successful in improving health-related quality of life and reducing the burden of disease in these persons.

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Compliance with Ethics Guidelines

Conflict of Interest

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Human and Animal Rights and Informed Consent

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Keywords

syndemics; severe mental illness; HIV; substance abuse; triply diagnosed; drug-drug interactions; treatment guidelines; depression; schizophrenia; bipolar disorder; anxiety disorder; PTSD; PATH+

Introduction

A majority of HIV/AIDS patients in every clinical center suffer from co-occurring affective disorders (e.g. major depression and bipolar disorder), substance abuse disorders, cognitive disorders, psychotic disorders and/or anxiety disorders. Often these “syndemic patients” have often been excluded from randomized clinical trials investigating new drugs and other treatments. This practice emphasizes the internal validity of experiments over the external validity of having samples that equate to those living in the “real world” where people often have multiple co-morbid illnesses. Consequently, there has been a missed opportunity to provide informed guidance to clinicians faced with patients who have these comorbid problems. Syndemic illness refers to the co-occurrence of two or more diseases or conditions within a population where there is some biological interaction or synergy that exacerbates the negative effects of the diseases or illnesses and complicates treatment¹. There has been a growing interest in syndemics and their treatment as the health and public health community has increasingly recognized that health disparities are largely linked to social conditions including social ecological factors such as poverty, stress, violence, and other adverse conditions that contribute to environmental toxicity. Here we address syndemic illness and their treatment for persons with HIV and a serious mental illness (SMI). Importantly, SMI is not a diagnosis per se, rather it is used to refer to a broad category of persons who are disabled by any number of mental illnesses, and is often used to determine eligibility for a variety of entitlements.

A now established body of research documents that persons with mental illness are at increased risk for contracting and transmitting HIV.^{2,3} This increased risk is thought to be due to high rates of substance use including injection drug use (IDU), risky sexual behavior, sexual victimization, and prostitution among those with SMI.⁴ Recently, there has been an increased emphasis on having both inpatient and outpatient mental health settings offer routine, opt-out HIV testing to improve case finding among persons with mental illness and promoting their linkage to infectious disease care⁵. Adherence to HIV treatment regimens is sometimes markedly compromised when a person has an SMI, which can pose a public health threat by increasing community viral load and potentially developing ART resistant virus strains. When this happens, the person with mental illness may serve as a vector of HIV transmission. Therefore, there is a need for methods of improving continuity between increasing their access to HIV treatment, then reinforcing their treatment adherence. Research also makes clear that these adverse outcomes are far from inevitable, as people with SMI receiving good quality care can achieve adherence rates comparable to non-SMI counterparts. In fact, the evidence reviewed here shows that they can adhere to treatments with appropriate supports, and some have found that they are less likely to discontinue ART than others⁶.

Prevalence Estimates from Convenience Samples

Risk factors associated with HIV infection among persons with SMI mirror those in the general population and include unprotected sex and injection drug use (IDU).^{3,7-11} The evidence needed to establish accurate estimates of co-occurrence have come from several sources. First, in samples of patients with SMI during the 1990s and early 2000s using convenience samples, estimations of HIV prevalence ranged from 1%–23%¹²⁻¹⁶ Prevalence

estimates observed from these studies vary a great deal mainly due to methodological differences related to sampling frames, particularly the reliance on convenience samples, which tended to be restricted to institutional or geographically restricted areas, as well as different approaches to adjustment for confounding effects of factors associated with HIV. Given the low absolute rates of infection, estimates were also necessarily affected by small sample sizes. The extent to which these early prevalence estimates reflect current infection patterns is not known.

Prevalence Estimates from Administrative Data

A second source of data come from administrative health care claims from Medicaid, often linked to other administrative data sources, such as state HIV or AIDS registry files. These likewise report evidence of elevated associations. For example, in an analysis of claims linked to the New Jersey HIV/AIDS registry, Walkup and colleagues found 5.7% had a diagnosis of schizophrenia², which can be compared to general population prevalence rate for schizophrenia of around 1%¹⁷. After controlling for a range of socio-demographic variables available through welfare records, Blank and colleagues found schizophrenia spectrum disorder patients were 1.5 times as likely to have claims indicative of HIV infection, and those major affective disorder were 3.8 times as likely³. Administrative medical records from a national sample from the Veterans Administration also point to elevated rates of HIV in severely mentally ill patients⁷.

Estimates based on true epidemiological samples are rare. Perhaps due to shortcomings in existing detection systems, these estimates are often limited in their ability to shed light on people with more severe psychotic illnesses; they offer psychiatric diagnoses based on structured interviews with carefully designed sampling frames. A recent study using the National Epidemiologic Survey on Alcohol and Related Conditions reported that, compared to their HIV-negative counterparts, men with HIV were significantly more likely to merit a range of diagnoses, including major depressive disorder/dysthymia, and any personality disorder¹⁸.

Prevalence Estimates from Remnant Blood

More recently, some findings suggest administrative claims may produce underestimates when not all HIV diagnoses are captured and for those that are, they may not be reliably linked to confirmed HIV positive tests within administrative databases. In order to address this issue, Rothbard, Blank and colleagues conducted HIV testing on remnant blood specimens collected from patients on two inpatient psychiatric units in the City of Philadelphia¹⁶. When using this more direct case ascertainment strategy, HIV infection was observed in 10.1% of patients. In contrast, when the review was restricted to chart review only, a full one-third of the individuals identified by remnant blood testing as HIV positive did not include documentation of an HIV positive diagnosis. These results identify some serious shortcomings even in inpatient care, which suggests that persons with mental illness are likely underserved with regard to identification of infectious diseases including HIV.

A Lack of Treatment Guidelines

Relatively few guidelines have been developed for clinicians who provide treatment for persons with comorbid HIV/AIDS and mental illness, and the ones that have been provided by the American Psychiatric Association may now be considered outdated¹⁹. Previous studies have attempted to query clinicians regarding their preferred treatment options for PLWHA who have co-occurring psychiatric disorders. One web-based survey of the membership of the Organization of AIDS Psychiatry found among the 39% of responding clinicians that first-line medication for depression was escitalopram/citalopram; first line

treatment for psychosis and secondary mania was quetiapine; and first line medication treatment for anxiety was clonazepam²⁰. Another national survey queried members of the American Academy of HIV Medicine regarding how they made decisions regarding initiating HAART for HIV+ people with schizophrenia²¹ and found that clinicians recognized the importance of recommending antiretroviral treatment to HIV infected people with co-occurring schizophrenia and avoided using antiretroviral medication with known neuropsychiatric side effects. One result of these kinds of studies has been a fledgling effort toward developing biopsychosocial curricular components of residency training for psychiatrists²².

There is a growing need to establish an evidentiary base of how to translate and implement interventions that have been shown to be effective in other populations among PLWHA with co-occurring psychiatric disorders. Toward that end we discuss research conducted within a prior two year period (2011–2103) to identify emerging themes as well as more enduring and challenging tasks associated with testing and treatment adherence for individuals at risk for HIV as well as people living with HIV.

Treatment Challenges

Major Depression and Bipolar Affective Disorder

Depression and other affective disorder are common co-morbidities of all chronic illnesses including HIV infection, where they provide particular challenges to clinical care. They diminish people's ability to adhere to treatment and engage in self-care, quality of life, and biomedical outcomes. It is probable that they also interfere with an ability to benefit from other health promotion interventions²³. A meta-analytic review found that, across 95 independent samples, depression was significantly associated with medication non-adherence²⁴.

Prevalence estimates of major depressive disorder among persons living with HIV/AIDS (PLWHA) range from 20% to as high as 37%²³. This is more than three times the rate of major depression in the general population, which has been shown to range between 5% and 12%²⁵. Because HIV is a chronic and life-threatening illness and like other such illnesses, can be stressful to manage, people living with HIV/AIDS (PLWHA) are particularly vulnerable to depression and other affective disorders. The life-threatening nature of HIV infection itself may instigate fears of impending mortality. Moreover, the medical sequelae of HIV infection such as HIV Associated Neurocognitive Disorders (HAND), associated opportunistic infections, and the side effects of antiretroviral treatment can mimic symptoms of depression (i.e., fatigue, concentration problems, somatic symptoms, decreased appetite/weight loss). From a cognitive-behavioral perspective, these physical symptoms can be part of a cycle of continued depression²³. Other factors that might account for the high level of depression and other affective disorders among PLWHA are unique to HIV. Specifically, PLWHA disproportionately belong to socially disadvantaged and marginalized populations who are already at risk for depression because of their racial, ethnic, or sexual minority status, poverty, current or prior substance use, sex work, and trauma and the argument has been made that providing quality treatment to these individuals is effective prevention²⁶. Because HIV is associated with all of these marginalized statuses, many PLWHA face high levels of stigma. Like stigma for mental illness, HIV stigma can lead to problems including nondisclosure of HIV serostatus, social isolation, and stress which further enhances the risk of depression and other affective disorders.

Depression rates do not appear to decline with age in HIV populations as they do in the general population²⁷. This is important because as many as one quarter of all U.S. HIV+ adults are now 50 years or older²⁸. As people live longer due to medical advances,

depression in a gradually aging HIV cohort will remain an issue that needs to be addressed clinically and accounted for in HIV research. While there is evidence that the presence of severe psychiatric illness can negatively impact HIV care, particularly medication adherence, studies also underline the importance of individualized assessment and the potential positive impact of good psychiatric and substance abuse care. Carrico, Bangsberg, and colleagues used a mobile outreach van to recruit a probability sample of homeless and unstably housed men²⁹. Those who tested positive for HIV were given the Diagnostic Interview Schedule to screen for psychiatric disorder. Participants on HAART were compared to those eligible for HAART but not receiving it. Mental health treatment in the past 90 days significantly increased the odds of HAART receipt. No significant impact on odds of HAART receipt was found for current SMI, major depression, or PTSD, but among those on HAART, SMI was independently associated with six times higher viral load. Associations between progression of HIV disease and depression have been linked to its impact on medication non-adherence in an analysis of outcome data from participants in a behavioral intervention³⁰.

Psychotherapeutic interventions may be well suited to address the psychosocial difficulties as well as the distress associated with HIV. Of note, telephone-based cognitive behavioral therapy (T-CBT) has emerged as a feasible, acceptable and efficacious treatment for major depression. One recent randomized controlled trial found that among HIV positive people with major depression those randomized to receive T-CBT were as likely as those randomized to face-to-face psychotherapy treatment to have significant reductions in depression. However, those who received the T-CBT were significantly more likely to maintain their adherence to antiretroviral medication compared to the face-to-face treatment. This may suggest that T-CBT may not only reduce depressive symptoms but do so in a way that improves adherence to antiretroviral medication³¹.

Bipolar disorder, also known as manic-depressive illness, causes unusual shifts in mood, energy, activity levels, and the ability to carry out day-to-day tasks. Symptoms of bipolar disorder can be quite severe and can result in a manic state where thinking and judgment are significantly impaired. Diagnostic criteria for bipolar disorder includes but is not limited to behaving impulsively and engaging in pleasurable, high-risk behaviors including high-risk sexual behaviors. These impulsive, high-risk behaviors in the context of impaired judgment may put people in the manic phase of bipolar disorder at increased risk for becoming infected with HIV as well as for transmitting it to others.

Research with PLWHA shows that they are significantly more likely to have bipolar disorder than the general population. A recent study of HIV-infected patients in Brazil found high rates of bipolar disorder (BD) on the Mood Disorder Questionnaire (MDQ)³². The sample included 196 HIV-infected adults who were interviewed with the Mood Disorder Questionnaire (MDQ). Positive MDQ screening was found in 13.2% (N=26) and the BD diagnosis was confirmed in 8.1% (N=16) of the sample. This represents almost four times higher prevalence of BD among the PLWHA in the sample (8.1%) than in the general population from the USA (2.1%). The variables associated with the diagnoses of BD were sex with commercial partners, sex outside the primary relationship, alcohol use disorders, and illicit drug use. The most common psychiatric comorbidity in the BD group was substance abuse (61.5%).

Another recent study in the US examined HIV in individuals with bipolar disorder (BD). HIV transmission risk behavior was examined among 63 patients with BD, major depressive disorder, and no mood disorder; half also had substance use disorders (SUDs). Patients with BD were more likely than others to report unprotected intercourse with HIV-negative partners and less than 95% adherence to antiretroviral medications. In multivariate models,

BD and SUD were independent predictors of both risk behaviors. Participants with poorer medication adherence were more likely to have detectable HIV viral loads and unprotected intercourse with HIV-negative partners. Patients with BD deserve careful evaluation and HIV prevention services to reduce HIV transmission risk behaviors³³.

Anxiety Disorders

Studies examining the prevalence of anxiety disorders among HIV-infected individuals suggest that as many as 16–36% of HIV-infected individuals have anxiety disorders³⁴ and the HIV Cost and Services Utilization Study (HCSUS) study found that 16% of HIV-infected individuals in their sample met criteria for generalized anxiety disorder, and that 10.5% met criteria for panic attacks³⁵. Among PLWHA with anxiety symptoms, adjustment disorder with anxious mood was found to be most common, followed by generalized anxiety disorder (GAD) and panic disorder (PD). Adjustment disorder can be distinguished from other anxiety disorders, as the severity of symptoms for anxiety disorders are of greater severity than those exceed typically found with adjustment disorders. Anxiety disorders are also a common co-morbidity among those with depression, underlining the importance of careful assessment for anxiety symptoms among those presenting with depression. SSRIs are a common treatment and effective for anxiety disorders, however, Vitiello and colleagues found that 63% of the medications prescribed for anxiety among HIV-infected individuals were benzodiazepines.³⁶ That finding was of some concern considering the high rates of substance abuse among HIV-infected persons and the potential for abuse of benzodiazepines. Hopefully, the use of benzodiazepines to treat anxiety among persons who are HIV infected has declined markedly in the decade since that review was conducted.

Posttraumatic stress disorder (PTSD) is a highly prevalent chronic and disabling psychiatric disorder that is frequently comorbid with major depression.³⁷ Among individuals who are HIV-infected, the rate of lifetime PTSD and incidence of HIV-related PTSD has been estimated at 54% and 40% respectively³⁸. Despite the high co-occurrence and harmful effects of PTSD in HIV-infected individuals, there is relatively little research on the efficacy of treating PTSD in this population and not all studies have found antidepressant medication to be efficacious in treating HIV-positive individuals with PTSD³⁹. Prolonged Exposure (PE) therapy is a well-supported psychotherapeutic treatment for PTSD and has demonstrated efficacy in a wide range of trauma populations. PE has been shown to be effective in reducing symptoms of PTSD and symptoms of comorbid depression in one study to date⁴⁰.

Schizophrenia

Schizophrenia spectrum disorders are a complex constellation of severe psychiatric illnesses that are characterized by positive symptoms (i.e., hallucinations and delusions), negative symptoms (i.e., alogia, anhedonia), disorganized thinking and cognitive impairment that leads to social and occupation dysfunction. Onset of schizophrenia is typically in late adolescence and early adulthood in both men and women, during the developmental period where sexuality and sexual behaviors typically increase in frequency and importance. This dynamic combined with the increased vulnerability to abuse and exploitation of persons with disordered thinking makes these persons particularly vulnerable to contracting and transmitting HIV and other infectious diseases. Antipsychotic agents are the treatments of choice regardless of the underlying diagnosis. Open studies and case reports support the use of standard antipsychotic agents for psychotic symptoms in PLWHA, and there have been recommendations made that the atypical antipsychotics are efficacious with fewer extrapyramidal side-effects than traditional antipsychotic medications like haldol and thioridazine⁴¹. However, there is consensus that the widespread use of many psychiatric medications, particularly the newer atypical antipsychotics, heighten the risk of obesity and

metabolic syndrome. In general, studies suggest that individuals experience greater weight gain with the atypical neuroleptics than with older antipsychotics such as haloperidol⁴²; however weight gain with older neuroleptics such as chlorpromazine and thioridazine is also well documented⁴³.

What is needed are evidence-based treatment guidelines based on biological and behavioral studies of the treatment of mental illness among individuals in treatment for HIV/AIDS to develop innovative, integrated treatments to optimize psychiatric, behavioral, and medical outcomes and to achieve a better understanding of the biological mechanisms underlying these combined illnesses and treatments⁴⁴.

Treatment for Co-occurring Substance Abuse and Mental Illness among HIV positive Individuals (Triply Diagnosed Persons)

The interaction between symptoms of mental illness and HIV risk behaviors is complex and recursive, and the symptom to infection pathway needs to be understood in the context of multiple environmental and behavioral factors. As with any serious chronic illness, HIV itself often produces depression and anxiety in persons, and the virus has been shown to have direct neurotoxic effects that can result in HIV-associated Neurocognitive Disorder (HAND), a complex syndrome characterized by a wide variety of neurological and performance deficits. The severity of mental illness symptoms has been found to be associated with higher risk for being HIV infected in a study that examined the association of HIV risk and psychiatric symptom severity using the Colorado Symptom Index (CSI)⁴⁵. That study found a 47% increased risk for HIV among persons with CSI scores greater than 30 (a criterion score for severe psychiatric symptoms) compared to those with scores lower than 30, indicating that psychiatric symptom severity was associated with HIV infection.

To further add to the complexity of the problem, there is a now established empirical base that clearly demonstrates the co-morbidity between HIV, mental illness, and substance use⁴⁶. There is compelling evidence that the addition of substance abuse profoundly raises the risk of HIV in people with mental illness. In a large sample of patients with schizophrenia spectrum disorders treated through the VA system, Himelhoch and his colleagues found an interaction where people with schizophrenia and co-morbid substance abuse were at markedly greater risk for HIV infections, but in the absence of a substance use diagnosis people with schizophrenia alone were actually at lower risk for HIV infections than the general VA population.⁷ These findings have been echoed in a paper using Medicaid claims to examine new HIV diagnoses among SMI patients in 8 states⁴⁷.

Care must be taken in drawing conclusions from data patterns based on diagnosis, and in translating findings into clinical practices⁴⁸. As we noted earlier, HIV testing practices among SMI can produce undercounts. If people with SMI but no substance abuse are particularly unlikely to be tested, HIV diagnoses in this group will underestimate true rates. Given that underestimates are possible, the clear evidence that cases of HIV continue to go undetected in psychiatric settings, and the probability that many people who present with an SMI eventually develop substance use problems, integrated service delivery with prevention and treatment services provided for both disorders seems desirable. Including substance use in HIV risk assessment for those presenting with an SMI is needed, and availability and promotion of HIV testing should be increased across settings. The spread of routine testing may provide improved opportunities to estimate true rates of infection across groups and, more important, should reduce the probability of missed cases.

Clearly, comprehensive routine opt-out HIV testing and screening for HIV risk among persons with mental illnesses needs to include a substance abuse screen. As such, research

geared toward community implementation of HIV prevention interventions that are relevant to persons with SMI and substance abuse has great public health significance, since these individuals seem disproportionately prone to contracting HIV themselves, and perhaps to spreading the disease to others.

Medication Monitoring and Drug-Drug Interactions

When prescribing psychotropic medication in the context of antiretroviral therapy, it is important to monitor for untoward side effects, as well as to consider possible drug-drug interactions. For example, people prescribed second generation antipsychotic medication are at increased risk for developing symptoms associated with the metabolic syndrome. These symptoms include weight gain, hyperglycemia and hyperlipidemia. Similar symptoms associated with the metabolic syndrome are also associated with treatment with antiretroviral medications (i.e., protease inhibitors). Clearly monitoring of weight, fasting blood glucose, and lipid profiles is integral to treatment for people taking any of these medications. Clinicians need to also be careful to review and identify any drug-drug interactions (i.e., cytochrome P-450 system) between antiretroviral medication and psychotropic medications. For example, specific benzodiazepines may be contraindicated when taken with protease inhibitors and care must be taken when prescribing methadone in the presence of specific non-nucleoside reverse-transcriptase inhibitors (NNRTIs). A careful history about use of over the counter medications and herbal remedies is also recommended. In particular, St. Johns Wort may be contraindicated when used in conjunction with antiretroviral treatment.

Treatment Innovations: Preliminary Evidence for Tailored Treatment and Nurse Health Navigators

Preventing AIDS through Health for HIV Positive persons (PATH+) was a regimen management intervention study for persons who also had a SMI that was carried out by advanced practice nurses (APNs) who provided in-home services and coordinated participants' care^{10,49,50}. In PATH+ an adaptive treatment design⁵¹ implemented through a "intervention cascade" was used to titrate the intensity (and expense) of the intervention to actual adherence outcomes. As described by Blank & Eisenberg¹⁰, the PATH+ intervention cascade is an individually tailored intervention to promote adherence in HIV positive persons with co-occurring mental illnesses. The PATH+ intervention consisted of assignment of the services of an APN who provided in-home consultations and coordinated medical and mental health services for one year. The APNs collaborated with prescribing providers, pharmacists, and case managers to organize medication regimens and help participants cope with barriers to medication adherence and promote the participant's ability to self-care. The protocol included a meeting with the participant at a minimum of once a week. The basic intervention consisted of psycho-education along with pillboxes and beeping watches and was provided to all participants in the intervention group. In addition, the APN served a health navigator, and coordinated physician and other appointments for the client and would also attend them with the patients when there was a problem with a medication, communication, or other issues needing physician attention.

Adherence to HIV and psychiatric medications was calculated weekly. If adherence fell below 80%, the intervention cascade was implemented until adherence was maintained equal to or above 80% for three weeks. The intervention cascade represented a gradual increase in intensity and included activation of social networks, the use of reminder beepers with alphanumeric displays, and then prepaid cellular phones to encourage participants to follow their regimen. If all else failed, the final step in the intervention cascade was directly observed therapy.

A total of 238 community-dwelling, HIV-positive subjects with SMI who were in treatment at urban CMHC's between 2004 to 2008 were enrolled. The main outcome measures were viral load and CD4 count. Results of the intervention showed significant reductions in viral load at 12 months¹⁰, and latent growth curve models showed significant changes in viral load, CD4, and health-related quality of life over 24 months⁵².

Conclusion

The increased risk for HIV infections among persons with severe mental illness and the disproportionate burden of disease it represents for these people require more attention and more effective individualized treatments. Here, we briefly outline what is known regarding HIV risk and treatment for persons with schizophrenia, depression and other affective disorders, bipolar disorders, and anxiety disorders including PTSD. A brief discussion of what little information exists regarding drug-drug interactions between psychotropic medications and anti-retrovirals is included. Moving away from DSM-diagnostic groupings, we then go on to discuss prevalence and treatment issues for triply diagnosed PLWHA with substance abuse or dependence, and a co-occurring severe mental illness. We use an example from Preventing AIDS through Health for Positives (PATH+), an intervention that was individually tailored to promote adherence to complex treatment regimens among these persons, to show that these individuals can be treated successfully when given appropriate supports.

References

1. Singer, M. Introduction to syndemics: A critical systems approach to public and community health. Wiley.com; 2009.
2. Walkup J, Crystal S, Sambamoorthi U. Schizophrenia and major affective disorder among medicaid recipients with HIV AIDS in New Jersey. *American Journal of Public Health*. Jul; 1999 89(7): 1101–1103. [PubMed: 10394325]
3. Blank MB, Mandell DS, Aiken L, Hadley TR. Co-occurrence of HIV and serious mental illness among Medicaid recipients. *Psychiatric Services*. 2002; 53(7):868–873. [PubMed: 12096171]
4. Gottesman, Groome CS. HIV/AIDS risks as a consequence of schizophrenia. *Schizophrenia Bulletin*. 1997; 23(4):675–684. [PubMed: 9366003]
- *5. Blank MB, Himelhoch SS, Balaji AB, Metzger DS, Dixon LB, Rose CE. A Multisite Study of the Prevalence of HIV using Rapid Testing in Mental Health Settings. *American Journal of Public Health*. in press. The objective was to estimate HIV prevalence and risk factors among persons receiving treatment in mental health settings in Philadelphia and Baltimore. 1062 individuals were tested for HIV who were receiving services in three settings: University-based inpatient psychiatric units (N=288), assertive community treatment programs (ACT, N=273), and community mental health centers (CMHCs, N=501). The proportions with confirmed positive HIV test results were 5.9% for inpatient units, 5.1% for ICM programs, and 4.0% for CMHCs. HIV infection was associated with black race, homosexual or bisexual identity, HCV infection, and overall psychiatric symptom severity. The authors recommend routine opt-out testing for all inpatient and outpatient mental health treatment settings.
6. Himelhoch S, Brown CH, Walkup J, et al. HIV patients with psychiatric disorders are less likely to discontinue HAART. *AIDS (London, England)*. 2009; 23(13):1735.
7. Himelhoch S, McCarthy JF, Ganoczy D, Medoff D, Dixon LB, Blow FC. Understanding associations between serious mental illness and HIV among patients in the VA health system. *Psychiatric services*. Sep; 2007 58(9):1165–1172. [PubMed: 17766561]
8. Himelhoch S, Chander G, Fleishman JA, Hellinger J, Gaist P, Gebo KA. Access to HAART and utilization of inpatient medical hospital services among HIV-infected patients with co-occurring serious mental illness and injection drug use. *General hospital psychiatry*. Nov-Dec;2007 29(6): 518–525. [PubMed: 18022045]

- *9. Himelhoch S, McCarthy JF, Ganoczy D, et al. Understanding Associations Between Serious Mental Illness and Hepatitis C Virus Among Veterans: A National Multivariate Analysis. *Psychosomatics*. Jan-Feb;2009 50(1):30–37. The public health literature demonstrates disturbingly high HIV risk for persons with a serious mental illness (SMI), who are concurrently co-morbid for substance abuse (SA). Many HIV positives have not been tested, and therefore do not know their status, but for individuals who are triply diagnosed, adherence to HIV treatment results in meaningful reductions in viral loads and CD4 counts. Barriers to treatment compliance are reviewed, low threshold/low intensity community based interventions are discussed, and preliminary evidence is presented for the efficacy of the Intervention Cascade, defined as an integrated intervention delivered by specially trained nurses who individualize a treatment compliance intervention in real time as an adaptive response to demand characteristics of the individual. [PubMed: 19213970]
10. Blank MB, Eisenberg MM. Tailored treatment for HIV+ persons with mental illness: the intervention cascade. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2013; 63:S44–S48.
11. Meade CS, Sikkema KJ. HIV risk behavior among adults with severe mental illness: A systematic review. *Clinical Psychology Review*. Jun; 2005 25(4):433–457. [PubMed: 15914265]
12. Susser E, Valencia E, Conover S. Prevalence of HIV-infection among psychiatric patients in a New York City men's Shelter. *American Journal of Public Health*. Apr; 1993 83(4):568–570. [PubMed: 8460736]
13. Silberstein C, Galanter M, Marmor M, Lifshutz H, Krasinski K, Franco H. HIV-1 AMONG INNER-CITY DUALY DIAGNOSED INPATIENTS. *American Journal of Drug and Alcohol Abuse*. 1994; 20(1):101–113. [PubMed: 8192129]
14. Rosenberg SD, Goodman LA, Osher FC, et al. Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness. *American Journal of Public Health*. Jan; 2001 91(1):31–37. [PubMed: 11189820]
15. Cournos F, McKinnon K. HIV seroprevalence among people with severe mental illness in the United States: A critical review. *Clinical Psychology Review*. 1997; 17(3):259–269. [PubMed: 9160176]
16. Rothbard AB, Blank MB, Staab JP, et al. Previously Undetected Metabolic Syndromes and Infectious Diseases Among Psychiatric Inpatients. *Psychiatric services*. 2009; 60(4):534–537. [PubMed: 19339330]
17. Kessler RC, Birnbaum H, Demler O, et al. Prevalence and correlates of nonaffective psychosis: Results from NCS-R. *Biological Psychiatry*. Apr 15; 2005 57(8):108S–109S.
18. Lopes M, Olfson M, Rabkin J, et al. Gender, HIV status, and psychiatric disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *The Journal of clinical psychiatry*. 2012; 73(3):384–391. The prevalence of 12-month psychiatric disorders among HIV-positive and HIV-negative adults was stratified by sex to examine the differential increase in risk of a psychiatric disorder as a function of the interaction of sex and HIV status using the National Epidemiologic Survey on Alcohol and Related Conditions Wave 2. HIV-positive men were more likely than HIV-negative men to have any mood disorder, major depressive disorder/dysthymia, any anxiety disorder, and any personality disorder. The same comparisons were not significant in comparisons of HIV positive and HIV negative women. [PubMed: 22053858]
19. association Ap. Practice guideline for the treatment of patients with HIV/AIDS. *American Psychiatric Pub*; 2000.
20. Freudenreich O, Goforth HW, Cozza KL, et al. Psychiatric treatment of persons with HIV/AIDS: an HIV-psychiatry consensus survey of current practices. *Psychosomatics*. 2010; 51(6):480–488. 159 members of the Organization of AIDS Psychiatry (OAP) participated in a web-based survey to determine consensus on current treatment trends in AIDS psychiatry. With a response rate of only 39% (n=69), findings should be carefully considered but promising trends in agreement were observed for first-line treatment for depression (escitalopram/citalopram), for psychosis and secondary mania (quetiapine), and for anxiety (clonazepam). [PubMed: 21051679]
21. Himelhoch S, Powe NR, Breakey W, Gebo KA. Schizophrenia, AIDS and the decision to prescribe HAART: results of a national survey of HIV clinicians. *J Prev Interv Community*. 2007; 33(1/2): 109–120. [PubMed: 17298934]

22. Cohen MA, Forstein M. A Biopsychosocial Approach to HIV/AIDS Education for Psychiatry Residents. *Academic Psychiatry*. 2012; 36(6):479–486. This article discusses the importance of HIV/AIDS training for psychiatry residents and proposes an HIV/AIDS curriculum using a biopsychosocial approach that can be integrated into the standard 4 year residency training programs. [PubMed: 23154699]
23. Simoni JM, Safren SA, Manhart LE, et al. Challenges in addressing depression in HIV research: assessment, cultural context, and methods. *AIDS and behavior*. 2011; 15(2):376–388. Depression, as a common co-morbidity of HIV infection is associated with reduced quality of life and poor health outcomes. This paper reviews diagnostic, screening, and symptom-rating measures of depression and includes a discussion of cross-cultural measurement issues. [PubMed: 21046221]
- *24. Gonzalez JS, Batchelder AW, Psaros C, Safren SA. Depression and HIV/AIDS treatment nonadherence: a review and meta-analysis. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2011; 58(2):181–187. A meta-analysis of 95 independent samples was conducted of the relationship between depression and HIV medication nonadherence in order to evaluate the overall effect size and examine potential methodological and measurement moderators. Depression was significantly associated with nonadherence, with larger effects for studies that collected data via interviews versus self-administered questionnaires and when considered along a continuum rather than as a dichotomous variable. No relationship was observed for assessment interval (ie, cross-sectional vs. longitudinal), sex, IV drug use, sexual orientation, clinical severity, or study location. Depression, even at subclinical levels, should be included within HIV behavioral interventions.
25. Kessler RC, Birnbaum H, Bromet E, Hwang I, Sampson N, Shahly V. Age differences in major depression: results from the National Comorbidity Survey Replication (NCS-R). *Psychological medicine*. 2010; 12(2):225. [PubMed: 19531277]
26. Kalichman, SC. *HIV Treatments as Prevention (TasP): Primer for Behavior-based Implementation*. Springer; 2013.
27. Rabkin JG, McElhiney MC, Ferrando SJ. Mood and substance use disorders in older adults with HIV/AIDS: methodological issues and preliminary evidence. *Aids*. 2004; 18:43–48.
28. Smith RD, Delpech VC, Brown AE, Rice BD. HIV transmission and high rates of late diagnoses among adults aged 50 years and over. *Aids*. 2010; 24(13):2109–2115. [PubMed: 20616697]
- *29. Carrico AW, Bangsberg DR, Weiser SD, Chartier M, Dilworth SE, Riley ED. Psychiatric correlates of HAART utilization and viral load among HIV-positive impoverished persons. *AIDS (London, England)*. 2011; 25(8):1113. A cross-sectional community-recruited study of 227 HIV-positive homeless or marginally homeless participants examined psychiatric correlates of highly active antiretroviral therapy utilization and viral load. Investigators reported a diagnosis of severe mental illness (SMI) was independently associated with higher viral load than those without an SMI diagnosis. Authors emphasize the importance of ‘test and treat’ among homeless SMI/HIV positives.
30. Carrico AW, Riley ED, Johnson MO, et al. Psychiatric risk factors for HIV disease progression: The role of inconsistent patterns of anti-retroviral therapy utilization. *Journal of acquired immune deficiency syndromes (1999)*. 2011; 56(2):146. Outcome data from 603 participants randomized to a behavioral intervention examined whether inconsistent patterns of ART utilization partially mediated the effects of depression and substance use on higher HIV viral load over a 25-month follow-up. Elevated affective symptoms of depression independently predicted ART discontinuation, and use of stimulants at least weekly independently predicted intermittent ART utilization. After controlling for the average self-reported percentage of ART doses taken and baseline T-helper (CD4+) count, elevated depressive symptoms predicted a 50% higher mean viral load, and weekly stimulant use predicted a 137% higher mean viral load. These effects became non-significant after accounting for inconsistent patterns of ART utilization, providing evidence of partial mediation. Inconsistent patterns of ART utilization may partially explain the effects of depression and stimulant use on hastened HIV disease progression. [PubMed: 21116186]
- *31. Himelhoch S, Medoff D, Maxfield J, et al. Telephone Based Cognitive Behavioral Therapy Targeting Major Depression Among Urban Dwelling, Low Income People Living with HIV/AIDS: Results of a Randomized Controlled Trial. *AIDS and behavior*. 2013:1–9. A manualized telephone based cognitive behavioral therapy (T-CBT) intervention was compared to face-to-face therapy among 34 low-income, urban dwelling HIV infected depressed participants of a pilot

randomized controlled trial, with reduced depression a primary outcome., and medication adherence as secondary outcome. No between group differences were observed with participants in both groups displaying reductions in depressive symptoms. Participants in the T-CBT group displayed better treatment adherence. Study suggests the potential for T-CBT as an alternative to f2f treatment. [PubMed: 23054037]

32. de Sousa Gurgel W, da Silva Carneiro AH, Barreto Rebouças D, et al. Prevalence of bipolar disorder in a HIV-infected outpatient population. *AIDS care*. 2013;1–5. (ahead-of-print). Prevalence of bipolar disorder (BD) was assessed among 196 HIV-infected adult Brazilian outpatients. Mood Disorder was found in 13.2% (N=26) and the Bipolar Disorder was confirmed in 8.1% (N=16) of the sample, a BD prevalence almost four times higher among the HIV-infected than in the general USA population. The most common psychiatric comorbidity in the BD group was substance abuse (61.5%). [PubMed: 22568569]
33. Meade CS, Bevilacqua LA, Key MD. Bipolar Disorder is Associated with HIV Transmission Risk Behavior Among Patients in Treatment for HIV. *AIDS and behavior*. 2012; 16(8):2267–2271. HIV transmission risk behavior was examined among 63 patients with bipolar disorder (BD), major depressive disorder, and no mood disorder; half had substance use disorders (SUDs). BD patients displayed highest risk behaviors relative to the other groups and poorest treatment adherence. [PubMed: 22614744]
34. Chander G, Himelhoch S, Moore RD. Substance abuse and psychiatric disorders in HIV-positive patients. *Drugs*. 2006; 66(6):769–789. [PubMed: 16706551]
35. Tsao JC, Dobalian A, Moreau C, Dobalian K. Stability of anxiety and depression in a national sample of adults with human immunodeficiency virus. *The Journal of nervous and mental disease*. 2004; 192(2):111–118. [PubMed: 14770055]
36. Vitiello B, Burnam MA, Bing EG, Beckman R, Shapiro MF. Use of psychotropic medications among HIV-infected patients in the United States. *American Journal of Psychiatry*. 2003; 160(3): 547–554. [PubMed: 12611837]
37. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. POSTTRAUMATIC-STRESS-DISORDER IN THE NATIONAL COMORBIDITY SURVEY. *Archives of General Psychiatry*. Dec; 1995 52(12):1048–1060. [PubMed: 7492257]
- *38. Martin L, Kagee A. Lifetime and HIV-Related PTSD Among Persons Recently Diagnosed with HIV. *Aids and Behavior*. Jan; 2011 15(1):125–131. Eight-five recently diagnosed HIV-positive patients in the Western Cape, South Africa participated in a cross-sectional study of lifetime rates of PTSD and HIV-related PTSD, resulting in a lifetime rate for PTSD of 54.1% and HIV-related PTSD of 40%. This demonstrates the degree of stress associated with an HIV diagnosis, and highlights the importance of considering the individual's psychological preparation for positive test results. [PubMed: 19082880]
39. Himelhoch S, Medoff DR. Efficacy of antidepressant medication among HIV-positive individuals with depression: A systematic review and meta-analysis. *Aids Patient Care and Stds*. Dec; 2005 19(12):813–822. [PubMed: 16375613]
40. Foa EB, Hembree EA, Cahill SP, et al. Randomized trial of prolonged exposure for posttraumatic stress disorder with and without cognitive restructuring: Outcome at academic and community clinics. *Journal of Consulting and Clinical Psychology*. Oct; 2005 73(5):953–964. [PubMed: 16287395]
41. Benton T, Blume J, Dube B. Treatment considerations for psychiatric syndromes associated with HIV Infection. *Future Medicine*. 2010; 4(2):231–245.
42. Rummel-Kluge C, Komossa K, Schwarz S, et al. Head-to-head comparisons of metabolic side effects of second generation antipsychotics in the treatment of schizophrenia: a systematic review and meta-analysis. *Schizophrenia research*. 2010; 123(2):225–233. [PubMed: 20692814]
43. Allison DB, Newcomer JW, Dunn AL, et al. Obesity among those with mental disorders: a National Institute of Mental Health meeting report. *American journal of preventive medicine*. 2009; 36(4):341–350. [PubMed: 19285199]
44. Walkup J, Blank MB, Gonzalez JS, et al. The impact of mental health and substance abuse factors on HIV prevention and treatment. *Jaids-Journal of Acquired Immune Deficiency Syndromes*. 2008; 47:S15–S19.

- *45. Wu ES, Rothbard A, Blank MB. Using Psychiatric Symptomatology to Assess Risk for HIV Infection in Individuals with Severe Mental Illness. *Community Mental Health Journal*. Dec; 2011 47(6):672–678. The Colorado Symptom Index (CSI) was used to identify vulnerable subgroups within the severely mentally ill population at elevated risk for HIV infection. Baseline data on 228 HIV positive and 281 HIV negative participants from two clinical trials, years to HIV diagnosis served as the primary endpoint. A CSI score ≥ 30 was associated with a 47% increased risk for HIV infection ($P < 0.01$). This study establishes the foundation for using CSI scores to identify a vulnerable subgroup within the SMI community. Further studies should develop effective approaches to mitigate psychiatric symptomatology in order to examine the impact on HIV transmission risky behaviors. [PubMed: 21479681]
46. Dévieux JG, Malow R, Lerner BG, et al. Triple jeopardy for HIV: substance using severely mentally ill adults. *Journal of prevention & intervention in the community*. 2007; 33(1–2):5–18. [PubMed: 17298927]
- *47. Prince JD, Walkup J, Akincigil A, Amin S, Crystal S. Serious mental illness and risk of new HIV/AIDS diagnoses: an analysis of Medicaid beneficiaries in eight states. *Psychiatric services*. 2012; 63(10):1032–1038. Medicaid claims data in 5 states was linked to compare the influence of substance abuse, HIV and mood disorder to identify risk factors for psychiatric hospitalization and early readmission within 3 months of discharge. Logistic and Cox regression revealed 24% of beneficiaries ($N=129,524$) with mood disorder were hospitalized, and 24% of that group were re-hospitalized within the 3 month review period. The addition of substance abuse accounted for 36% of initial hospitalizations and 50% of readmissions. Comorbid disorders should be treated within a multi-discipline partnership between mental health, infectious disease, and substance abuse professionals. [PubMed: 22855268]
- *48. Cournois F, Guimarães MD, Wainberg ML. HIV/AIDS and Serious Mental Illness: A Risky Conclusion. *Psychiatric services*. 2012; 63(12):1261–1261. Authors provide a counter-argument to the Prince, Walkup, Akincigil et al 2013 *Psychiatric Services* paper which concluded that “for their sample “a severe mental illness diagnosis in the absence of a substance abuse diagnosis was not highly associated with increased risk of a new HIV/AIDS diagnosis””. Authors point to the lack of full data and inadequate analyses, as well as to the difficulty of focusing on one diagnostic category to the exclusion of others, when substance abuse and mental illnesses are often inextricably related. [PubMed: 23203364]
49. Lee AK, Hanrahan NP, Aiken LH, Blank MB. Perceived facilitators and barriers to the implementation of an advanced practice: nursing intervention for HIV regimen adherence among the seriously mentally ill. *Journal of psychiatric and mental health nursing*. 2006; 13(5):626–628. [PubMed: 16965484]
- *50. Hanrahan NP, Wu E, Kelly D, Aiken LH, Blank MB. Randomized Clinical Trial of the Effectiveness of a Home-Based Advanced Practice Psychiatric Nurse Intervention: Outcomes for Individuals with Serious Mental Illness and HIV. *Nursing research and practice*. 2011; 2011 Two-hundred and thirty-eight community-dwelling individuals with HIV and serious mental illness (SMI) were randomly assigned either to an intervention group that received care management from an advanced practice psychiatric nurse or to a control group that received treatment as usual. Those in the intervention group demonstrated reductions in depression and improvements in the physical component of health-related quality of life, highlighting the promise of using advanced practice psychiatric nurses to improve quality of care and outcomes for complex patients.
51. Collins L, Murphy S, Bierman K. A Conceptual Framework for Adaptive Preventive Interventions. *Prevention Science*. Sep 01; 2004 5(3):185–196. [PubMed: 15470938]
- *52. Blank M, Hennessy M, Eisenberg M. Increasing Quality of Life and Reducing HIV Burden: The PATH+ Intervention. *AIDS & Behavior*. in press. The heightened risk of persons with a serious mental illness (SMI) to contract and transmit human immunodeficiency virus is a public health problem. In order to test the effectiveness of a community-based advanced practice nurses intervention to promote adherence to HIV and psychiatric treatment regimens, 238 HIV-positive participants who also were in treatment for a serious mental illness were randomized to a nurse led intervention, Preventing AIDS Through Health for Positives (PATH+), or treatment-as-usual. The study examined viral load and CD4 count at baseline, 12 and 24 months, and health-related quality of life measures (SF-12 Mental and Physical Health) at baseline, 3, 6, 12, and 24 months.

Participants were followed for 12 months after PATH ended in order to examine any radiating effects of decay of the intervention. Latent growth curve model using three data points for biomarkers (baseline, 12 & 24 months) and five data points for health related quality of life (baseline, 3, 6, 12, & 24 months) shows moderate to excellent fit for modeling changes in CD4, viral load, and mental SF-12 subscales. This project demonstrates the effectiveness of PATH+ and its community-based, individually-tailored intervention cascade, to improve outcomes of individuals with HIV/SMI. With appropriate support, persons with SMI and HIV can successfully adhere to treatment and achieve improvements in health-related quality of life and biomarker health status indicators.