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The Association of Major Depression and Selected Health Behaviors among HIV-positive Adults Receiving Medical Care in Georgia: Findings from the Georgia Medical Monitoring Project, 2009-2012

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THE ASSOCIATION OF MAJOR DEPRESSION AND SELECTED HEALTH BEHAVIORS AMONG HIV-POSITIVE ADULTS RECEIVING MEDICAL CARE IN GEORGIA: FINDINGS FROM THE MEDICAL MONITORING PROJECT, 2009-2012

BY

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2. Maggio D, **Culbreth R,** Spears N, Kelly J, Drenzek C. Stigma and Discrimination through the Eyes of Women Living with HIV: An analysis from Georgia MMP data. Center for AIDS Research (CFAR) Networking Meeting: Emory University Rollins School of Public Health. Atlanta, Georgia 2014.
3. **Culbreth R**, Kelly J, Maggio D, Murphy-Hoefer R, Drenzek C. Surviving HIV and dying for a smoke: Implications of tobacco use among people living with HIV. Scientific Retreat on Tobacco Related Research. Charleston, South Carolina 2014.
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Abstract

Introduction:

Currently there are approximately 1.2 million people in the United States living with HIV and it is estimated that 25.6% of HIV-positive adults suffer from depression. The purpose of this study is to examine the contribution of depression on substance use and medication adherence specifically among HIV-positive adult Georgians receiving medical care for HIV.

Methods:

Secondary data with a probability sample of 608 HIV-positive adults who took part in the 2009-2012 Georgia Medical Monitoring Project (MMP) were analyzed. Descriptive analysis and multivariate logistic regression models were conducted to assess relationships between depression with current cigarette smoking, injection drug use, other non-injection drug use, and medication adherence, adjusting for sociodemographic covariates (age, gender, race, and education). All analyses accounted for non-response and complex sampling design and were performed using SAS 9.2 (Cary, NC).

Results:

Among HIV-positive adults in Georgia, approximately 9.2% met the criteria for major depression; 15.2% of women and 6.9% of men had major depression. Heterosexual adults also had a higher percentage of major depression (11.9%) compared to adults who identified as bisexual (8.3%) or homosexual (6.1%). Major depression was also highest among young adults (17.1%) and adults with high school diploma or GED (13.0%). Major depression was associated with a greater odds of current cigarette smoking (3.04; 95% CI: 1.48, 6.23); injection drug use (5.62; 95% CI: 0.96, 32.81), and other non-injection drug use (2.17; 95% CI: 1.10, 4.25), after adjusting for sociodemographic variables. Major depression was also associated with a greater odds of ART medication non-adherence, 2.52 (95% CI: 1.20, 5.28), after adjusting for gender.

Conclusion:

As previously found in the general population, we found significant associations between depression and smoking and other non-injection drug use among HIV-positive adults. Major depression was also associated with a greater odds of ART medication non-adherence, which is also consistent with the literature. Because HIV-positive adults have ongoing encounters with healthcare providers, screening and treatment for depression and other co-morbid substance use is needed to reduce an additional health burden in this population.

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CHAPTER I: Introduction

1.1 Background

Approximately 1.2 million people within the United States are currently living with Human Immunodeficiency Virus (HIV), and nearly 14% are not aware of their HIV infection ("CDC - HIV/AIDS"). The CDC estimates 50,000 new HIV infections each year ("CDC - HIV/AIDS"). According to the Georgia Department of Public Health HIV/AIDS Epidemiology Section, approximately 50, 436 people were living with HIV in Georgia as of December 31, 2012 (*The Georgia Department of Public Health Fact Sheet: HIV Surveillance, Georgia, 2012*). Georgia has the sixth highest HIV prevalence among adults and adolescents in the United States, and Georgia ranked fourth highest in the United States for new HIV infections in 2011 (*The Georgia Department of Public Health Fact Sheet: HIV Surveillance, Georgia, 2012*).

If left untreated, HIV leads to acquired immunodeficiency syndrome (AIDS). HIV impairs the immune system by destroying CD4 cells. HIV is classified into three stages which are measured by CD4 counts. Stage three is when CD4 levels are the lowest, classified as AIDS. Although there is no cure at this time, treatment with antiretroviral therapy (ART) is highly effective at improving the quality and longevity of life among people living with HIV. ART lowers a person's viral load and decreases the risk of transmission (*The Georgia Department of Public Health Fact Sheet: HIV Surveillance, Georgia, 2012*).

Adults with HIV experience multiple comorbid social, behavioral, physical, and mental health problems. For example, adults with HIV may deal with stigma and discrimination, and this may lead to chronic stress and substance use. Adults with HIV also may engage in more risk taking behaviors such as unprotected sex or needle-sharing injection drug use, and because many persons may not know they are infected, risk taking behaviors by persons with HIV may further increase the likelihood of spreading the virus.

While individuals living with HIV are living longer lives compared to the era before ART, complications and barriers still exist linking and retaining individuals with HIV to treatment and care. Specific comorbidities are common to people living with HIV. Mental illness, specifically depression, disproportionately affects this population. The presence of depression among HIV-positive adults is strongly suspected to be a barrier to accessing and remaining in care.

1.2 Purpose of the study

The purpose of this study is to examine the association of major depression with current cigarette smoking, injection drug use, other non-injection drug use, and medication adherence, among adults in Georgia receiving medical care for HIV infection using the Georgia Medical Monitoring Project Data, 2009-2012.

1.3 Hypotheses

The four null hypotheses will be tested using multivariate logistic regression: (1) Among adults residing in Georgia living with HIV, major depression will have no association with current cigarette smoking, (2) Among adults residing in Georgia living with HIV, major depression will have no association with injection drug use, (3) Among adults residing in Georgia living with HIV, major depression will have no association with other

non-injection drug use, and (4) Among adults residing in Georgia living with HIV, major depression will have no association with ART medication adherence.

CHAPTER II: Literature Review

2.1 Epidemiology of HIV

Approximately 1.2 million people within the United States are currently living with Human Immunodeficiency Virus (HIV) ("CDC - HIV/AIDS"). Currently, African Americans are most affected by HIV in the United States. African American's rate of infection is nearly 8 times compared to whites ("CDC - HIV/AIDS"). African Americans also have a higher proportion of new HIV infections, a higher prevalence of HIV infections, and a higher proportion of persons ever diagnosed with AIDS ("CDC - HIV/AIDS"). An estimated 44% of all new HIV infections among individuals 13 or older were African Americans, and among those, an estimated 70% were men. More new HIV infections were among African American men who have sex with men, ages 13 to 24, than other men who have sex with men ("CDC - HIV/AIDS").

In the United States, 75% of all adults living with HIV were men, and the majority of those individuals were men who have sex with men ("CDC - HIV/AIDS"). Among women, most new HIV infections are from heterosexual contact ("CDC - HIV/AIDS"). As with men, African American women are disproportionately affected by HIV compared to other races; nearly 64% of HIV-positive women are African American. Also, women overall are not receiving adequate care for their HIV in the United States. Only 45% of HIV-positive women were retained in care ("CDC - HIV/AIDS").

Similar trends are observed in Georgia compared to national HIV epidemiology. According to the Georgia Department of Public Health HIV/AIDS Epidemiology Section, approximately 50, 436 people were living with HIV in Georgia as of December

31, 2012 (*The Georgia Department of Public Health Fact Sheet: HIV Surveillance, Georgia, 2012*). Georgia has the sixth highest HIV prevalence among adults and adolescents in the United States, and Georgia ranked fourth highest in the United States for new HIV infections in 2011 (*The Georgia Department of Public Health Fact Sheet: HIV Surveillance, Georgia, 2012*). Men account for 78% of new HIV infections, and 55% of all new HIV infections were African American.

2.2 Epidemiology of Depression among Adults in the U.S. Population

During 2009-2011, an annual average of 19.9% of adults had a mental illness, including individuals with depression, schizophrenia, and bipolar disorders (Centers for Disease Control and Prevention (CDC), 2013). Among these individuals, the highest proportion of mental illness was among adults ages 18 to 24 and among women. An estimated 23.4% (95% CI, 22.9-23.9) of women had a mental illness compared with 16.1% (95% CI, 15.7-16.6) of men (Centers for Disease Control and Prevention (CDC), 2013). The median state percentage of adults with any mental illness was 20.4%, and Georgia had a 17.2% percentage of adults with a mental illness (Centers for Disease Control and Prevention (CDC), 2013). A recent examination of NHANES 2009-2010 revealed that the prevalence of depressive symptoms among adults ages 18 and older was 25.7% (Wittayanukorn, Qian, & Hansen, 2014). Among the 25.7% experiencing depressive symptoms, 36.6% were classified as having moderate to severe depression (Wittayanukorn et al., 2014). Furthermore, among those classified as having moderate to severe depression, only 38.7% were receiving antidepressant medication or seeing a mental health professional (Wittayanukorn et al., 2014).

Major depressive disorder, as defined by the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (DSM-IV), includes experiencing five or more depressive symptoms (American Psychiatric Association, 2000). These symptoms can include feeling sad or empty, diminished interest in activities, significant weight loss, insomnia or hypersomnia, psychomotor agitation, fatigue, feelings of worthlessness, and an inability to concentrate (American Psychiatric Association, 2013).

There are multiple scales and instruments currently used to assess depression among the adult population. The Patient Health Questionnaire (PHQ-9) is one such instrument, which has become an increasingly popular tool in surveillance systems to assess the 9 criteria for depression as defined by the DSM-IV (American Psychiatric Association, 2000; K. Kroenke, Spitzer, & Williams, 2001). Recently, a PHQ-8 became available that consisted of an 8-item version of the PHQ-9 (Kurt Kroenke et al., 2009). PHQ-8 has demonstrated strong validity and reliability as a measure to assess current depression (Kurt Kroenke et al., 2009).

2.3 Depression among Adults living with HIV

Among HIV-infected individuals, depression is the most common neuropsychiatric disorder that affects these individuals (Nanni, Caruso, Mitchell, Meggiolaro, & Grassi, 2015). The prevalence of depression among HIV-infected individuals is anywhere between 18 and 81 percent (Arseniou, Arvaniti, & Samakouri, 2014). Depression also disproportionately affects HIV-positive individuals compared to HIV-negative individuals (Bing et al., 2001). Using the National Medical Monitoring Project (MMP) and the Behavioral Risk Factor Surveillance System (BRFSS), the prevalence of any depression among HIV-positive adults in care was 25.6% (95% CI:

23.8%-27.4%) compared to 9.1% (95% CI: 8.9%-9.4%) of adults in the general population who had any depression (Do et al., 2014). An estimated 12.4% (95% CI: 11.2%, 13.7%) of HIV-positive adults had major depression compared to 4.1% (95% CI: 3.9%, 4.2%) who had major depression in the general population (Do et al., 2014). This estimate of 25.6% of HIV-positive adults with any depression is also higher than the estimated 19.9% of adults in the general population who had a mental illness (Centers for Disease Control and Prevention (CDC), 2013). Compared to the general population, HIV positive persons are between two and seven times more likely to be diagnosed with major depression (Hinkin, Castellon, Atkinson, & Goodkin, 2001; Do et al., 2014). Depression among people living with HIV is known to have an effect on several health outcomes and health behaviors (Arseniou et al., 2014).

The relationship between depression and HIV infection is complicated, and the directionality of causation is often unclear. Depression does not only frequently occur after HIV diagnosis, but depression can be a risk factor for HIV transmission (Nanni et al., 2015). Adults with severe mental illness (SMI), including those with depression, are more likely to engage in risky sexual behavior or use injection drugs, therefore increasing HIV transmission risk (Meade & Sikkema, 2005). In the study by Do et al., adults who engaged in one or more HIV risk behaviors had a depression prevalence twice the depression prevalence of adults who did not engage in HIV risk behaviors (2014).

Biological Etiologies of Depression among persons living with HIV

Depression also frequently occurs after HIV diagnosis. Depression within the HIV-positive population has several etiologies, including biological and psychosocial factors (Arseniou et al., 2014). HIV infection may play a role in secondary depression by

altering biological elements within the brain, leading to depression. One indication that the HIV virus has infected the central nervous system is the presence of neurocognitive defects, which also may potentially cause depression (Gibbie et al., 2006). HIV infection has been linked to alterations of neural networks and white matter structure, alterations of brain morphology, somatostatin dysregulation, and tryptophan degradation (Gibbie et al., 2006). Several studies have examined brain structure alterations among HIV-negative individuals with major depression, and they have found several brain structures actually morph over time (Milak et al., 2005; Sheline, 2000). These certain brain structures, including basal ganglia, orbitofrontal cortex, and neural networks, are also vulnerable to HIV infection, which may cause secondary depression (Arseniou et al., 2014). Long-term studies are needed to further examine this relationship, but there is evidence linking HIV infection and depression within the brain structures.

Another biological mechanism that has been hypothesized as linking HIV infection to depression is hypothalamus-pituitary-thyroid (HPT) dysfunction (Arseniou et al., 2014). HPT dysfunction, among the HIV-negative population, is known to cause depression, along with mood disorders and dementia. HIV infection of the CNS may alter hypothalamus and thyroid communication; therefore, HIV infection of the CNS may cause depression through this mechanism (Langford, Baron, Joy, Del Valle, & Shack, 2011).

Psychosocial Etiologies of Depression among persons living with HIV

Apart from the biological factors explaining depression diagnoses post-HIV infection, psychosocial factors among HIV-positive adults also contribute to the depression etiology in this population. Among the general population, people who are

newly diagnosed with a chronic illness or disease exhibit elevated levels of depression (DeJean, Giacomini, Vanstone, & Brundisini, 2013). Among HIV positive individuals, changes in social support structure and body image, perceived stigma, and occupational disability contribute to an increase risk of depression (Olatunji, Mimiaga, O'Cleirigh, & Safren, 2006). Among a study assessing the emotions of newly diagnosed men and women in the San Francisco area, a qualitative analysis revealed several common themes about initial diagnosis, including concerns about dying, stigma, and a threat to identity (Moskowitz, Wrubel, Hult, Maurer, & Acree, 2013).

Depression's Impact on the Progression of HIV

Depression is not only harmful to individuals living with HIV and their sense of well-being, but one study revealed depressive symptoms were associated with a quicker development of an AIDS condition compared to individuals without depressive symptoms (J. Leserman et al., 2002). This rapid progression can be due to a variety of factors, including individuals with depressive symptoms adhering less to HIV medication regimen than individuals without depressive symptoms (Soller et al., 2011). Chronic depression, as well as stressful events and trauma, may negatively influence disease progression by decreasing CD4 T lymphocytes and increasing risk for mortality (Leserman, 2003; Leserman, 2008). The extent of this relationship of depression to biomarkers still needs to be explored; depression may influence psychosocial and behavioral risk factors, which subsequently influence an increase in viral load or decrease in CD4 T lymphocytes (Schuster, Bornovalova, & Hunt, 2012).

Early studies revealed depression has a substantial influence on the immune system. In addition to the influences of depression on the progression of HIV disease, this

is further worsened by depression's negative influence on the production of cytotoxic lymphocytes (Herbert & Cohen, 1993). Hyperactivity of the HPA axis, which results from major depression, increases glucocorticoid circulation (Pariante & Lightman, 2008). Glucocorticoids have an effect on the production of interleukins and interferons, which have a direct impact on lymphocytes' mechanism of fighting infectious agents (Schuster et al., 2012).

In addition to these studies, other researchers sought to evaluate depression's effect on the immune system in patients on antiretroviral therapy. A small study in Italy revealed a significant difference in the number of natural killer cells between depressed individuals and non-depressed individuals (Alciati, Gallo, Monforte, Brambilla, & Mellado, 2007). These participants were all receiving antiretroviral therapy.

2.4 Depression and Cigarette Smoking among Adults living with HIV

The association between depression and cigarette smoking among the general population

Among the general United States adult population, a strong relationship between mental illness and tobacco use exists in the general U.S. adult population and also across US states (Dube et al., 2009; McClave et al., 2009). During 2009-2011, a yearly average of 19.9% of adults ages 18 and older were living with a mental illness, and among these adults, 36.1% were current smokers (Centers for Disease Control and Prevention (CDC), 2013). Among the general adult population ages 18 and older, 21.4% of adults are current smokers, substantially lower than the smoking prevalence among those living with a mental illness (Centers for Disease Control and Prevention (CDC), 2013). Among Georgians, an estimated 24% (95% CI, 18.8-30.1) of adults with a mental illness smoke. Potential reasons for the association between mental illness and tobacco use is the

psychoactive properties of nicotine, which may help to ameliorate negative affective states that are symptoms of many types of mental illnesses, including major depression (McClave, McKnight-Eily, Davis, & Dube, 2010; Strine et al., 2012; Trosclair & Dube, 2010).

Depression and cigarette smoking among persons living with HIV

While mental illnesses, including depression, have a known association with cigarette smoking, the general adult population living with HIV also experience a higher smoking prevalence compared to the general adult population in the United States (Browning, Wewers, Ferketich, & Diaz, 2013; Centers for Disease Control and Prevention (CDC),"BRFSS," 2013). Studies have reported smoking prevalence in the range of 40-70% among persons living with HIV, compared to the general population smoking prevalence of 21.4% (Centers for Disease Control and Prevention (CDC), 2013). In 2013, the Behavioral Risk Factor Surveillance System (BRFSS) estimated only 17.8% of adults are current smokers, a decrease from the previous estimate of 21.4% (Centers for Disease Control and Prevention (CDC),"BRFSS," 2013). Mdodo et al, 2015 examined smoking prevalence and quit ratios among HIV adults in care who participated in the Medical Monitoring Project compared to adults who participated in the National Health Interview Survey in 2009 (2015). Smoking prevalence among adults was 42.4% (95% CI, 39.7% to 45.1%) compared to 20.6% of adults in the general population (Mdodo et al., 2015). Adults living with HIV were nearly twice as likely to smoke, and less likely to quit smoking (quit ratio, 32.4% vs. 51.7%) (Mdodo et al., 2015). Adults living with HIV are disproportionately affected by cigarette smoking compared to the general adult population.

Depression may be a factor in the high cigarette smoking prevalence observed in people living with HIV (Browning et al., 2013). Due to the high proportion of depression among HIV-positive individuals, smoking may in fact help to mitigate the effects of depression, as seen in the general adult population (Burkhalter, Springer, Chhabra, Ostroff, & Rapkin, 2005). HIV-positive individuals that currently smoke also have lower quit rates compared to the general adult population, and a high prevalence of depression may impact quit attempts (Burkhalter et al., 2005).

Shuter, Bernstein, and Moadel examined smoking behaviors and beliefs among persons living with HIV (2012). These individuals were receiving care, and most of the individuals explained that cigarette smoking helped them cope with anger, depression, or anxiety (Shuter et al., 2012). Among these participants, 73.3% stated they were currently depressed or experienced depression in the past (Shuter et al., 2012).

The increased burden of cigarette smoking among persons living with HIV

Cigarette smoking increases risk for diseases for HIV-positive smokers, including cardiovascular disease, pneumonia, lung cancer, and liver cancer (Helleberg et al., 2013). HIV-positive smokers are more susceptible to develop chronic obstructive pulmonary disorder (COPD) compared to smokers in the general population (Crothers et al., 2006). One study revealed liver cancer risk is synergistically increased by HIV infection and current tobacco use (Helleberg et al., 2013). The authors also reported a substantial increase in mortality among HIV-positive smokers compared to HIV-infected non-smokers (Helleberg et al., 2013). In another study, Helleberg, et al, examined associations between smoking and mortality among individuals in care with more than one year after initiation on antiretroviral therapy (ART), excluding injection drug users (Helleberg et

al., 2015). The mortality rate ratio (MRR) which compared HIV-infected smokers with HIV-infected nonsmokers was 1.94 (95% CI 1.56-2.41). HIV-positive smokers also experienced a higher mortality from cardiovascular disease [MRR 6.28 (95% CI 2.19-18.0)] (Helleberg et al., 2015). The loss life-years associated with smoking was 7.9 (95% CI 7.1-8.7) (Helleberg et al., 2015).

2.5 Depression and Substance Use among Adults living with HIV

Previous research has demonstrated a relationship between depression and substance use in persons living with HIV. Studies have estimated between 10% and 28% of persons living with HIV have co-occurring substance use disorders and mental illness disorders, including depression (Burnam et al., 2001; Dausey & Desai, 2003). A national study that utilized a probability sample of HIV-positive individuals in care revealed that drug dependence was independently associated with a number of factors, including screening positive for a psychiatric disorder, including depression (Bing et al., 2001). Berger-Greenstein et al. estimated a 72% prevalence of depression among HIV-positive substance users in a low-income, urban setting (2007). Depression and substance use disorders are also related to low medication adherence, essentially creating a complicated mechanism of disease progression (Magidson et al., 2014).

Researchers have also found that depressive symptoms are associated with an increase in risky behaviors, which have an even larger impact on HIV-positive substance users, particularly injection-drug users (Johnson, Rabkin, Lipsitz, Williams, & Remien, 1999). Depressive symptoms have been related to an increase in needle-sharing, which increases both the risk of transmissibility of HIV as well as a new infection of a different strain of HIV to those already infected (Johnson et al., 1999; Berger-Greenstein et al.,

2007). Persons who are infected with more than one strain of HIV have an increased probability of experiencing resistance to antiretroviral medications (Berger-Greenstein et al., 2007).

Although the relationship between depression and substance use has been explored among persons living with HIV, few articles examine the relationship between depression and use of specific drugs, especially non-injection drugs, among persons living with HIV in care. A study which examined co-occurring substance use disorders with psychological distress found the strongest relationship among opioid users (McCabe, Feaster, & Mitrani, 2014). Opioid users had three times the odds of having co-occurring psychological distress (OR=2.75, p=0.035) (McCabe et al., 2014). This article also assessed relationships between psychological distress and use of other substances, including cannabis, alcohol, and sedatives; however, these relationships were not statistically significant (McCabe et al., 2014).

2.6 Depression and HIV Medication Adherence

Depression has been linked to a decrease in HIV medication adherence in more than 95 studies (Gonzalez, Batchelder, Psaros, & Safren, 2011). This meta-analytic review found that across 95 independent samples depression was significantly ($P<0.01$) related to medication non-adherence (r=0.19; 95% CI 0.14-0.25) (Gonzalez et al., 2011). However, contradicting results were found in a study assessing medication adherence among HIV-positive substance users with a mental illness, including those with depression (Berger-Greenstein et al., 2007). The participants were actively receiving care for HIV, and 72.9% of participants had major depression disorder (Berger-Greenstein et al., 2007). The researchers found that participants who reported a high number of

depression symptoms were also likely to report a high rate of medication adherence compared to individuals reporting a smaller number of depression symptoms (Berger-Greenstein et al., 2007). The authors reasoned that depressed individuals are more likely to be concerned with longevity of life and their health, and they are more likely to take their medications. They also proposed that medication adherence could have been falsely reported by these individuals, possibly due to their depression interfering with memory recall or social desirability bias (Berger-Greenstein et al., 2007).

Although many studies have assessed the relationship of depression to HIV medication adherence, articles have revealed inconsistent results. Few articles also explore the relationship between depression and medication adherence among individuals receiving continuous care for HIV (Berger-Greenstein et al., 2007). Other researchers have sought to examine the relationships between depression, non-medication adherence, and other variables.

Medication adherence is measured in a variety of ways. Although medication adherence is measured primarily by self-reported questionnaires or interviews, medication adherence can also be measured by viral load (Bonner, Mezochow, Roberts, Ford, & Cohn, 2013). Most HIV-positive individuals who are adhering to antiretroviral medications are virally suppressed.

2.7 Summary of Literature Review and Gaps

Individuals living with HIV and co-morbid depression experience more adverse health behaviors, such as medication non-adherence, current cigarette smoking, and substance use, compared to individuals living without depression. Untreated depression negatively affects multi-dimensional aspects of life for persons living with HIV.

Abstaining from substance use and cigarette smoking behaviors has been shown to prolong life for this population. Furthermore, adhering to ART medication promotes healthier, longer lives while substantially decreasing the risk of HIV transmission. However, these important behaviors are negatively impacted by depression. Since depression has such a high prevalence in this population compared with the general population, identifying and treating depression has enormous implications for persons living with HIV.

Although a substantial amount of literature exists around depression among persons living with HIV, few studies have consistently evaluated individuals living with HIV who are currently receiving medical care. By analyzing Medical Monitoring Project participants in Georgia, this study can provide a unique perspective of the association of depression on certain health behaviors among individuals currently receiving medical care for HIV. Most studies reviewed have examined the relationship between depression and adverse health outcomes; however, no studies to date have assessed the relationship between depression and adverse health outcomes among HIV-positive adults in Georgia receiving care. The results will inform public health professionals and healthcare providers on the importance of screening and treatment of depression among this population.

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CHAPTER III: Manuscript

THE ASSOCIATION OF MAJOR DEPRESSION AND SELECTED HEALTH BEHAVIORS AMONG HIV-POSITIVE ADULTS RECEIVING MEDICAL CARE IN GEORGIA: FINDINGS FROM THE MEDICAL MONITORING PROJECT, 2009-2012

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Abstract

Introduction:
Currently there are approximately 1.2 million people in the United States living with HIV and it is estimated that 25.6% of HIV-positive adults suffer from depression. The purpose of this study is to examine the contribution of depression on substance use and medication adherence among HIV-positive adults receiving medical care for HIV.

Methods:
Secondary data with a probability sample of 608 HIV-positive adults who took part in the 2009-2012 Georgia Medical Monitoring Project (MMP) were analyzed. Descriptive analysis and multivariate logistic regression models were conducted to assess relationships between depression with current cigarette smoking, injection drug use, other non-injection drug use, and medication adherence, adjusting for sociodemographic covariates (age, gender, race, and education). All analyses accounted for non-response and complex sampling design.

Results:
Among HIV-positive adults in Georgia, approximately 9.2% met the criteria for major depression; 15.2% of women and 6.9% of men had major depression. Heterosexual adults also had a higher percentage of major depression (11.9%) compared to adults who identified as bisexual (8.3%) or homosexual (6.1%). Major depression was also highest among young adults (17.1%) and adults with high school diploma or GED (13.0%). Major depression was associated with a greater odds of current cigarette smoking (3.04; 95% CI: 1.48, 6.23); injection drug use (5.62; 95% CI: 0.96, 32.81), and other non-injection drug use (2.17; 95% CI: 1.10, 4.25), after adjusting for sociodemographic variables. Major depression was also associated with a greater odds of ART medication non-adherence, 2.52 (95% CI: 1.20, 5.28).

Conclusion:
As previously found in the general population, we found significant associations between depression and smoking and other non-injection drug use among HIV-positive adults. Because HIV-positive adults have ongoing encounters with healthcare providers, screening and treatment for depression and other co-morbid substance use is needed to reduce an additional health burden in this population.

Key Words: Depression, substance use, cigarette smoking, antiretroviral medication adherence, HIV, Behavior

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Introduction

Approximately 1.2 million people within the United States are currently living with Human Immunodeficiency Virus (HIV) ("CDC - HIV/AIDS"). According to the Georgia Department of Public Health HIV/AIDS Epidemiology Section, approximately 50, 436 people were living with HIV in Georgia as of December 31, 2012 (*The Georgia Department of Public Health Fact Sheet: HIV Surveillance, Georgia, 2012*). Georgia has the sixth highest HIV prevalence among adults and adolescents in the United States, and Georgia ranked fourth highest in the United States for new HIV infections in 2011 (*The Georgia Department of Public Health Fact Sheet: HIV Surveillance, Georgia, 2012*).

While individuals living with HIV are living longer lives compared to the era before antiretroviral therapy (ART), complications and barriers still exist linking and retaining individuals with HIV to treatment and care. Specific comorbidities are common to people living with HIV. Mental illness, specifically depression, disproportionately affects this population, and depression is strongly suspected to be one barrier to accessing and remaining in care. Among HIV-infected individuals, depression is the most common neuropsychiatric disorder that affects these individuals (Nanni, Caruso, Mitchell, Meggiolaro, & Grassi, 2015). Compared to the general population, HIV positive persons are between two and seven times more likely to be diagnosed with major depression (Hinkin, Castellon, Atkinson, & Goodkin, 2001; Do et al., 2014).

Depression among people living with HIV is known to have an effect on several health outcomes and health behaviors, including medication adherence (Arseniou, Arvaniti, & Samakouri, 2014). Depression has been linked to a decrease in HIV medication adherence in more than 95 studies (Gonzalez, Batchelder, Psaros, & Safren, 2011). However, Berger-Greenstein et al found that participants who reported a high number of depression symptoms were also likely to report a high rate of medication adherence compared to individuals reporting a smaller number of depression symptoms (2007).

Other adverse health behaviors, including cigarette smoking and substance use, have also been associated with depression (McClave, McKnight-Eily, Davis, & Dube, 2010; Strine et al., 2012; Trosclair & Dube, 2010). For example, among persons with any mental illness, 36.1% are current smokers, substantially higher than the general population (CDC, 2013). The psychoactive properties of nicotine in tobacco, may be used to ease symptoms of mental illness, including major depression (McClave et al., 2010; Strine et al., 2012; Trosclair & Dube, 2010). Due to the high proportion of depression among HIV-positive individuals, the nicotine from smoking cigarettes may in fact help to mitigate the effects of depression, as seen in the general adult population (Burkhalter, Springer, Chhabra, Ostroff, & Rapkin, 2005). Adults living with HIV are nearly twice as likely to smoke, and less likely to quit smoking (quit ratio, 32.4% vs. 51.7%) (Mdodo et al., 2015). Substance use also has demonstrated an association with depression, among both the general population and those with HIV. Studies have estimated between 10% and 28% of persons living with HIV have co-occurring substance use disorders and mental illness disorders, including depression (Burnam et al., 2001;

Dausey & Desai, 2003). Depression and substance use disorders are also related to low medication adherence, essentially creating a complicated mechanism of disease progression (Magidson et al., 2014).

The purpose of this study is to examine the excess burden of depression on current cigarette use, injection drug use, non-injection drug use, and ART medication adherence, among adult Georgians receiving medical care for HIV infection using the Georgia Medical Monitoring Project Data, 2009-2012. By analyzing depression's association with these health behaviors, individuals involved in care of HIV-positive persons can determine the importance of screening and treating depression.

Methods

Sample and Data Source

The Georgia Medical Monitoring Project (MMP) is a surveillance system that collects data on behavioral and clinical aspects of persons living with HIV who are currently receiving medical care ("Georgia Medical Monitoring Project (MMP) | Georgia Department of Public Health"). For the purposes of the present study, a secondary analysis was conducted using 2009, 2010, 2011, and 2012 aggregate MMP data. Institutional Review Board at Georgia State University determined the study to be exempt.

MMP consists of a three-stage, probability sampling method, and Georgia is one of 26 states and cities across the United States to participate ("Georgia Medical Monitoring Project (MMP) | Georgia Department of Public Health"). MMP project areas are estimated to include over 80% of the total HIV/AIDS patients in the United States. Interviews are conducted either face-to-face or via phone to ascertain behavioral

information, and medical record abstractions are used to obtain clinical information. To be eligible to participate, individuals were required to be HIV-positive, 18 years of age or older at the time of the interview, and actively receiving medical care for HIV. Data from the Georgia MMP are weighted to produce a representative sample of all adult Georgians receiving medical care for HIV (McNaghten et al., 2007; Blair et al., 2011; Frankel et al., 2012). Once facilities are selected and agree to participate, patient lists are generated and a random sample of 400 Georgia patients are randomly selected. Patient and facility response rates are combined into one response rate to report for each year of MMP. For 2009, the combined response rate was 27.39%, the combined response rate for 2010 was 17.58%, the combined response rate for 2011 was 23.23%, and the combined response rate for 2012 was 34.71%.

Measures

Independent Variables

Depression is measured in MMP using the Eight-Item Patient Health Questionnaire (PHQ-8) (Kurt Kroenke et al., 2009; K. Kroenke, Spitzer, & Williams, 2001). The PHQ-8 was adopted from the PHQ-9, which assesses the nine criteria associated with depression as defined by the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (DSM-IV) (American Psychiatric Association, 2000). The ninth item that was omitted from the PHQ-8 assesses suicidal ideations, and due to the majority of interviewers not being trained mental health providers, this item was removed to create a more widely used tool, the PHQ-8 (Kurt Kroenke et al., 2009; K. Kroenke et al., 2001). The PHQ-8 has demonstrated to be closely comparable to the PHQ-9 (Kurt Kroenke, Spitzer, Williams, & Löwe, 2010). According to a systematic review of the PHQ-9, the

measure has demonstrated internal reliability or 0.86 to 0.89 and external reliability of 0.84 in identifying depression in both clinical settings and general population settings (Kurt Kroenke et al., 2010).

Methods used to identify individuals with major depression are consistent with the DSM-IV criteria (American Psychiatric Association, 2000) as well as methods used to identify major depression in a national MMP study (Do et al., 2014). The PHQ-8 asks if the individuals experienced certain symptoms within the last two weeks. Individuals were considered to have major depression if the individual had five out of the eight symptoms "more than half the days" out of the last two weeks, and the individual answered "more than half the days" in response to at least one of the first two questions: 1) "Little pleasure in doing things", 2) "Feeling down, depressed, or hopeless" (Kurt Kroenke et al., 2009; Do et al., 2014).

Dependent Variables

Injection drug use

Participants who responded that they had used injection drugs in the past 12 months were defined injection drug use. The interviewer explains that injection drugs for non-medical purposes include using drugs with a needle, "either by mainlining, skin popping, or muscling." The participant can identify which drug (heroin, cocaine, heroin and cocaine together, crack, methamphetamine, amphetamines, oxycontin, steroids or hormones, or any other drug) and how often the individual used the drug.

Other non-injection drug use

Participants who responded that they had used other non-injection drugs in the past month (methamphetamines, amphetamines or stimulants, crack, cocaine, downers

such as Valium, Ativan, Xanax, painkillers such as Oxycontin, Vicodin, Percocet, hallucinogens such as LSD, or mushrooms, and other drugs like ecstasy, heroin or opium, marijuana, amyl nitrate, GHB, or ketamine) and how often they used the drug during the past 12 months (daily, weekly, monthly, less than monthly, never, refused, or don't know).

Current Cigarette Smoking

For the descriptive analysis, current cigarette smoking was categorized as current cigarette smoker, former cigarette smoker, and never smoker. Cigarette smoking was assessed using the CDC criteria used to assess current smoker status ("CDC Disability and Health Data System (DHDS)"). Individuals were defined as current smokers if the individual answered "Yes" to "Have you smoked at least 100 cigarettes in your entire life?" and if the individual answers "Daily," "Weekly," or "Monthly" in response to "How often do you smoke cigarettes now?" ("CDC Disability and Health Data System (DHDS)"). To meet the criteria of a former cigarette smoker, participants answered "Yes" to "Have you smoked at least 100 cigarettes in your entire life?" and "Never" to "How often do you smoke cigarettes now?" Never smokers were classified if participants answered "No" to "Have you smoked at least 100 cigarettes in your entire life?"

Individuals were classified as current smokers or non-smokers for the purpose of the logistic regression analysis. Current smokers were classified using the same methodology as the descriptive analysis, and former smokers were categorized with never smokers into the non-smoker category.

ART Medication Adherence

ART medication adherence was assessed using several questions. Adults who reported ever taking any antiretroviral medicines were included in the analysis. Participants who responded they were not currently taking antiretroviral medicines due to reasons other than doctor advisement, but had taken antiretroviral medicines in the past, were classified as non-adherent. If participants reported their antiretroviral medicines consisted of special instructions, such as taking medication with food or with plenty of fluids, and they reported following those instructions "Never," "Rarely," or "About half of the time," they were classified as non-adherent. Participants who reported "Most of the time" or "Always" regarding following their instructions were classified as adherent. Also, if participants reported "Never," "Rarely," or "About half of the time," to specific scheduling instructions for ART medications in the past 3 days, they were classified as non-adherent. Participants were classified as adherent if they reported following their scheduling instructions "Most of the time" or "Always." Furthermore, if individuals reported missing their ART medications in the past week, 1-2 weeks ago, or 3-4 weeks ago, the participants were classified as non-adherent. If the participant reported the last time they missed their ART medication as 1-3 months ago, more than 3 months ago, or reported never skipping medications, they remained classified as adherent.

Drug holidays were also taken into consideration in assessing for medication adherence. Participants who responded "Yes" to the question, "Have you ever purposefully taken a 'drug holiday' from your antiretroviral medicines that wasn't recommended by your doctor?" were classified as non-adherent, whereas participants who responded "No" were classified as adherent.

Participants were excluded from the medication adherence analysis if they were never prescribed antiretroviral medicines due to their doctor's recommendations or if they had never taken antiretroviral medicines. Participants were also excluded from the analysis if they reported having taken ART medicines in the past, were not currently taking ART medicines, but reported participating in an HIV clinical trial. Individuals who refused to answer or did not know if they were taking antiretroviral medicines were also excluded.

Statistical Analyses

All statistical analyses were conducted using SAS 9.2 (SAS Institute, Inc., Cary, NC). Demographic variables between individuals with major depression and individuals without major depression were ascertained. All analyses accounted for the complex survey design and included weights, cluster and stratum variables. Multivariate logistic regression was conducted to assess associations between depression and dependent variables using procedures which accounted for complex sampling design. Logistic regression took into account various confounders based upon bivariate analyses of confounders in this dataset and previously documented confounders in the literature.

Results

Demographic characteristics (Table 1) displayed differences among adults with major depression and those without major depression. The overall total weighted percentage of adults with major depression, 9.2% (95% CI: 6.8%, 11.7%), were similar to findings in a national MMP study, which found 12.4% (95% CI: 11.2%, 13.7%) of adults had major depression (Do et al., 2014). A greater percentage of females, 15.2%, were classified as having major depression (95% CI: 8.8%, 21.6%) compared to 6.9% of males

(95% CI: 4.6%, 9.1%). An estimated 11.9% (95% CI: 7.8%, 16.1%) of heterosexuals classified as having major depression, a higher percentage than those who identified as bisexual, 8.3% (95% CI: 2.2%, 14.4%), or homosexual, gay, or lesbian, 6.1% (95% CI: 3.0%, 9.2%). A higher proportion of individuals whose highest education achieved was a high school education or GED met the criteria for major depression, 13.0% (95% CI: 8.2%, 17.8%), compared to individuals with a higher level of education.

Adults who reported non-adherence to ART medication had a higher percentage of major depression, 20.8% (95% CI: 8.8%, 32.8%) compared to adults who reported adherence to ART medication, 8.2% (95% CI: 5.8%, 10.6%). Among all participants, 9.7% (95% CI: 7.1%, 12.3%) met the criteria for non-adherence to ART medication. Among those who reported not currently taking antiretroviral medicines, reported reasons for non-adherence included due to doctor advisement or delay, 24.7% (95% CI: 10.1%, 39.2%), due to side effects, 22.4% (95% CI: 9.4%, 35.4%), worried about ability to adhere, 7.4% (95% CI: 3.8%, 11.0%), or due to money or insurance issues, 26.4% (95% CI: 11.9%, 40.8%). As previously mentioned, participants who reported non-adherence due to doctor advisement to delay or stop treatment were excluded from the analysis. Logistic regression analyses (Table 2) examined the associations between ART medication adherence and major depression. After adjusting for gender, major depression was associated with a higher odds of non-adherence to medication, 2.52 (1.20, 5.28), compared to adults without major depression.

A higher percentage of current cigarette smokers had major depression, 16.1% (95% CI: 11.1%, 21.0%), compared to former cigarette smokers, 4.4% (95% CI: 0.5%, 8.4%), and non-smokers, 5.9% (95% CI: 2.7%, 9.2%). Multivariate logistic regression

analyses compared current smokers to non-smokers. After adjusting for age, gender, race, and education, the odds of current cigarette smoking among individuals with major depression was 3.04 (95% CI: 1.48, 6.23) times the odds of current cigarette smoking among individuals without major depression.

Injection drug users had a much higher percentage of adults with major depression, 28.2% (95% CI: 2.4%, 54.0%) compared to non-injection drug users, 9.0% (95% CI: 6.5%-11.5%). However, due to the small sample size of unweighted individuals with major depression, the confidence interval is unstable. The adjusted odds ratio for persons with major depression and the association of injection drug use was 5.62 (95% CI: 0.96, 32.81). Both the injection drug odds ratio and the non-injection drug odds ratio were adjusted for age, gender, race, and education. Non-injection drug users also had a similar distribution of individuals with major depression as injection drug users. Among non-injection drug users, 14.2% (95% CI: 8.3%, 20.1%) had major depression compared to 7.7% (95% CI: 5.0%, 10.5%) of those who did not use non-injection drugs who had major depression. The adjusted odds ratio for non-injection drug use and major depression was 2.17 (95% CI: 1.10, 4.25).

Discussion

Adults with major depression were more likely to report current cigarette smoking, non-injection drug use in the past 12 months, and ART medication non-adherence compared with individuals without major depression. Even after adjusting for potential confounders, these relationships were significant. Although injection drug users had a wide confidence interval and was not statistically significant, a larger raw sample

size would likely yield a significant relationship between major depression and injection drug use.

The association of depression and medication non-adherence is one that has been found in numerous studies, including a recent meta-analysis of 95 studies which showed a positive relationship between depression and medication non-adherence (Gonzalez, Batchelder, Psaros, & Safren, 2011). While we examined non-adherence through a multitude of self-reported measures, the association of depression and medication adherence could also be explored using viral load. Although the literature has demonstrated self-reported medication adherence and viral load are both consistent at operationalizing medication adherence, viral load suppression would be able to reveal who is virally suppressed and therefore medication adherent. Also, viral load levels could be longitudinally studied comparing adults with and without depression to examine if a difference exists with regards to change in viral loads over time, which would also reveal which adults remain in care. Furthermore, in this questionnaire, adults could report reasons why they are not currently taking antiretroviral medicines or why they haven't ever taken antiretroviral medicines. While "feeling down or depressed" was an option as a reason for non-adherence, this was not selected by any participants.

The associations with injection and non-injection drugs are commonly found in the literature among the general population, as well as in adults living with HIV. Self-reported drug use is likely under reported, and the prevalence of injection and non-injection drug use is likely higher. Adults who are not in care may have an even higher prevalence of injection and non-injection drug use.

Limitations

Several limitations should be noted in our study. Due to the small sample of transgender persons, this gender category was excluded from logistic regression analyses (unweighted n=4, weighted n=159). Future studies should include larger sample sizes of transgender persons when examining the relationship between depression and behaviors, especially as this is a group that experiences health disparities, even among HIV-positive persons.

All measures examined were self-reported, which introduces the possibility of recall bias and potentially social desirability bias, especially with assessing previous drug use. As previously mentioned, injection drug users composed a small sample size (unweighted n= 8, weighted n=274). This is likely an underestimate of the true parameter of injection drug use. Future studies that include larger samples of HIV-positive persons would likely solve this issue. Also, obtaining medical histories or medical chart abstractions regarding previous injection drug use within the past 12 months could also be a more accurate estimate of injection drug use, as opposed to the self-reported measure.

Medication adherence analyses excluded individuals who had never taken antiretroviral medicines and individuals whose doctors delayed antiretroviral treatment due to CDC guidelines and recommendations for antiretroviral medicines prior to 2012. Since the guidelines post 2012 include recommending all persons living with HIV to be prescribed antiretroviral medicines, the effects of this policy may take a few years to be evident. Evaluating the association between medication adherence and major depression after this guideline change would be of interest.

The MMP questionnaire does not assess whether or not the individual is taking medication for depression. By knowing whether or not an individual is taking antidepressants, analyses could be conducted on those with untreated depression. Persons with untreated depression experience more adverse health outcomes than those with treated depression. Associations of treated depression and medication adherence could be examined to evaluate if a difference exists compared to associations of untreated depression and medication adherence in this population of Georgians to evaluate if these associations are consistent with the literature.

Lastly, the burden of depression among HIV-positive adults currently receiving care may underestimate the overall burden of depression among HIV-positive adults. Those seeking medical care may be more health-conscious. These individuals may also have less adverse health behaviors than the general HIV-positive population in the United States.

Implications and Recommendations

The associations of depression with these health behaviors have enormous implications for depression treatment and screening for HIV-positive persons. Guidelines do exist for HIV specific care providers that take into account screening and treatment of depression (Aberg et al., 2009). Screening for depression has not been consistently implemented in HIV care provider settings, although recommended as part of HIV medical care guidelines (Shacham et al., 2009). Shacham et al demonstrated the PHQ-9 as a feasible screening tool for HIV care providers (2009).

Smoking cessation programs for individuals with HIV should also address potential depression. Tobacco use and cigarette smoking has additional implications for

HIV-positive individuals, including increasing risks for cardiovascular disease, pneumonia, lung cancer, and liver cancer (Helleberg et al., 2013). Studies have demonstrated a substantial increase in mortality among smokers living with HIV, more than smoking or HIV alone (Helleberg et al., 2013). HIV providers and infectious disease providers need to recognize the importance of tobacco cessation within this population. Shuter, Bernstein, et al. examined smoking behaviors among people living with HIV, and 83% of participants revealed their primary care provider discussed smoking cessation with them (2012). However, only 32.8% were referred to a quit line and 5.3% were referred to a smoking cessation program (Shuter et al., 2012).

A recent review assessed tobacco cessation programs among HIV-positive persons (Moscou-Jackson, Commodore-Mensah, Farley, & DiGiacomo, 2014). Interventions which incorporated cell phone cessation strategies were the most successful at smoking cessation rates (Vidrine, Arduino, Lazev, & Gritz, 2006; Vidrine, Marks, Arduino, & Gritz, 2012). The review concluded that the most successful interventions were adjusted to address specific needs of people living with HIV (Moscou-Jackson et al., 2014). Also, interventions that addressed co-occurring substance use and psychiatric disorders were also more successful at achieving tobacco cessation than interventions that did not address these comorbidities (Moscou-Jackson et al., 2014).

Future studies should also aim at assessing substance use and smoking cessation interventions that incorporate depression screening and treatment. Depression could be the underlying factor impeding successful treatment of co-occurring substance use and tobacco use. The treatment of depression could increase the overall well-being of persons

living with HIV, as well as having an effect on the reduction of substance or cigarette smoking behaviors.

Table 1. Demographic characteristics among adults with major depression and without major depression

	Major Depression			Without Major Depression			Total MMP Participants		
	N*	**Weighted N**	**Percentage (95% CI)**	**N**	**Weighted N**	**Percentage (95% CI)**	**N**	**Weighted N**	**Percentage (95% CI***
Gender									
Male	29	977	6.88% (4.63%-9.12%)	392	13,224	93.12% (90.88%-95.37%)	421	14,201	70.20% (64.46%-75.93%)
Female	22	893	15.21% (8.78%-21.64%)	144	4,977	84.79% (78.36%-91.22%)	166	5,870	29.02% (23.58%-34.46%)
Transgender**	0	---	---	4	159	---	4	159	---
Sexual Orientation									
Homosexual, gay, or lesbian	14	483	6.11% (3.03%-9.18%)	220	7,421	93.89% (90.82%-96.97%)	234	7,903	39.27% (31.28%-47.26%)
Bisexual	6	188	8.30% (2.16%-14.43%)	60	2,076	91.70% (85.57%-97.84%)	66	2,264	11.25% (8.96%-13.54%)
Heterosexual	29	1,150	11.94% (7.76%-16.11%)	252	8,483	88.06% (83.89%-92.24%)	281	9,633	47.86% (41.58%-54.14%)
Other**	2	50	---	5	276	---	7	326	---
Race/Ethnicity									
Alaskan Native/American Indian**	0	---	---	2	77	---	2	77	---
Asian**	0	---	---	2	78	---	2	78	---
Black/African American	28	1,054	7.87% (4.56%-11.17%)	365	12,346	92.13% (88.83%-95.44%)	393	13,400	66.37% (61.81%-70.93%)
White/Caucasian	16	589	12.93% (8.13%-17.73%)	121	3,967	87.07% (82.27%-91.87%)	137	4,556	22.57% (17.82%-27.31%)
Multi-Racial	6	190	10.20% (2.40%-18.00%)	45	1,674	89.80% (82.00%-97.60%)	51	1,864	9.24% (6.33%-12.13%)
Hispanic/Latino**	1	36	---	4	177	---	5	213	---
Age									
18-24**	6	233	---	30	1,137	82.95% (70.67%-95.24%)	36	1,371	6.78% (4.68%-8.87%)
25-34**	9	271	---	70	2,374	89.76% (81.73%-97.80%)	79	2,645	13.07% (10.34%-15.81%)
35-44**	7	305	---	162	5,675	94.89% (90.52%-99.26%)	169	5,980	29.56% (25.91%-33.22%)
45-54	23	872	12.90% (8.01%-17.79%)	174	5,892	87.10% (82.21%-91.99%)	197	6,764	33.44% (30.17%-36.70%)
$\geq$ 55**	6	187	---	102	3,189	94.46% (90.11%-98.80%)	108	3,376	16.69% (14.02%-19.36%)
Education									
High School/GED	30	1,148	13.04% (8.24%-17.85%)	225	7,656	86.96% (82.15%-91.76%)	255	8,804	43.52% (36.33%-50.71%)
Some college	15	524	7.05%	200	6,907	92.95%	215	7,431	36.73%

			(3.31%-10.79%)			(89.21%-96.69%)			(32.35%-41.12%)
Bachelor's Degree**	4	142	---	77	2,566	94.76% (89.92%-99.60%)	81	2,708	13.39% (9.30%-17.47%)
Post-graduate studies**	2	56	---	38	1,230	95.67% (89.51%-100%)	40	1,286	6.36% (3.72%-8.99%)
Total	51	1,870	9.24% (6.78%-11.70%)	540	18,360	90.76% (88.30%-93.22%)	591	20,230	100%

*Unweighted N totals may not add up consistently due to missing variables. Missing variables were not reported if they comprised less than 10% of the total sample size.
**Weighted percentages were suppressed if estimates had a coefficient of variance >30%.
***Column percentages reported for total MMP participant column, whereas row percentages are reported for characteristics comparing major depression and no major depression.

Table 2. Associations of major depression with dependent variables

	Row percent	Unadjusted OR**	P-Value	Adjusted OR***	P-Value
Dependent Variables					
Medication Non-Adherence					
No Major depression	8.45% (6.0, 10.9)	1.00 Referent		1.00 Referent	
Major Depression	21.3% (9.6, 33.1)	3.01 (1.26, 7.18)	0.01*	2.52 (1.20, 5.28)	0.01*
Current smoker					
No Major Depression	32.3% (27.6, 37.0)	1.00 Referent		1.00 Referent	
Major Depression	62.4% (46.3, 78.4)	3.48 (1.75, 6.91)	0.0004*	3.04 (1.48, 6.23)	0.003*
Non-injection Drug Use					
No Major Depression	22.3% (18.0, 26.5)	1.00 Referent		1.00 Referent	
Major Depression	36..1% (21.8, 50.5)	1.98 (1.06, 3.70)	0.03*	2.17 (1.10, 4.25)	0.03*
Injection Drug Use****					
No Major Depression	---	1.00 Referent		1.00 Referent	
Major Depression	---	3.99 (1.06, 14.99)	0.04*	5.62 (0.96, 32.81)	0.06

*Significant values at P<0.05.
**Unadjusted OR obtained from bivariate analyses.
***Adjusted based upon bivariate analyses and the presence of confounders in the literature among noted variables. Medication adherence was adjusted for gender. Current cigarette smoking, non-injection drug use, and injection drug use were adjusted for age, gender, race, and education.
****Percentages suppressed if coefficient of variation >30%.

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Table 3.a. Demographics among adults reporting adherence to ART medication and persons reporting non-adherence to ART medication

	Adherence to ART medication			Non-adherence to ART medication			Total MMP Participants		
	N*	**Weighted N**	**Percentage (95% CI)**	**N**	**Weighted N**	**Percentage (95% CI)**	**N**	**Weighted N**	**Percentage (95% CI)**
Gender									
Male	385	12,912	72.56% (67.29%-77.83%)	27	889	46.55% (28.69%-64.41%)	412	13,802	70.04% (64.46%-75.61%)
Female	134	4,764	26.88% (21.67%-31.88%)	28	981	51.35% (33.28%-69.42%)	162	5,745	29.16% (23.86%-34.45%)
Transgender**	3	119	---	1	40	---	4	159	---
Sexual Orientation									
Homosexual, gay, or lesbian	211	7,103	40.26% (32.75%-47.78%)	16	536	28.06% (14.09%-42.03%)	227	7,639	39.07% (31.46%-46.68%)
Bisexual**	55	1,832	10.39% (7.77%-13.01%)	7	254	---	62	2,087	10.67% (8.19%-13.16%)
Heterosexual	248	8,502	48.20% (41.65%-54.74%)	32	1,097	57.41% (43.55%-71.27%)	280	9,599	49.10% (42.86%-55.33%)
Other**	4	203	---	1	23	---	5	226	---
Race/Ethnicity									
American Indian/Alaskan Native**	1	31	---	0	---	---	1	31	---
Asian**	2	78	---	0	---	---	2	78	---
African American	344	11,711	66.16% (60.65%-71.67%)	41	1,381	72.30% (52.55%-92.06%)	385	13,093	66.76% (61.97%-71.55%)
White	124	4,094	23.13% (18.10%-28.16%)	10	318	16.66% (7.64%-25.69%)	134	4,413	22.50% (17.60%-27.41%)
Multi-Racial**	44	1,572	8.88% (6.01%-11.75%)	5	211	---	49	1,783	9.09% (6.09%-12.09%)
Hispanic/Latino**	5	213	---	0	---	---	5	213	---
Age									
18-24	29	1,110	6.24% (4.06%-8.41%)	4	132	---	33	1,242	6.30% (4.24%-8.37%)
25-34	66	2,218	12.47% (9.59%-15.34%)	8	276	---	74	2,495	12.66% (9.80%-15.51%)
35-44	142	4,888	27.47% (24.00%-30.93%)	17	615	32.21% (19.34%-45.09%)	159	5,503	27.93% (24.53%-31.33%)
45-54	176	6,137	34.49% (30.77%-38.20%)	20	640	33.51% (21.57%-45.45%)	196	6,777	34.39% (31.08%-37.71%)
≥ 55	109	3,442	19.34% (16.08%-22.60%)	6	176	---	115	3,618	18.36% (15.44%-21.28%)
Education									
High School/GED	231	8,019	45.06% (35.51%-54.62%)	24	835	43.68% (30.88%-56.49%)	255	8,854	44.93% (36.60%-53.26%)
Some college	186	6,406	36.00%	20	656	34.33%	206	7,062	35.84%

			(29.50%-42.50%)			(20.13%-48.53%)			(30.45%-41.22%)
Bachelor's Degree**	72	2,371	13.32% (9.44%-17.20%)	8	284	---	80	2,655	13.47% (9.47%-17.48%)
Post-graduate studies**	33	999	5.62% (3.60%-7.63%)	4	136	---	37	1,136	5.76% (3.76%-7.77%)
Major Depression									
Yes	38	1,417	8.21% (5.83%-10.59%)	11	385	20.82% (8.84%-32.80%)	49	1,802	9.24% (6.78%-11.70%)
No	470	15,840	91.79% (89.41%-94.17%)	43	1,463	79.18% (67.20%-91.16%)	513	18,360	90.76% (88.30%-93.22%)
Total	508	17,258	90.33% (87.75%-92.91%)	54	1,847	9.67% (7.09%-12.25%)	562	19,105	100%

*Unweighted N totals may not add up consistently due to missing variables. Missing variables were not reported if they comprised less than 10% of the total sample size.
**Weighted percentages were suppressed if estimates had a coefficient of variance >30%.
***Column percentages reported

Table 3.b. Demographics among adults who used injection drugs in the past 12 months and persons who did not use injection drugs in the past 12 months

	Injection Drug Use in the Past 12 Months**			No Injection Drug Use in the Past 12 Months			Total MMP Participants		
	N*	**Weighted N**	**Percentage (95% CI)**	**N**	**Weighted N**	**Percentage (95% CI)**	**N**	**Weighted N**	**Percentage (95% CI***
Gender									
Male	7	238	---	424	14,354	69.69% (63.89%-75.49%)	431	14,592	69.91% (64.00%-75.83%)
Female	1	36	---	172	6,085	29.54% (24.04%-35.04%)	173	6,121	29.33% (23.72%-34.92%)
Transgender	0	0	---	4	159	---	4	159	---
Sexual Orientation									
Homosexual, gay, or lesbian	6	206	---	231	7,819	38.25% (30.52%-45.98%)	237	8,025	38.74% (30.81%-46.67%)
Bisexual	1	36	---	66	2,276	11.14% (8.75%-13.52%)	67	2,313	11.16% (8.81%-13.52%)
Heterosexual	1	32	---	292	10,021	49.02% (42.62%-55.42%)	293	10,053	48.52% (42.12%-54.93%)
Other	0	---	---	7	325	---	7	325	---
Race/Ethnicity									
Alaskan Native/American Indian	0	---	---	2	77	---	2	77	---
Asian	1	49	---	1	29	---	2	78	---
African American	0	---	---	408	13,950	68.04% (63.51%-72.57%)	408	13,950	67.14% (62.48%-71.81%)
White	6	189	---	132	4,404	21.48% (16.77%-26.20%)	138	4,593	22.11% (17.33%-26.89%)
Multi-Racial	1	36	---	50	1,828	8.92% (6.19%-11.65%)	51	1,864	8.97% (6.17%-11.78%)
Hispanic/Latino	0	---	---	5	213	---	5	213	---
Age									
18-24	1	49	---	36	1,362	6.61% (4.53%-8.70%)	37	1,411	6.76% (4.71%-8.81%)
25-34	2	68	---	79	2,665	12.94% (10.47%-15.41%)	81	2,733	13.10% (10.51%-15.68%)
35-44	2	52	---	169	5,976	29.01% (25.40%-32.63%)	171	6,028	28.88% (25.38%-32.38%)
45-54	3	105	---	197	6,800	33.01% (29.73%-36.30%)	200	6,905	33.08% (29.78%-36.39%)
≥ 55	0	---	---	117	3,701	17.97% (15.18%-20.75%)	117	3,701	17.73% (14.94%-20.52%)
Education									

High School/GED	1	32	---	266	9,228	44.80% (37.26%-52.33%)	267	9,259	44.36% (36.91%-51.82%)
Some college	5	152	---	213	7,401	35.93% (31.24%-40.63%)	218	7,553	36.19% (31.65%-40.73%)
Bachelor's Degree	2	90	---	81	2,683	13.03% (9.10%-16.95%)	83	2,773	13.29% (9.23%-17.34%)
Post-graduate studies	0	---	---	40	1,286	6.24% (3.62%-8.87%)	40	1,286	6.16% (3.58%-8.74%)
Major Depression									
Yes	2	77	---	49	1,792	8.98% (6.45%-11.51%)	51	1,870	9.24% (6.78%-11.70%)
No	6	197	---	534	18,163	91.02% (88.49%-93.55%)	540	18,360	90.76% (88.30%-93.22%)
Total	**8**	**274**	**---**	**600**	**20,597**	**98.69% (97.65%-99.72%)**	**608**	**20,871**	**100%**

*Unweighted N totals may not add up consistently due to missing variables. Missing variables were not reported if they comprised less than 10% of the total sample size.
**Weighted percentages were suppressed if estimates had a coefficient of variance >30%.
***Row percentages reported

Table 3.c. Demographics among adults who used non-injection drugs in the past 12 months and persons who did not use non-injection drugs in the past 12 months

	Non-Injection Drug Use in the Past 12 Months			No Non-Injection Drug Use in the Past 12 Months			Total MMP Participants		
	N*	**Weighted N**	**Percentage (95% CI)**	**N**	**Weighted N**	**Percentage (95% CI)**	**N**	**Weighted N**	**Percentage (95% CI)**
Gender									
Male	111	3,880	80.66% (72.83%-88.49%)	320	10,712	66.70% (60.45%-72.94%)	431	14,592	69.91% (64.00%-75.83%)
Female	25	885	18.39% (10.83%-25.95%)	148	5,236	32.60% (26.70%-38.50%)	173	6,121	29.33% (23.72%-34.92%)
Transgender**	2	46	---	2	113	---	4	159	---
Sexual Orientation									
Homosexual, gay, or lesbian	72	2,462	52.04% (27.80%-41.81%)	165	5,563	32.21% (27.80%-41.81%)	237	8,025	38.74% (30.81%-46.67%)
Bisexual**	14	486	---	53	1,827	11.43% (8.76%-14.10%)	67	2,313	11.16% (8.81%-13.52%)
Heterosexual	49	1,711	36.16% (24.76%-47.56%)	244	8,342	52.19% (46.23%-58.14%)	293	10,053	48.52% (42.12%-54.93%)
Other**	1	73	---	6	252	---	7	325	---
Race/Ethnicity									
American Indian/Alaskan Native**	0	0	---	2	77	---	2	77	---
Asian**	1	49	---	1	29	---	2	78	---
African American	84	2,995	62.77% (51.90%-73.65%)	324	10,956	68.45% (63.96%-72.93%)	408	13,950	67.14% (62.48%-71.81%)
White	41	1,425	29.87% (18.25%-41.50%)	97	3,168	19.79% (15.75%-23.83%)	138	4,593	22.11% (17.33%-26.89%)
Multi-Racial	11	302	---	40	1,562	9.76% (6.44%-10.09%)	51	1,864	8.97% (6.17%-11.78%)
Hispanic/Latino**	0	---	---	5	213	1---	5	213	---
Age									
18-24	18	575	11.96% (6.96%-16.97%)	19	836	5.20% (3.10%-7.31%)	37	1,411	6.76% (4.71%-8.81%)
25-34	22	760	15.79% (9.13%-22.45%)	59	1,974	12.29% (9.53%-15.04%)	81	2,733	13.10% (10.51%-15.68%)
35-44	42	1,444	30.01% (20.89%-39.13%)	129	4.584	28.54% (24.42%-32.67%)	171	6,028	28.88% (25.38%-32.38%)
45-54	40	1,546	32.13% (23.18%-41.08%)	160	5,360	33.37% (29.54%-37.21%)	200	6,905	33.08% (29.78%-36.39%)
≥ 55**	16	486	---	101	3,214	20.01% (17.03%-22.99%)	117	3,701	17.73% (14.94%-20.52%)
Education									

High School/GED	61	2,066	42.95% (31.60%-54.31%)	206	7,193	44.79% (37.31%-52.26%)	267	9,259	44.36% (36.91%-51.82%)
Some college	52	1,874	38.96% (28.39%-49.53%)	166	5,679	35.36% (30.13%-40.59%)	218	7,553	36.19% (31.65%-40.73%)
Bachelor's Degree	17	561	11.66% (5.81%-17.50%)	66	2,212	13.77% (9.33%-18.21%)	83	2,773	13.29% (9.23%-17.34%)
Post-graduate studies	8	309	---	32	977	6.08% (3.61%-8.55%)	40	1,286	6.16% (3.58%-8.74%)
Major Depression									
Yes	18	676	14.19% (8.26%-20.12%)	33	1,194	7.72% (4.98%-10.46%)	51	1,870	9.24% (6.78%-11.70%)
No	119	4,086	85.81% (79.88%-91.74%)	421	14,273	92.28% (89.54%-95.02%	540	18,360	90.76% (88.30%-93.22%)
Total	**138**	**4,811**	**23.05% (18.93%-27.17%)**	**470**	**16,601**	**76.95% (72.83%-81.07%)**	**608**	**20,871**	**100%**

*Unweighted N totals may not add up consistently due to missing variables. Missing variables were not reported if they comprised less than 10% of the total sample size.
**Weighted percentages were suppressed if estimates had a coefficient of variance >30%.
***Column percentages reported

Table 3.d. Demographics among current smokers, former smokers, and never-smokers

	Current Smokers			Former Smokers			Never-Smokers			Total MMP Participants		
	N	**Weighted N**	**Percentage (95% CI)**	**N**	**Weighted N**	**Percentage (95% CI)**	**N**	**Weighted N**	**Percentage (95% CI)**	**N**	**Weighted N**	**Percentage (95% CI)**
Gender												
Male	151	5,082	68.02% (58.55%-77.48%)	87	2,934	68.96% (58.97%-78.95%)	192	6,551	72.23% (65.82%-78.65%)	430	14,567	70.05% (64.28%-75.82%)
Female	61	2,344	31.37% (21.84%-40.90%)	39	1,321	31.04% (21.05%-41.03%)	72	2,405	26.52% (19.72%-33.32%)	172	6,070	29.19% (23.71%-34.67%)
Transgender**	2	46	---	0	---	---	0	113	---	4	159	---
Sexual Orientation												
Homosexual, gay, or lesbian	79	2,706	36.21% (23.89%-45.53%)	40	1,437	34.39% (23.10%-45.68%)	118	3,883	43.19% (36.65%-49.73%)	237	8,025	38.88% (31.05%-46.71%)
Bisexual	21	643	8.61% (4.42%-12.80%)	18	600	14.36% (8.36%-20.37%)	27	1,044	11.62% (8.04%-15.19%)	66	2,288	11.08% (8.71%-13.45%)
Heterosexual	113	4,099	54.87% (42.88%-66.85%)	65	2,069	49.50% (39.24%-59.77%)	114	3,833	42.64% (36.44%-48.84%)	292	10,002	48.46% (42.18%-54.73%)
Other**	1	23	---	1	73	---	5	229	---	7	325	---
Race/Ethnicity												
American Indian/ Alaskan Native**	0	---	---	1	46	---	1	31	---	2	77	---
Asian**	0	---	---	1	29	---	1	48	---	2	78	---
African American	132	4,652	62.26% (55.18%-69.34%)	79	2,639	62.60% (52.64%-72.57%)	195	6,584	73.04% (67.39%-78.68%)	406	13,875	67.02% (62.38%-71.67%)
White	56	1,898	25.40% (18.45%-32.35%)	33	1,098	26.05% (17.35%-34.75%)	49	1,598	17.72% (12.29%-23.16%)	138	4,593	22.19% (17.44%-26.94%)
Multi-Racial**	23	796	10.65% (6.07%-15.23%)	11	403	---	17	666	7.38% (3.06%-11.71%)	51	1,864	9.01% (6.17%-11.84%)
Hispanic/Latino**	3	126	---	0	---	---	2	87	---	5	213	1.03% (0.31%-1.75%)
Age												
18-24**	12	408	---	3	154	---	22	849	9.36% (5.92%-12.80%)	37	1,411	6.79% (4.73%-8.84%)
25-34**	34	1,298	17.37% (11.74%-23.00%)	1	19	---	46	1,417	15.62% (12.13%-19.11%)	81	2,733	13.14% (10.54%-15.75%)
35-44	63	2,186	29.25% (22.46%-36.05%)	29	1,117	26.26% (18.34%-34.18%)	79	2,725	30.04% (24.29%-35.80%)	171	6,028	28.98% (25.48%-32.50%)
45-54	75	2,660	35.60% (27.06%-44.14%)	44	1,486	34.93% (25.64%-44.23%)	79	2,683	29.59% (23.99%-35.18%)	198	6,830	32.84% (29.50%-36.18%)
≥ 55	30	920	12.31% (8.62%-16.00%)	48	1,456	34.23% (25.59%-42.87%)	39	1,324	14.60% (10.49%-18.72%)	117	3,701	17.80% (15.00%-20.59%)
Education												
High School/GED	123	4,366	58.44% (50.00%-66.88%)	50	1,598	37.56% (27.47%-47.66%)	94	3,295	36.33% (28.44%-44.21%)	267	9,259	44.53% (36.90%-52.15%)
Some college	72	2,545	34.06% (27.38%-40.75%)	49	1,722	40.46% (33.45%-47.47%)	95	3,211	35.41% (29.09%-41.73%)	216	7,477	35.96% (31.27%-40.64%)
Bachelor's Degree	14	409	5.47% (2.13%-8.81%)	20	690	16.22% (8.71%-23.72%)	49	1,674	18.46% (13.14%-23.78%)	83	2,773	13.33% (9.30%-17.37%)
Post-graduate	5	151	---	7	245	---	28	890	9.81%	40	1,286	6.18%

studies**									(4.90%-14.72%)			(3.61%-8.76%)
Major Depression												
Yes**	29	1,166	16.06% (11.13%-20.99%)	6	179	---	16	524	5.93% (2.66%-9.21%)	51	1,870	9.28% (6.80%-11.76%)
No	180	6,094	83.94% (79.01%-88.87%)	115	3,876	95.58% (91.63%-99.52%)	243	8,314	94.07% (90.79%-97.34%)	538	18,284	90.72% (88.24%-93.20%)
Total	**214**	**7,472**	**35.93% (30.74%-41.12%)**	**126**	**4,255**	**20.46% (16.92%-24.00%)**	**266**	**9,069**	**43.61% (38.27%-48.95%)**	**606**	**20,796**	**100%**

*Unweighted N totals may not add up consistently due to missing variables. Missing variables were not reported if they comprised less than 10% of the total sample size.
**Weighted percentages were suppressed if estimates had a coefficient of variance >30%.
***Row percentages reported

Table 3.e. Bivariate associations of major depression with demographic variables

Demographic Variables	Unadjusted Odds Ratio	P-Value
Gender		
Male	1.00 Referent	
Female	2.09 (1.24, 3.50)	0.006*
Race		
White	1.00 Referent	
Black/African American	0.58 (0.30, 1.12)	0.10
Other	0.76 (0.27, 2.10)	0.60
Education		
High School/GED	1.00 Referent	
Post-High School	0.45 (0.23, 0.87)	0.02*
Age	0.99 (0.96, 1.02)	0.46

*Significance at $p<0.05$