ENTRY INTO HIV MEDICAL CARE, RECEIPT OF CASE MANAGEMENT SERVICES, DEPRESSION, AND ART ADHERENCE AMONG ADULTS WITH HIV IN NORTH CAROLINA

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ABSTRACT

Damon Floyd Ogburn: Entry into HIV medical care, receipt of case management services,
depression, and ART adherence among adults with HIV in North Carolina
(Under the direction of Victor J. Schoenbach)

Engagement in HIV care is important for optimal clinical outcomes and reductions in
transmission, particularly in Southern states. Delayed care initiation remains prevalent. While
individual-level risk factors are established, barriers to prompt care initiation associated with
characteristics of HIV testing facilities are not well defined. Upon care initiation, persons may
benefit from the provision of case management services. Little has been published about whether
case management services reduce depression or improve ART adherence.

We analyzed 2015 enhanced HIV/AIDS Reporting System data for North Carolina (NC)
to estimate the cumulative incidence of persons initiating HIV care by time since diagnosis and
in relation to (1) patient-level characteristics and (2) characteristics of the facility where HIV was
diagnosed. Of 1,269 adults newly diagnosed in 2015, 84.9% were linked to care < three months
from diagnosis; 63% initiated care within one month. Initiating care at ≥ three months was
associated with younger age, IDU transmission, diagnosis at a site without co-located HIV care
among males but not females, diagnosis at a facility with a higher diagnosis volume, and
diagnosis at a sexually transmitted disease clinic (STD), HIV counseling and testing site, or a
non-traditional testing facility setting such as a jail.

For the examination of persons in HIV care, we used NC data for 2009-2013 from the
Medical Monitoring Project. Depression prevalence was higher among the 53.2% who had

received case management services than among those who had not, though the adjusted association was observed only among patients living above the poverty level. No differences in ART adherence were observed by receipt of case management services. Though ART adherence was high overall, depressed persons with HIV were less likely to be adherent.

HIV clinicians, case managers, and intervention specialists working with persons diagnosed at high volume STD clinics, HIV counseling and testing sites, and non-traditional testing facilities should be provided with resources to ensure persons are promptly enrolled in care. Depression persisted, suggesting the need for resources for case managers, providers, and mental health professionals. Combining data sources for persons living with HIV will be essential to monitor the HIV continuum in NC.

I dedicate this dissertation research to my parents, Dr. and Mrs. Floyd and Trevia A. Ogburn, as well as my brother, Dr. Kenyon D. Ogburn.

To my relatives, gone yet not forgotten, thank you for your perseverance and sacrifice. Thank you for leading by example!

To my family, closest friends and colleagues – thank you! I will forever be grateful for your encouragement and support!

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LIST OF ABBREVIATIONS

ADAP	AIDS Assisted Drug Program
AETC	AIDS Education and Training Center
AIC	Akaike information criterion
AIDS	Acquired immune deficiency syndrome
aOR	Adjusted odds ratio
aPR	Adjusted prevalence ratio
aRR	Adjusted relative risk
ART	Antiretroviral therapy
ARTAS	Antiretroviral Treatment Access Study
ARV	Antiretroviral
CBO	Community-based organization
CDC	Centers for Disease Control and Prevention
CES-D	Center for Epidemiologic Studies-Depression
CI	Confidence interval
DAG	Directed acyclic graph
DHHS	Department of Health and Human Services
DUA	Data use agreement
eHARS	enhanced HIV/AIDS Reporting System
ER	Emergency room
HAART	Highly Active Antiretroviral Therapy
HIV	Human immunodeficiency virus
HPTN	HIV Prevention Trials Network

HR	Hazard ratio
HRSA	Health Resources and Services Administration
ID	Identification
IDU	Injection drug use
IRB	Institutional review board
MMP	Medical Monitoring Project
MRA	Medical record abstraction
MSM	Men who have sex with men
NC	North Carolina
NHAS	National HIV/AIDS Strategy
OR	Odds ratio
PHQ-8	Patient Health Questionnaire (8 item)
PR	Prevalence ratio
PrEP	Pre-exposure prophylaxis
PSU	Primary sampling unit
RW	Ryan White
STD	Sexually transmitted disease
TB	Tuberculosis
US	United States
VL	Viral load

CHAPTER ONE: OVERVIEW

Interventions focused on persons living with the human immunodeficiency virus (HIV) are of great importance for reducing HIV comorbidities, improving clinical outcomes and survival, and preventing further transmission. Initial HIV prevention strategies focused on reductions in sexual partners,[1] changes in sexual behaviors,[1-3], increase in condom usage,[2, 3] and abstinence.[3] Although these behavioral approaches have been shown to be effective at reducing HIV transmission, the more recent "test-and-treat" strategy is much more powerful.[4] Early HIV detection with prompt linkage to HIV medical care including initiation of and adherence to antiretroviral (ART) therapy dramatically reduces HIV transmission.[4, 5]

Despite widespread endorsement of the new strategy, failure to promptly initiate care upon initial detection is common, leading to ongoing HIV transmission and more rapid progression to the acquired immune deficiency syndrome (AIDS) as defined by CD4 criteria.[6] A meta-analysis of time to enter care between 1995 and 2009 found that 28% of HIV-positive people entered care more than 3 months after initial diagnosis.[7] A study measuring access to HIV primary care in the St. Louis, MO area found that 10% to 20% of newly diagnosed individuals did not enter care even after three years following diagnosis.[8] In Southern states disproportionately affected by HIV, the prevalence of delayed linkage to HIV medical care among people living with HIV is not clear. Factors such as sex,[9, 10] age,[9-12] race,[13-15] socioeconomic status,[12, 13] health insurance,[14-16] geographic location,[12, 13] education,[12] and mental health status[12] have been associated with delayed entry into HIV medical care. Several studies

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have demonstrated that initial HIV diagnosis at larger medical facilities in urban areas or at facilities with co-located HIV clinical care significantly decreased delayed entry into HIV medical care.[10, 17-20] The type of facility at initial HIV diagnosis may also be a factor. In New York City surveillance data, patients diagnosed at a community testing site, city correctional system, and sexually transmitted disease (STD) or tuberculosis (TB) clinic were less likely to initiate HIV medical care within three months of initial diagnosis than patients diagnosed at sites with co-located medical care.[20]

Further along the HIV care continuum,[21] according to a meta-analysis of 31 ART adherence studies, only 55% of HIV-infected persons reached adequate levels of adherence upon initiation of and linkage to HIV medical care.[22] ART adherence is essential to achieve good clinical and immunologic outcomes, particularly viral suppression.[23-25] Given how crucial viral suppression is both to patient survival and also to preventing further transmission,[6] it is also important to address any unmet needs that may compromise ART adherence and viral suppression. Depression, the most prevalent psychiatric disorder among HIV-infected patients other than substance use disorders, has serious effects on a patient's quality of life and course of illness.[26] Numerous prospective and cross-sectional studies have demonstrated significant associations of depression or depressive symptoms with ART non-adherence and discontinuation,[25, 27-29] and poorer virological response and immunological failure.[23, 30, 31]

One approach to facilitating treatment of depression or depressive symptoms among HIV-infected persons is the provision of case management services. Several studies of case management services for recently diagnosed, persons with HIV reported greater linkage to care, receipt of ART, and virologic success.[19, 32-34] However, few studies have examined the utilization of case management services in relation to unmet psychosocial and social service needs among

persons with HIV who have initiated HIV care. HIV patients who were aware of their status but had not been retained in care within the past six months or never initiated care had lower mental health scores than persons who received some HIV care services, and did not have case managers.[35]

The goal of the present research is to examine (1) potential patient and testing facility barriers to linkage to care, and (2) the use of HIV case management services in relation to HIV-related mental health and clinical outcomes. Using North Carolina (NC) data from two national surveillance databases – the enhanced HIV/AIDS Reporting System (eHARS, 2015) and the Medical Monitoring Project (MMP, 2009-2013) – we will address the following aims:

1.1   Aim 1

Specific Aim 1. Estimate the cumulative incidence of persons initiating HIV medical care following diagnosis, examine patient-level sociodemographic and behavioral characteristics associated with delay in initiating care, and assess time to care initiation in relation to characteristics of the facility where HIV was diagnosed.

1.2   Aim 2

Specific Aim 2. Estimate the prevalence of probable current depression and 100% ART dose adherence in the past three days in relation to the receipt of case management services in the previous 12 months.

The proposed research aims to identify barriers along the HIV care continuum in North Carolina, where HIV/AIDS incidence is higher than the national average. Results can be used to evaluate areas for improvement in linkage to HIV medical care and to assess the utilization of case management support services in relation to depression and ART adherence, which

ultimately affect retention in care and the achievement of optimal clinical and survival outcomes for persons living with HIV as well as preventing further transmission of the virus.

CHAPTER TWO: BACKGROUND AND SIGNIFICANCE

2.1   HIV Epidemic in the Southern United States

The Centers for Disease Control and Prevention (CDC) estimate that more than 1.2

million people living in the United States (US) are infected with HIV. Approximately 1 in 8

(~13%) HIV-infected persons are unaware of their HIV status.[36] The number of incident cases

remains stable at approximately 50,000 cases per year; however, several subpopulations are

disproportionately affected. Blacks represent 12% of the U.S. population but accounted for

approximately 44% of new HIV infections in 2010. Hispanics represent 16% of the population,

but accounted for roughly 21% of incident infections in the same year. Approximately 62% of

persons receiving an HIV diagnosis in 2011 were men who have sex with men (MSM).[36] Young

black MSM between the ages of 18 and 30 are at greatest risk for HIV infection.[37]

The District of Columbia and sixteen states that comprise the Southern region of the US

carry a severe HIV burden.[38] Six southern states (NC, South Carolina, Alabama, Georgia,

Louisiana, Mississippi) – the Deep South[39] – have similar HIV/AIDS epidemic profiles. The

Deep South has a history of challenges including high STD rates, poor medical infrastructures,

high poverty levels, and considerable numbers of persons lacking health insurance. Minority

groups, particularly blacks, are disproportionately affected by these factors, which are related to

the higher HIV/AIDS incidence rates observed in this region.[39, 40]

By the end of 2013, approximately 36,300 people were living with HIV infection in

NC.[41] An estimated 6,500 (17.9%) were unaware of their HIV status. During 2013, 1,525

individuals were newly diagnosed, including 1,513 over 13 years of age, for an adult/adolescent incidence rate of 18.7 per 100,000/year.[41] By 2015, the most recent year for which data are available, the number of adult/adolescent incident HIV cases diagnosed had decreased to 1,336, an HIV incidence rate of 15.9 per 100,000/year.[42] Although incidence decreased, the high rates of undiagnosed and untreated HIV, along with aforementioned factors, enable ongoing HIV transmission. Moreover, 2015 adult/adolescent HIV incidence in NC continued to be much higher in the black population, with their share of new diagnoses nearly twice the percentage of blacks in the state's adult/adolescent population.[42]

Challenges to removing barriers to HIV testing and treatment in NC, particularly among minorities, include historical factors specific to the Deep South. Two more commonly described challenges are poverty and rurality, which limit access to healthcare. Between 2009 and 2010, 19% of the 19-64 year old population was at or below the federal poverty line.[43] Since NC has not adopted the Affordable Care Act's Medicaid expansion, persons above the poverty line may have even greater difficulty accessing healthcare than the poor.[44] In 2006, the CDC reported that NC had the highest rate of HIV and AIDS cases in rural areas.[43] Since most HIV care management is available only in urban areas, HIV-infected rural residents often travel significant distances to receive care.[45] Rural communities often experience shortages of trained medical and mental health professionals,[40, 46] lack of public and personal transportation,[40, 46] lack of knowledge regarding HIV prevention,[46] and few systems of support and counseling for HIV-infected persons.[45, 46] In addition, persons living with HIV in rural areas face greater stigma from community members than persons living in or near urban areas.[39]

With the continuing problem of HIV and an especially high HIV burden among specific subpopulations, there remains a need for research to identify specific barriers that impede HIV

testing, treatment initiation, and adherence, as well as potential facilitators including counseling and case management services, to assist NC HIV prevention strategists in fielding interventions that reduce transmission.

2.2   HIV Prevention Strategies

In 2003, the CDC along with other government agencies released guidelines for incorporating HIV prevention into the medical care of HIV-infected persons. New and existing strategies such as risk screening, behavioral interventions, and partner notification and counseling were suggested in these guidelines.[47] In 2010, the US government created a plan known as the 'The National HIV/AIDS Strategy' (NHAS) with a goal of addressing the national HIV epidemic. Building on the strategies implemented in 2003, the Strategy has three main goals: reduce HIV incidence; increase access to care and optimize health outcomes for people living with HIV; and reduce HIV-related health disparities. In addition, the strategy set an overall goal of reducing HIV incidence by 25% by the year 2015.[48] States with a high HIV burden, such as NC, and metropolitan cities serve as focal points, as described by specific action steps listed within the proposed strategy. In 2014, the federal government allotted a total of $29.5 billion towards combating HIV, with the majority (55%) for HIV care and the least amount (3%) for HIV prevention services.[49]

Prevention services vary on both state and local levels, and often include involvement with community organizations. Early HIV prevention strategists focused on reductions in sexual partners,[1] reductions in risky sexual behaviors,[1-3] increased condom usage [2, 3] and abstinence.[3] However, the primary focus shifted towards identification of HIV-infected persons through routine testing and linkage to care. An additional objective was to increase the number of persons who are aware of their HIV serostatus to 90% or better by 2015.[48] The goals set in 2010, as well

as lessons learned, contributed to 'The National HIV/AIDS Strategy: Updated to 2020' in 2015.

This Strategy maintains the original plan of action outlined in 2010 with an additional goal of

achieving a more coordinated national response to HIV. Emphasis is now placed on increasing

testing; linking and retaining in care 85% of HIV-infected persons within one month of

diagnosis; and achieving viral suppression among 80% of persons living with HIV. In addition,

the Strategy aims to increase access to pre-exposure prophylaxis (PrEP). A focus on

subpopulations with the highest rates remains key.[50]

In 2011 the landmark HIV Prevention Trials Network (HPTN) 052 phase III clinical trial

assessing the effects of early initiation of antiretroviral (ARV) therapy on heterosexual HIV

transmission among serodiscordant couples reported that immediate treatment reduced HIV

transmission by 96%;[51] efficacy was 93% at the trial's conclusion in 2016. Among the 1,171

heterosexual couples with complete follow-up data, 78 HIV infections occurred. A total of 46 out

of 78 infections were partner-linked. Approximately 93% (n=43) of these infections occurred

among partnerships where the HIV-infected person delayed initiation of ART treatment.[52, 53]

Findings are expected to be comparable within the homosexual community as well. The

ongoing PARTNERS Study, which has enrolled over 1,000 serodiscordant couples (40%

homosexual) has not reported any transmissions among couples where the HIV-infected person

has an undetectable viral load.[54] These findings have shaped the way in which HIV prevention

efforts are guided worldwide. World Health Organization guidelines now recommend immediate

ART treatment for all HIV-infected persons regardless of CD4 count.[55] Clinicians no longer

recommend waiting until CD4 counts fall below a particular threshold. Studies have shown that

immediate treatment also results in a reduction in the risk of death or serious illness.[56]

Treatment as prevention has also evolved among persons at high risk of infection. The Pre-exposure Prophylaxis Initiative trial was an international study evaluating the efficacy and safety of once daily Truvada® for the prevention of HIV among men and transgender women who have sex with men. Truvada® was shown to provide 44% protection from HIV acquisition.[57] ARV prophylaxis for HIV prevention was also assessed among heterosexual partners. A randomized trial following 4,747 couples conducted in Kenya and Uganda reported a 67% relative reduction in the incidence of HIV among persons taking once-daily tenofovir and a 75% relative reduction in the incidence of HIV among persons taking Truvada®.[58] Given the efficacy of PrEP, the Food and Drug Administration approved its use in July 2012. In 2014, clinical practice guidelines were released to assist clinicians with prescribing PrEP and providing additional resources to their patients.[50]

2.3   The HIV Care Continuum

Effective test-and-treat HIV prevention strategies require identification and elimination of barriers along each step of the HIV care continuum, depicted in Figure 1. In 2013, President Obama and the White House administration established the HIV Care Continuum Initiative to accelerate progress towards this goal.[49] Specifically, the administration identified the following points along the continuum as requiring the greatest improvements: 1) awareness of status, 2) linkage to care, 3) engagement in care and 4) viral suppression.[50] With emphasis on the importance of the test-and-treat strategy, national testing efforts have increased. However, a large number of newly diagnosed, HIV-infected persons have already advanced to full blown AIDS by the time of diagnosis. High levels of viremia may lead to HIV comorbidities and increased likelihood of transmission to uninfected partners.[51] It is important to identify deficiencies in HIV control measures among subpopulations disproportionately affected by HIV.

Figure 1   The HIV care continuum
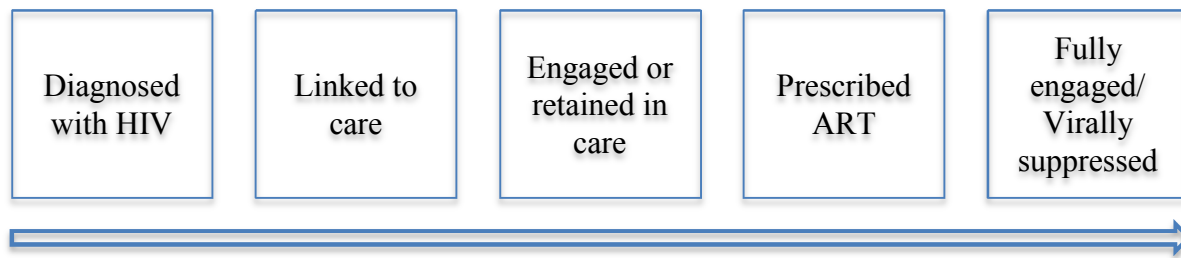
(Adapted from Gardner et al. 2011)

Besides the delay in diagnosing HIV, there is also delay in care initiation after diagnosis. In the US, delayed entry into HIV medical care is common. An estimated 75% of newly diagnosed persons initiate care six to twelve months after initial HIV diagnosis, while only 80%-90% link to care within three to five years.[59] In NC some 30,000 cases of HIV have been diagnosed and reported by the end of 2013 (Figure 2). Although the true number of persons seeking care was likely understated due to incomplete laboratory reporting, roughly half of these HIV-infected persons had one care visit during calendar year 2013. Approximately two-thirds of HIV-infected persons receiving at least one care visit in 2013 had a second visit three or more months later within the same year. In addition, viral suppression was documented for only 36.4% of the total cases.[41]

Figure 2   HIV care continuum among people with last known residence in North Carolina, 2009-2013
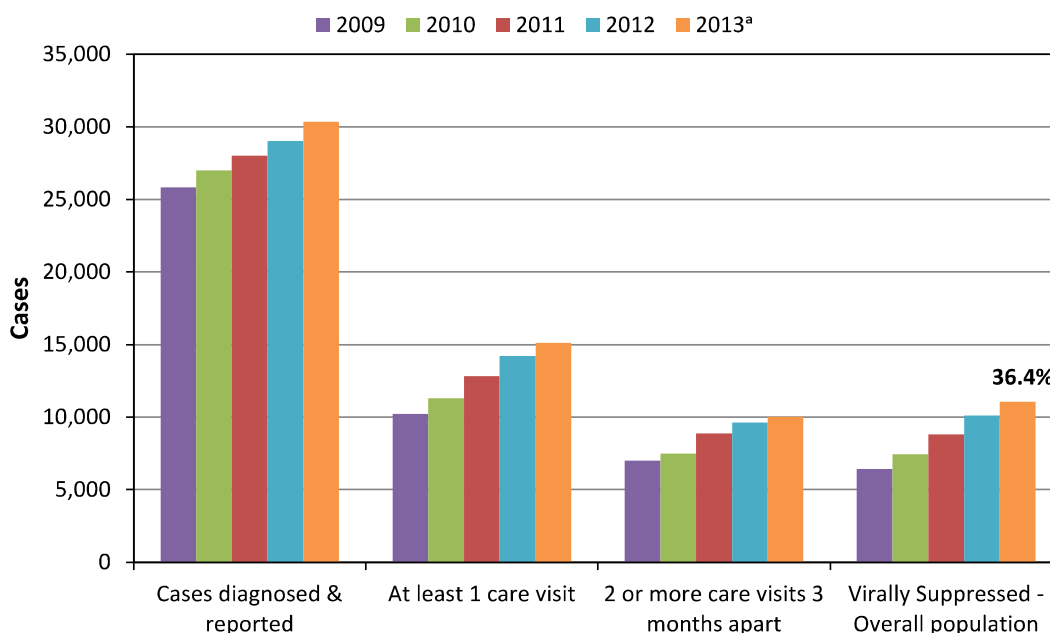
[a]2013 data are overestimated due to reporting delays for death information
[b]Legend: year shown refers to the year in which care measures were evaluated; cases were diagnosed and reported between the beginning of the epidemic and the end of the prior year.
Source: 2013 North Carolina HIV/STD Epidemiologic Profile

In 2015, additional data sources were available to measure points along the HIV care continuum in NC, including Ryan White (RW) service data, CAREWare, laboratory claims from Medicaid, and ARV medications dispensed from the AIDS Drug Assistance Program (ADAP) and Medicaid.[60] Of an estimated 35,700 persons living with HIV infection in NC in 2015, 32,130 (90%) were diagnosed and reported though 2014. Approximately 71% of those diagnosed and reported had at least one care marker (e.g., viral load (VL), CD4) in a year, and 59% were virally suppressed.[60] While these percentages were an improvement from previous estimates, barriers along each point of the continuum prevent many HIV-infected persons from ultimately achieving viral suppression.

2.4   Delayed Entry into HIV Medical Care

An estimated 17% to 29% of HIV-infected individuals do not enter care within six months of initial HIV diagnosis or initial clinic appointment (Table 1). The estimates vary on the basis of sample design and the defined time to entry to care.[7, 9, 10, 14, 16, 19, 20, 61] One prospective, five-year surveillance study conducted in St. Louis, Missouri reported that only 73% of newly diagnosed persons had evidence of an HIV primary care visit from 1998-2002.[8] Based on surveillance data for New York City residents diagnosed in 2003, 63.7% of newly diagnosed, HIV-infected persons initiated care within three months of diagnosis.[20] A study conducted in New York City using MMP surveillance data from 2007-2008 reported that among 513 persons in HIV care at the time of interview, 23% had entered care more than three months after initial diagnosis.[10]

Table 1   Studies examining delayed entry into HIV medical care

Source	Sample Design	Sample	% Delayed
> 3 months delayed entry into HIV care since baseline			
Turner et al. (*Arch Intern Med*, 2000)	national probability sample of persons in care	n = 1540, diagnosed by 02/93 and in care ≤ 3 years	29%
Turner et al. (*Arch Intern Med*, 2000)	national probability sample of persons in care	n = 1960, diagnosed by 02/95 and in care ≤ 1 year	17%
Torian et al. (*Arch Intern Med*, 2008)	New York City surveillance data	n = 1,928	19%
Reed et al. (*AIDS Patient Care STDS*, 2009)	US facility and population-based surveillance data	n = 3,942	28%
Jenness et al. (*AIDS Care*, 2012)	national probability sample of persons in care	n = 513	23%
> 4 months delayed entry into HIV care since baseline			
Marks et al. (*AIDS*, 2010)	meta-analysis	n = 6,586	28%
> 6 months delayed entry into HIV care since baseline			
Turner et al. (*Arch Intern Med*, 2000)	national probability sample of persons in care	n = 1540, diagnosed by 02/93 and in care ≤ 3 years	21%
> 12 months to delayed entry into HIV care since baseline			
Gay et al. (*AIDS*, 2006)	convenience sample	n = 348 (<u>note</u>: 37% initiated care at least once prior to study)	32%

The Supplement to HIV/AIDS Surveillance Project was a cross-sectional interview study designed to collect behavioral data from adults with HIV, most of whom had entered HIV care, in 18 states from 2000-2004. Among 3,942 respondents, 28% had delayed entry to care defined as three months or longer after initial diagnosis.[16] The Antiretroviral Treatment Access Study (ARTAS) examined time to care among recently diagnosed, HIV-infected persons in Atlanta, Baltimore, Los Angeles, and Miami. Only 60% of patients who received passive referrals to care linked to care within six months of initial diagnosis.[12] One cross-sectional study among patients living in NC initiating HIV medical care between 2000 and 2003 at the University of North Carolina HIV outpatient clinic reported that 32% of patients did not initiate care for at least one year after initial diagnosis.[9]

Factors associated with delayed entry into care include minority race[14, 15], injection drug use,[16] unemployment,[16] travel distance to care,[13] lacking private health insurance,[14-16] initial detection in a nonmedical environment,[20] and scheduling lag, defined as the time from the call to schedule a first patient visit to the appointment date.[14] Factors commonly identified as associated with difficulties in accessing HIV care in NC include rural residence, stigma, lack of transportation, and relatively few HIV-trained practitioners.[40] Race/ethnicity[13] and even laws and healthcare policies specific to some Southern states are relatively frequent barriers as well.[62]

Overall, though, little has been published detailing the relation of these patient characteristics, as well as of testing facility factors, to delayed entry to HIV medical care. In other areas of healthcare, co-location of medical services has been found to be significantly associated with more effective service delivery and better outcomes, which could have important implications for HIV linkage to care programs. One study examined no-show rates in coordinated vs. co-located integrated models of behavioral health care. Coordinated behavioral

health care was provided at a location separate from the primary care physician. Co-located care was provided in the same location as the primary care physician. Results showed that, among Medicaid patients, no-show rates for the co-located care group were significantly lower than for the coordinated care group ($p = 0.001$), which has important implications for integrating services into the offices of physicians, particularly for vulnerable populations.[63] A randomized trial assessed the efficacy of an integrated model of primary medical care for veterans with severe mental disorders. The integrated medical care clinic provided patients with on-site primary care as well as case management with collaboration from mental health providers. Researchers found that patients treated in the integrated care clinic were significantly more likely to have made a primary care visit, had greater average number of primary care visits, and had a significantly greater improvement in health as measured by a 36-Item Short-Form Health Survey.[64]

With regard to linkage to HIV medical care, The ARTAS-I was a CDC sponsored, two-arm randomized controlled trial comparing a brief strengths-based case management intervention with standard-of-care referral in linking recently diagnosed, HIV-infected persons to care. Due to successful, timely entry in the arm receiving case management services, ARTAS-II was funded to evaluate the same model in local and health state departments and community-based organizations (CBOs). Researchers used data from the ARTAS-II project, site visits, and project director reports to examine factors associated with timely linkage to HIV medical care. From October 2004 – June 2007, ARTAS-II obtained structural factor data from ten health departments or CBOs in rural, mid-sized and urban locations. Researchers found that in these settings, sites with co-located HIV medical care services had better linkage to care rates than non co-located sites (87% vs. 73%).[19]

Most research examining testing facility characteristics and time to entry into HIV medical care has assessed linkage models at large medical facilities or emergency departments in larger cities often co-located with HIV testing facilities. The rates of linkage to care within three months were often greater than 80-85%.[17, 18] However, even in large cities, initial diagnosis at sites in nonmedical environments (versus medical environments)[10] or sites without co-located HIV care (versus sites with co-located HIV care) was associated with delayed entry to care [community testing site (hazard ratio [HR], 1.9; 95% confidence interval [CI], 1.5-2.3); city jail (HR, 1.6; 95% CI, 1.2-2.0); STD/TB clinic (HR, 1.3; 95% CI, 1.1-1.6)].[20]

Notwithstanding the advantages of testing in facilities which have HIV medical care onsite, it is also important to consider how testing sites without co-located HIV medical care can facilitate patient initiation of care, since such sites detect many cases of HIV that would otherwise have gone undetected. This phenomenon is particularly relevant in resource-limited settings where access to medical care can be problematic, and a great need for general testing services remains. Thus, additional research is needed to assess the impact of various testing facility types on delayed entry into care in urban and rural settings in southern states such as NC and with a focus on subpopulations experiencing the highest rates of new HIV infections.

2.5 HIV and Depression

Once an HIV-infected person is engaged in care, it is crucial to address unmet needs that can compromise patient adherence and achievement of viral suppression. Depression, the most prevalent psychiatric disorder among HIV-infected patients after substance use disorders, has important implications for patient retention and quality of life.[26] Chander et al. reviewed depression prevalence estimates in the US among small, regional subpopulations of HIV-infected individuals prior to 2000, and reported estimates as high as 48%.[65] More recent prevalence

estimates of depression among HIV-infected persons engaged in care range from 20% - 30%.[66] These estimates are at least twice those of general population national depression prevalence estimates, which range from 4% - 7% based on data from the Behavioral Risk Factor Surveillance System.[67, 68] A 2014 study using national surveillance data for HIV-infected persons in care reported a 12.4% prevalence of major depression (95% CI, 11.2-13.7) and a 13.2% prevalence of other depression (95% CI, 12.0-14.4).[68]

Numerous prospective and cross-sectional studies have examined associations of depression or depressive symptoms with ART adherence, viral load, and immunological outcomes. A nested cohort analysis of 873 HIV-infected men in the Multicenter AIDS Cohort Study examined predictors and effects of highly active antiretroviral therapy (HAART) interruption and discontinuation. Approximately 28% of the study population was depressed, based on a Center for Epidemiologic Studies Depression (CES-D) Scale score greater than 15. Depression was significantly associated with HAART interruption [(adjusted odds ratio (aOR), 1.97; 95% CI, 1.38-2.80)] and HAART discontinuation (aOR, 1.42; 95% CI, 1.17-1.72).[25] A prospective study of 961 HIV-infected women participating in the Women's Interagency HIV Study examined the associations of race, sociodemographic, and behavioral characteristics with response to HAART. Approximately 50% of the women were classified as depressed (CES-D >16) at their last pre-HAART visit. Depression was found to be significantly associated with poorer virologic response (aOR, 0.81) and increased likelihood of immunologic failure (aOR, 1.98). In addition, depression was significantly associated with a higher risk of all-cause death, unrelated to AIDS (aOR, 1.65).[30]

A cross sectional study among 887 HIV-infected patients receiving HAART in western Denmark and central Copenhagen, part of a large population-based cohort, reported depression

prevalence of 47%. Researchers found that depression was significantly associated with increased odds of virological failure (aOR, 2.09; 95% CI, 1.19-3.68).[23] A study of 1910 HIV-infected patients reported that the 16% of patients with depression, measured using the Composite International Diagnostic Interview, were significantly more likely to be non-adherent to ART medication during the week prior to interview in comparison to patients who were not classified as depressed.[29]

Given empirical evidence of associations of depression with non-adherence and immunological failure, treatment of depression may improve outcomes among HIV-infected persons. A retrospective cohort study of HIV-infected persons who received clinical services from Denver Health reported lower antiretroviral adherence among depressed patients not on antidepressant treatment compared to depressed patients on antidepressants ($P = 0.012$).[69] However, antidepressant non-adherence and concurrent substance abuse can obstruct the efficacy of antidepressants.[26] Additional studies assessing the association between antidepressants and ART adherence are needed, particularly among subpopulations with higher HIV prevalence. In addition, more approaches to alleviating mental illness should be explored.

2.6   HIV Case Management Services

One potential resource for facilitating treatment of depression among HIV-infected persons is case management. Case management, as defined by the Commission for Case Manager Certification, is a 'collaborative process that assesses, plans, implements, coordinates, monitors and evaluates the options and services required to meet the client's health and human service needs'.[70] A clear need for case management services persists among HIV-infected persons. In one study, depression and associated quality-of-life, coping strategies, social support, and use of health and social services were assessed among HIV-infected persons (N=297) in

Ontario, Canada. Results showed that depression was common (54.2%), and associated with a diminished health status. Depressed, HIV-infected persons used significantly more community-based service organizations and crises centers. Findings suggested that caseworkers and service organizations could improve access to medications as well as quality of life for HIV-infected persons.[71]

The majority of studies examining case management services among HIV-infected persons assessed the impact of these services on linkage to care, unmet needs, utilization of ART medications, or clinical outcome indicators unrelated to mental health. In a 2005 study, recently diagnosed participants in the ARTAS study were randomized to either standard of care passive referral or case management for linkage to local HIV clinics. The study reported that a higher proportion of participants in the case-managed study arm (N=136) visited an HIV clinician in comparison to those in the standard of care arm (N=137) at least once within six months (78% vs. 60%; adjusted relative risk (aRR), 1.36; $P = 0.0005$, one-tail) and at least twice within twelve months (64% vs. 49%; aRR 1.41; $P = 0.006$, one-tail).[12] A 2001 study assessed the efficacy of case managers on unmet needs and on utilization of medical care and ART medications among a national probability sample of HIV-infected persons (N=2437). Contact with a case manager at baseline was significantly associated with decreased unmet need for income assistance [odds ratio (OR), 0.54; 95% CI, 0.36-0.91], health insurance (OR, 0.54; 95% CI, 0.33-0.89), home health care (OR, 0.29; 95% CI, 0.15-0.56), and emotional counseling (OR, 0.62; 95% CI, 0.41-0.94) at follow-up. In addition, contact with a case manager was associated with higher utilization of two-drug (OR, 1.58; 95% CI, 1.23-2.03) and three-drug (OR, 1.34; 95% CI, 1.00-1.80) antiretroviral regimens at follow-up.[72]

In a cross-sectional study of 1133 HIV-infected individuals identified through outreach programs who knew their status and were not newly diagnosed, 12% had not received HIV medical care in the six months prior to the interview. In multivariable analyses, those with no care were less likely to have a case manager ($p < 0.001$) or use mental health services ($p < .001$), and had poorer mental health scores ($p < 0.05$).[35] The ARTAS-II recruited HIV-infected persons from ten study sites in the US. Five sessions with a case manager were scheduled over a 90-day period. HIV-infected persons who had two-five sessions with a case manager were significantly more likely to engage in HIV care compared to those who had fewer than two sessions.[19]

A 2013 study assessed linkage, retention in care, and viral suppression among newly diagnosed and prevalent HIV-infected persons identified from the District of Columbia Department of Health, which funds facilities to provide HIV case management. HIV-infected persons receiving care in facilities funded to provide case management were significantly more likely to be retained in care (aOR, 4.13; 95% CI, 1.93-8.85) than HIV-infected persons receiving care in facilities not funded to provide case management, though similarly likely to be virally suppressed (aOR, 1.06; 95% CI, 0.68-1.62).[73] In another study, the health service utilization of 72 subjects receiving directly administered HAART was analyzed for its effect on viral load at six-months. In adjusted multivariable analyses, case management services were significantly associated with virologic suppression at six months (aOR, 5.8; 95% CI, 1.1-30.5, $P = 0.04$).[32]

Given the clinical benefits of case management services, it is essential that case management workers be adequately trained. A total of sixteen HIV/AIDS case managers across NC participated in a three-month case management training program and later enrolled clients who received adherence training. Data showed that case managers felt well positioned to provide services; however, common barriers were lack of reimbursement for their time, inadequate

training, and insufficient knowledge of HIV/AIDS and medications. Without appropriate training and resources, case managers may negatively affect client adherence, which may directly affect the client's mental and clinical outcomes.[74]

Further research on the various stages of the HIV continuum of care, including the potential benefits of case management services on management of depression and ART adherence, is desirable, particularly in Southern states experiencing a multitude of barriers to HIV medical care and higher incidence in subpopulations. NC has an integrated surveillance system with multiple programs collaborating to maximize disease prevention and treatment efforts. Educational guidelines for health professionals are established through the NC AIDS Education and Training Center (AETC) Program. Led by HIV clinical experts equipped to provide local training and education, this program was established by the Department of Health and Human Services (DHHS) and the Health Resources and Services Administration (HRSA). Clinicians receive technical and clinical information on services, such as PrEP, which is disseminated to the patient population.[75] In addition to NC AETC, other targeted programs and HIV resources in North Carolina include partner notification, counseling and referral services, Care and Prevention in the United States, ADAP, and RW funding.[41] The proposed research will use a subset of NC surveillance data to assist state public health officials to identify weak points along the HIV care continuum and help identify strategies for improvement.

CHAPTER THREE: RESEARCH PLAN AND METHODS

3.1   Study Design Overview

The two specific aims for this dissertation research are:

> **Specific Aim 1**. Estimate the cumulative incidence of persons initiating HIV medical
> care following diagnosis, examine patient-level sociodemographic and behavioral
> characteristics associated with delay in initiating care, and assess time to care initiation in
> relation to characteristics of the facility where HIV was diagnosed.
>
> **Specific Aim 2**. Estimate the prevalence of probable current depression and 100% ART
> dose adherence in the past three days in relation to case management utilization in the
> previous twelve months.

Both aims were accomplished by analyzing NC data included in national surveillance systems
developed by the US CDC.

For Aim 1 we analyzed population-based, surveillance data from the 2015 eHARS, a
system developed by the CDC to enable states to collect and update sociodemographic and
clinical data on HIV-infected persons. The state of NC requires named reporting of all HIV and
AIDS diagnoses, all viral load and CD4 cell count values, all positive Western blot tests for HIV
antibody, and all HIV genotypes.[76, 77] Information on the type of testing facility at initial
diagnosis and clinical time points, such as the date of initial HIV diagnosis and the date for the
first viral load and/or CD4 count, are included in the eHARS dataset.

For Aim 2 we analyzed data for 2009-2013 from the NC MMP. The MMP is a surveillance system designed to capture behavioral and clinical data from HIV-infected persons who have at least one HIV medical care visit during the survey window each year. MMP data are gathered from personal interviews with sampled patients and from abstraction of medical records

3.2   Study Setting

The NC Division of Public Health's Communicable Disease Branch uses eHARS to monitor all persons either diagnosed with HIV in NC or diagnosed with HIV in another state and now living in NC. The state-run, population registry maintains risk factor information, HIV/AIDS diagnosis dates, residence at diagnosis, and testing site, for regular surveillance reporting to the CDC. Selected laboratory values, including CD4 cell counts <200 cells/mm^3 and detectable viral loads, are also reported in eHARS.

MMP uses a 3-stage probability proportional to size sampling design to obtain nationally representative, annual cross-sectional samples of HIV-infected adults receiving outpatient HIV medical care in the United States.[78-80] For each annual data collection cycle, US states and territories are sampled first, followed by outpatient facilities providing HIV care, and finally by HIV-infected adults aged 18 years and older who have at least one medical care visit in a participating facility during January – April of the respective collection year (Figure 3). All 50 states, the District of Columbia, and Puerto Rico (defined as primary sampling units [PSUs]) are eligible for selection. For these PSUs, probability of selection is proportionate to the number of HIV-infected patients seen from January to April in the study year.[78]

Figure 3   Medical Monitoring Project, multi-stage sampling design, 2009-2013

Stage 1: State/Territory ("Site")
Population: All U.S. States, D.C., Puerto Rico
Sample: 23 project areas (16 states, 6 separately-funded metropolitan areas, Puerto Rico)

Stage 2: Facility (Provider)
Population: Facilities providing HIV care in sampled state - large and small, public and private
Sample: ~40-60 facilities per project area

Stage 3: Patient
Population: HIV-infected adults ≥ 18 years of age who received care at a sampled facility between January and the end of April
Sample: 0 - 125 patients per facility; 400 patients per site (minimum)

Participating project areas include sixteen states (California, Delaware, Florida, Georgia, Illinois, Indiana, Michigan, Mississippi, New Jersey, New York, NC, Oregon, Pennsylvania, Texas, Virginia, and Washington), six separately funded large metropolitan areas (Chicago, Houston, Los Angeles County, New York City, Philadelphia, and San Francisco) within five of the sampled states, and Puerto Rico.[68, 79] A facility sampling frame is developed in each of the 26 project areas. An eligible facility provides HIV medical care, which is defined as having providers who prescribe antiretroviral therapy or order CD4 or HIV viral load tests. Only providers who manage their own patients' HIV medical care are included in the facility sampling frame. Patients are then sampled from each facility with a third-stage sampling probability. Each patient sample is used for only one data collection cycle, with a new sample of patients drawn from participating facilities in each data collection cycle.[79] For our research, we will only be utilizing MMP surveillance data from the state of NC.

3.3   Study Population

The study population for Aim 1 was drawn from all HIV-infected persons at least 18 years of age, residing in NC and alive as of December 31, 2015 as recorded in eHARS.

The study population for Aim 2 was drawn from respondents to the 2009-2013 MMP questionnaires. Respondents for each MMP annual data collection cycle were sampled to be representative of HIV-infected adults at least 18 years old, who had at least one medical care visit at a NC participating facility between January and April in a data collection year. The three-stage sampling schema within NC for each year is provided below (Figure 4). While patients with complete interview and medical record abstraction (MRA) data were sampled, we only used interview data. Our MMP 2009-2013 analytical sample included a total of 910 respondents 18 years of age or older – 602 males (67.2%), 297 females (31.3%), 10 transgender persons (1.3%), and 1 intersex person (0.1%).

Figure 4   North Carolina Medical Monitoring Project sampling schema by year, 2009-2013
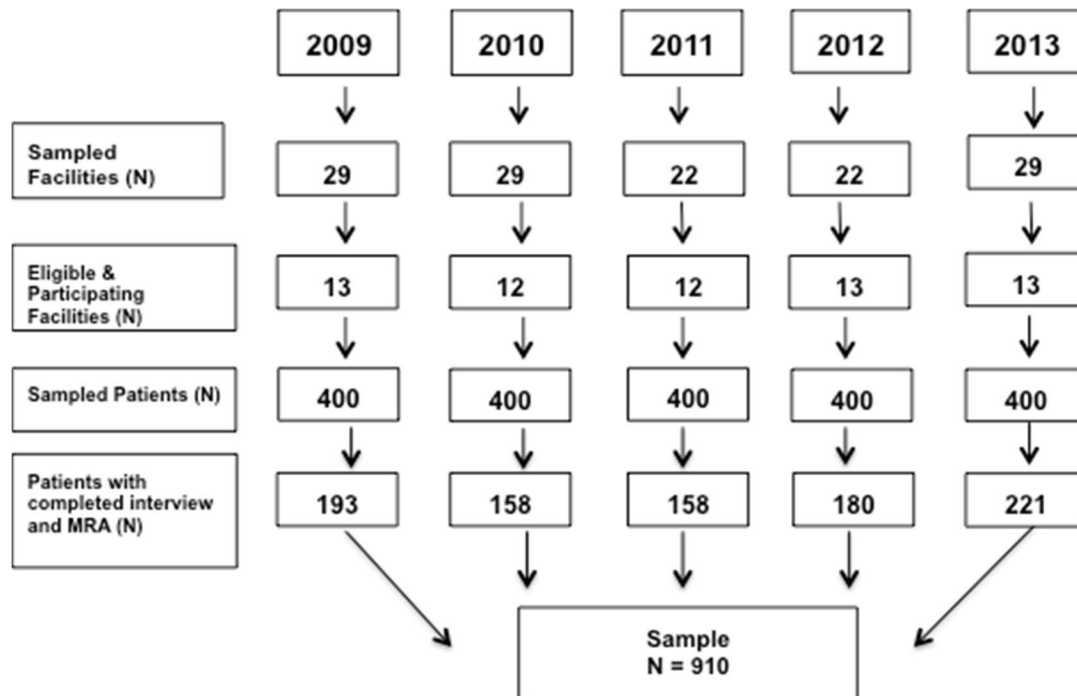
For each data collection year, the response rates among facilities and among patients in those facilities, adjusted for eligibility, were provided in the MMP response rate summary reports (Table 2). The facility response rate was calculated using the total number of eligible responding facilities and the total number of sampled participating eligible facilities. The adjusted patient response rate was calculated using the total number of sampled patients with overlapped interview data and MRA data, adjusted for eligibility. Although the response rates were lower than optimal, empirical research suggests that low response rates are not necessarily the result of nonresponse bias, particularly when probabilistic samples are drawn from well-constructed sampling frames.[81, 82]

Table 2   Summary of North Carolina response rates, 2009-2013

MMP Cycle	Facility Response Rate	Patient Response Rate	Combined Response Rate*
2009	72.22%	54.61%	39.44%
2010	66.67%	45.55%	30.37%
2011	60.00%	43.77%	26.26%
2012	68.42%	45.13%	30.88%
2013	87.50%	55.44%	48.51%

* = Facility response rate times patient response rate
Response rates provided by 2009-2013 MMP Response Rate Summary Reports[83]

3.4   Data Collection

enhanced HIV/AIDS Reporting System (eHARS)

Information obtained from each person diagnosed with HIV in NC is entered into a case report, which is then entered into eHARS. The data captured include the date of HIV diagnosis and clinical values and dates, obtained from laboratory testing such as CD4 counts and viral loads. Demographic and behavioral patient data include age, sex, race/ethnicity, and HIV transmission mode. The testing facility at initial HIV diagnosis was also recorded for most persons.

<u>Medical Monitoring Project (MMP) Questionnaire</u>

The most updated version of the MMP questionnaire used in our analyses had twelve sections. The first section (I) included participant identification (ID), facility ID, and the type and date of the interview. The next section (D) covered participant demographic characteristics such as type of residence, age, gender, education status, sexual orientation, and health insurance status. Participants were then asked to provide feedback on access to care (section A), including HIV testing and care experiences, sources of care, and met and unmet needs. The next section (R) gathered information on stigma and discrimination; quite often, HIV-infected individuals experiencing stigma and discrimination have difficulty taking prescribed HIV treatment medication and remaining adherent, which were ascertained in section T.

The largest portion of the questionnaire (section S) gathered information regarding sexual behaviors, including number of sex partners and types of sexual activity. In section U respondents reported on cigarette and alcohol use, non-injection drug use, and injection drug use. Section B assessed transmission risk factors, including questions about how participants may have acquired HIV and about their past partners' behaviors.

Sections P and M gathered information regarding prevention activities and depression, respectively. Depression was measured by asking the participant questions about his/her overall mood using the eight-item Patient Health Questionnaire depression scale (PHQ-8). This scale has been established as a valid diagnostic measure for depressive disorders in large population-based studies.[84]

The final two sections of the MMP questionnaire gathered information on respondents' gynecological and reproductive history (section G) and health conditions and preventive therapy (section C). Female respondents provided information regarding pelvic exams, Pap smears,

pregnancies and pregnancy outcomes. Specific health condition and preventive therapy questions included CD4 and VL dates, vaccination history and STD testing and diagnoses. An additional interview completion portion of the questionnaire (section E) confirmed respondent compensation, reassured confidentiality, and assessed the interviewer's confidence in the validity of the respondent's answers.

Medical Record Abstraction (MRA) – MMP Data

Though MRA data was not used in our analyses, these data were obtained from the medical charts of study participants with completed interview data to form an overlap dataset. In general, the MRA data gather the following information on respondents: patient demographics, a comprehensive medical history to include disease diagnoses and surgical histories, AIDS defining opportunistic illnesses, prophylaxis, hepatitis/*toxoplasma*/tuberculosis screening, immunizations, antiretroviral therapy, laboratory test results, HIV antiretroviral resistance testing, substance abuse, and mental health with an additional field for clinical notes and remarks.

Data Acquisition and Approval

eHARS and MMP data were made available through the NC Division of Public Health, Epidemiology Branch. A data use agreement (DUA) between the Division of Public Health and the University of North Carolina at Chapel Hill on behalf of the author of this dissertation authorized provision of data sets containing de-identified, protected health information. Appropriate safeguards (secured storage on an encrypted drive) were used to protect the data from misuse or inappropriate disclosure. All publications and/or presentations derived from the data provided under the DUA are to undergo the Division of Public Health, Epidemiology Section's clearance process.

The CDC have determined that MMP is a public health surveillance activity.[85] Because eHARS and MMP are not considered research, they are not subject to human subjects regulations including federal institutional review board (IRB review).[86] Funding for the MMP in NC was provided by a cooperative agreement (PS09-937) from the CDC. This doctoral dissertation does require oversight by the IRB at the University of North Carolina at Chapel Hill. The IRB determined that the dissertation research was exempt from full review because it is an activity using de-identified, secondary data conducted for public health purposes (IRB Review #: 14-2675).

3.5   Sample Weights

The MMP data were collected using a complex, multi-stage sampling scheme, which requires special analytical procedures.[87-91] Unequal selection probabilities, which necessitated weighted analysis, and appropriate methods for variance estimation were employed. The MMP-provided sample project area weights (pa_wgt_over), which adjust for nonresponse, and project area strata (pa_strat) and cluster (pa_clust) variables, which account for the design complexity, were applied to univariable, bivariable, and multivariable analyses using SAS 9.4, Cary, NC.

3.6   Analytic Methods

3.6.1   Patient and facility characteristics and time to HIV medical care initiation (Aim 1)

Measurements

Outcome: Time to initiation of HIV medical care was defined as the number of calendar days from the date of initial HIV diagnosis ('Day 0') to the date of the first CD4 or VL measurement. We calculated cumulative incidence of care initiation at various time points and, consistent with earlier studies,[10, 16, 20, 61] focused on delayed initiation defined as a first CD4 or

VL data ≥ three months since the date of HIV diagnosis (or no evidence of care) versus an earlier date.

Exposure: *Patient-level characteristics.* In relation to time to HIV care initiation, we examined age at initial HIV diagnosis (categorized at approximate quartiles: 17-24 years, 25-30 years, 31-44 years, and 45+ years), sex at birth (male, female), and race/ethnicity (non-Hispanic white, non-Hispanic black, and Hispanic/other). Due to small sample sizes, HIV-infected persons identifying as American Indian/Alaskan Native, Asian, Native Hawaiian/Pacific Islander, and multi-race were included in the Hispanic/other category. The following CDC hierarchical HIV transmission exposure categories were analyzed in relation to care initiation: MSM, injection drug use (IDU; including MSM/IDU), heterosexual transmission, and unknown HIV exposure.

Facility-level characteristics. We examined time to initiation of HIV care in relation to three characteristics of the facility at which the HIV diagnosis was made: whether HIV medical care was available at the facility (co-located HIV medical care), the total number of HIV diagnoses reported from the testing facility in 2015 (facility diagnosis volume, categorized at approximate quintiles), and a six-category version of the facility type code from eHARS. Descriptions of the strata of each facility characteristic are provided in Table 3.

Table 3   Classification of exposure

Testing Facility at Initial HIV Diagnosis
HIV medical care co-location
-    Site without co-located HIV medical care
-    Site with co-located HIV medical care (referent category)
Testing facility HIV diagnosis volume
-    15+ HIV diagnoses
-    7-14 HIV diagnoses
-    4-6 HIV diagnoses
-    2-3 HIV diagnoses
-    1 HIV diagnosis (referent category)
Testing facility type
-    Other/non-traditional[*]
-    STD clinic
-    HIV counseling & testing site
-    Inpatient hospital
-    Outpatient clinic
-    Outpatient private physician's office (referent category)

* Includes jails, prisons, blood bank and plasma centers, lab testing facilities, community centers, social service organizations, military processing centers, and university student health centers.

Data Analysis

All variables other than time to initiation of care were coded as dichotomous, nominal, or

ordinal categorical variables. ORs and 95% CIs were calculated using unconditional logistic

regression for bivariable associations of delayed entry into HIV medical care in relation to

patient sociodemographic and behavioral characteristics and testing facility characteristics. ORs

and 95% CIs were reported for comparability to published studies.[10, 16, 61] We would expect the

ORs to approximate relative risk estimates given a delayed initiation prevalence slightly greater

than 10%. We tested for collinearity, but did not observe any, among patient and facility risk

factors. Effect measure modification of the association between each patient and facility risk

factor and delayed care initiation by each additional patient and facility risk factor was examined

by comparing the Akaike Information Criterion (AIC) values of the reduced (main effects) and

full (main effects + interaction) models, where the model with the smaller AIC value was determined to have the better fit. This procedure indicated that including an interaction between sex and co-location of medical care improved model fit.

We then used multivariable unconditional logistic regression with a backward elimination modeling strategy with Wald chi-squared test $p < 0.10$ for retention to identify patient and facility risk factors independently associated with delayed entry into HIV medical care. The adjusted coefficients for facility volume displayed a clear dose-response relationship, so we elected to retain that variable despite its p-value of 0.25. Thus, all coefficients for patient and facility characteristics were adjusted simultaneously for the other characteristics, in a single multivariable, logistic regression model that included an interaction term for sex at birth with HIV co-location.

The Kaplan-Meier non-parametric product limit estimator was used to estimate the cumulative incidence of HIV care initiation according to days since HIV diagnosis. Persons either initiated care or were censored at the end of the date range for the data (June 15, 2016). The graphs of the cumulative incidence of HIV care initiation were stratified by testing facility characteristics: HIV care co-location, facility HIV diagnosis volume, and testing facility type. Facility HIV diagnosis volume was collapsed into low-volume (1-3 HIV diagnoses), medium-volume (4-14 HIV diagnoses), and high-volume (15+ HIV diagnoses) categories.

Of 1,269 participants, 14.1% (N=179) were diagnosed in a hospital as inpatients, and approximately 3.0% (N=33) had an initial HIV diagnosis occur in the emergency room (ER). Because some have argued that CD4/VL testing performed during an acute hospitalization or ER visit may not represent true HIV care initiation,[92] we conducted a sensitivity analysis that excluded these persons. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary,

NC). The IRB at the University of North Carolina at Chapel Hill determined that these analyses of data collected for public health surveillance purposes were exempt from full review (IRB # 14-2675).

3.6.2 HIV Case Management Utilization and Depression (Aim 2)

Measurements

Outcome: Depression was identified from responses on the PHQ-8.[84] The PHQ-8 assigns a score for the number of days in the previous two weeks that the respondent experienced each of the eight criteria for depression from the *Diagnostic and Statistical Manual of Mental Disorders, fourth* edition (DSM-IV).[93] Probable, current depression (we combined *major* with *other*) was defined based on Kroenke and Spitzer's 2002 algorithm of experiencing at least two depressive symptoms for "more than half the days" in the preceding two weeks, with at least one symptom being depressed mood or anhedonia. This diagnostic algorithm yields comparable judgments to a total PHQ-8 score of ≥ 10, which we also examined.[84, 94]

The prevalence of self-reported 100% ART dose adherence in the past three days was estimated using AIDS Clinical Trials Group measures.[95] ART dose was defined as either a single tablet or multiple tablets taken concurrently. At the time of interview, participants were asked, "In the past three days, were you 100% dose adherent to your ART medicine?" If the respondent missed part of a dose, they were instructed to report that incident as a missed dose. HIV-infected participants were recorded as either 100% ART dose adherent or not 100% ART dose adherent in the past 72 hours. We also analyzed the MMP question about ART schedule adherence.

Exposure: The exposure for aim two was utilization of case management services in the twelve-month period prior to the participant interview date. Case management services were examined dichotomously (Yes = 1, No = 0).

Additional covariates: Various characteristics were considered as potential correlates and/or effect measure modifiers of the associations between utilization of case management services in the previous twelve months and 1) probable current depression, and 2) 100% ART dose adherence in the past three days. Sociodemographic risk factors included age at interview (18-29, 30-39, 40-49, ≥ 50 years), gender (male, female, transgender/intersex), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic/Latino, other), sexual orientation (heterosexual, homosexual, bisexual, other/unclassified), education (< high school, high school or equivalent, > high school), yearly household income ($0-$19,999, $20,000-$39,999, $40,000-$74,999, ≥ $75,000), federal poverty level (living at or below, versus above, the poverty level, defined per 2012 standards using household income and size),[96] and health insurance (public or private, RW/ADAP only, uninsured). Because NC has many rural areas requiring long travel distances to visit medical providers, we examined the need for transportation assistance services in the previous twelve months (yes/no). Behavioral risk factors examined included alcohol consumption in the previous twelve months and current smoking status (yes/no).

Data Analysis

The distributions of sociodemographic and behavioral variables, the utilization of case management services in the previous twelve months, probable current depression, and 100% ART dose adherence in the past three days were summarized with unweighted counts and weighted percentages. All variables were coded as dichotomous, nominal, or ordinal categorical. Rao-Scott chi-square statistics accounting for survey design, and prevalence ratios (PRs) with 95% CIs were calculated for bivariable associations of sociodemographic and behavioral characteristics with 1) case management utilization in the previous twelve months, 2) probable current depression, and 3) 100% ART dose adherence in the past three days.

Effect measure modification was examined for each variable using a product interaction term and an adjusted Wald test with a 0.15 significance level. Potential confounders of the relation between case management utilization and probable current depression (Figure 5), as well as ART dose adherence (Figure 6), were selected *a priori* from literature and with the use of a directed acyclic graph (DAG). Adjusted PRs and 95% CIs were calculated using multivariable Poisson models with robust variance to account for violations of the distribution assumptions. We assessed possible collinearity among variables using variation inflation factors; no collinearity was noted. Analyses were performed using Stata version 14 (StataCorp, College Station, TX) and SAS 9.4 (SAS Institute, Cary, NC). Except where noted, all analyses incorporated the MMP-provided sample design and weights, to account for clustering, unequal selection, and nonresponse.

Figure 5   Causal diagram of the relationship between the receipt of case management services in the previous twelve months and probable, current depression
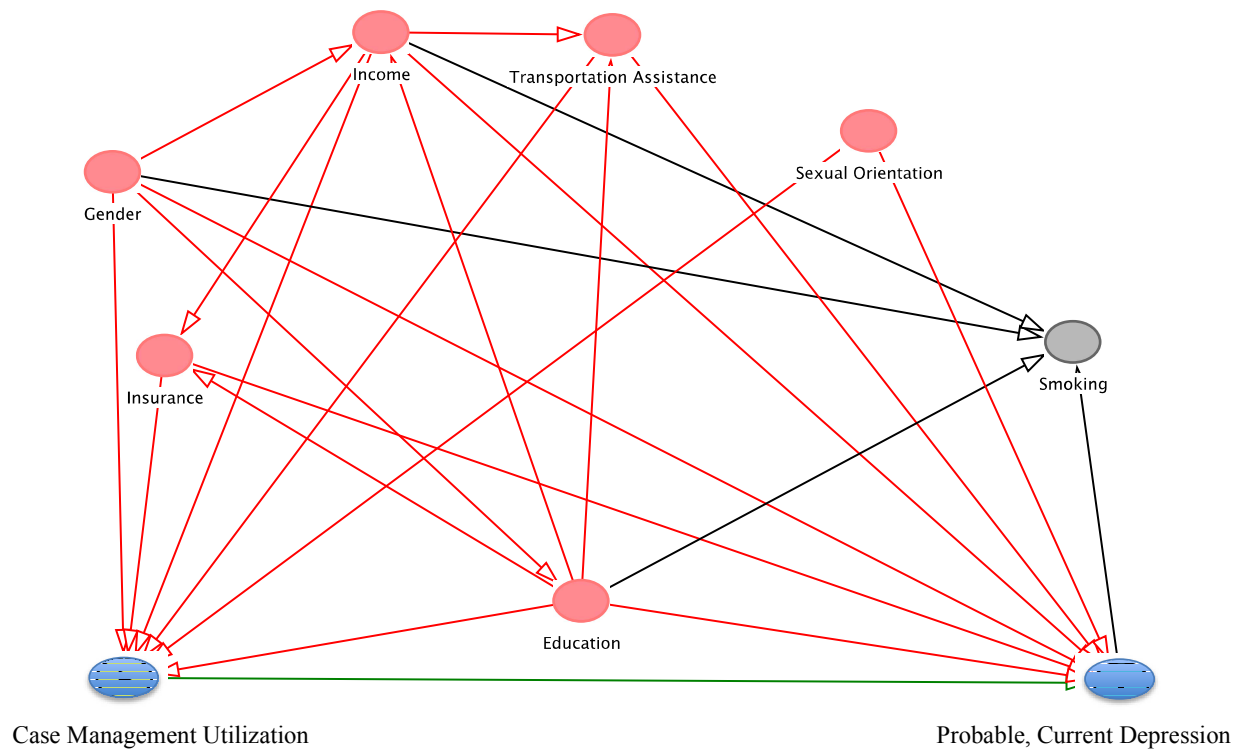
Figure 6   Causal diagram of the relationship between the receipt of case management
            services in the previous twelve months and ART dose adherence
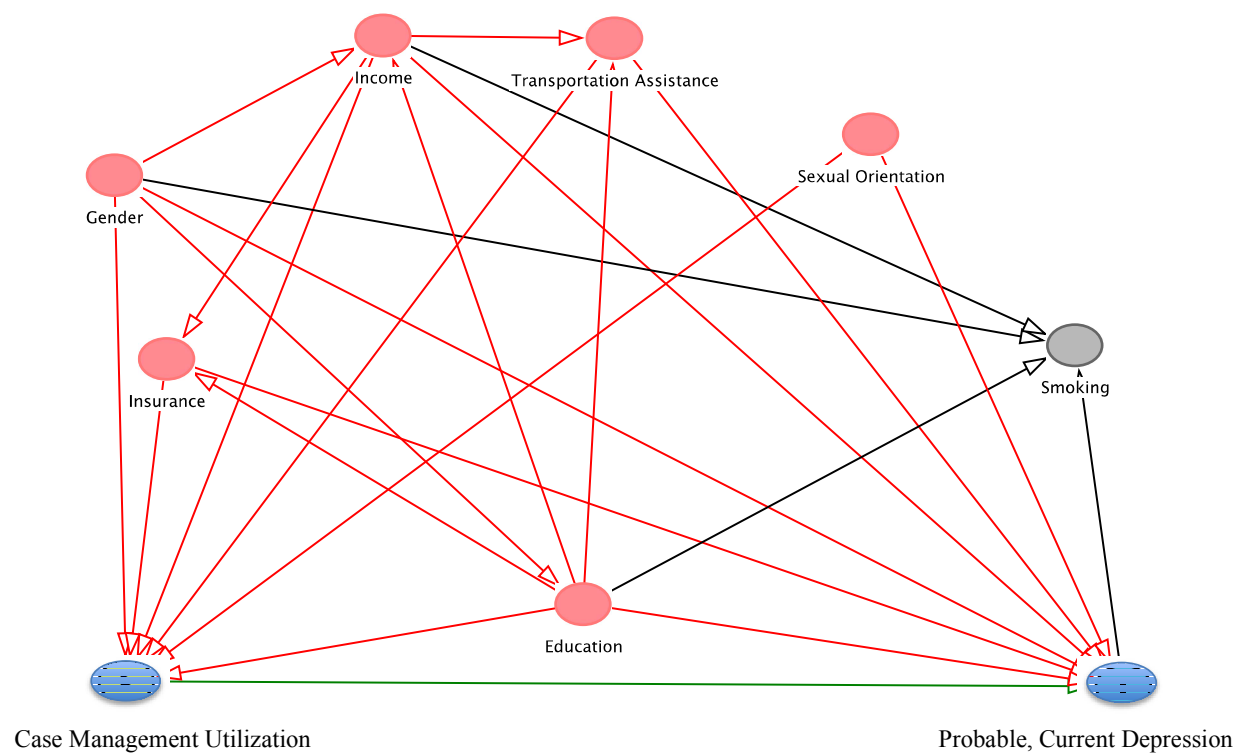
CHAPTER FOUR: DELAYED INITIATION OF HIV MEDICAL CARE AND ASSOCIATED PATIENT AND FACILITY CHARACTERISTICS AMONG ADULTS NEWLY DIAGNOSED WITH HIV IN NORTH CAROLINA

4.1 Background

Approximately 1.2 million people in the US were living with HIV as of 2015.[37] Although new HIV diagnoses declined 19% between 2005 and 2014,[37] incidence rates remain high among MSM (67% of incident cases), non-Hispanic blacks (45% of incident cases), Hispanics/Latinos (24% of incident cases), and residents of the South (HIV incidence 16.8 per 100,000 persons). Incidence rates (per 100,000 people) in the Northeast, West, and Midwest are lower at 11.6, 9.8, and 7.6, respectively.[37, 97]

The *NHAS: Updated to 2020* outlines strategic initiatives to prevent the spread of HIV. First put forward in 2010, the main goals of the Strategy are to improve the national response to the epidemic by reducing new HIV infections, increasing access to care while optimizing health outcomes, and reducing HIV-related health disparities and inequities.[50, 98] Given persistent transmission among specific demographic and geographic subpopulations despite increases in HIV testing rates, the 2020 update emphasizes improving key components of the HIV care continuum, namely timely initiation of HIV medical care upon diagnosis, prescription of and adherence to ART, retention in care, and achievement of viral suppression.[21, 50]

Focusing on each step of the HIV care continuum will help to identify and alleviate barriers to HIV care engagement and retention. Persons living with HIV in Southern states, especially, face major challenges to HIV care initiation due to shortages of trained medical and mental health professionals,[40, 46] lack of personal or public transportation,[40, 46] high STD rates

and poor medical infrastructures,[39, 40, 62] racial disparities,[62, 99] limitations in access to care due to lack of health insurance,[62] and few systems of support and counseling.[45] By 2013, NC met the 2015 NHAS goal of increasing HIV testing (ever tested) by four percentage points, from 44.2% to 48.4%.[100] Timely initiation of HIV care, with ART, significantly reduces the rate of HIV transmission [51] and also maximizes the benefits of treatment for the patient.[98]

Several studies have assessed delay in initiating HIV care following HIV diagnosis.[7, 9, 10, 16, 20, 61] These studies have used various time intervals following initial HIV diagnosis (commonly three, six, and twelve months) and study populations, including patients identified from public health surveillance in US cities and national probability samples of persons in care, to examine patient and testing facility characteristics as potential correlates of delayed care initiation. Patient-level characteristics associated with a delay (entry into HIV care three or more months after initial diagnosis) include male gender;[16] black,[61] Latino,[61] and non-white race;[20] younger age;[10] IDU;[10, 20] MSM and IDU HIV transmission exposure modes;[16] unemployment;[16] and birth outside of the US.[20] The national ARTAS-II project reported that persons diagnosed at HIV testing sites with co-located HIV care services entered HIV care significantly earlier than persons diagnosed at sites without co-located care.[101] In New York City, persons diagnosed at a community testing site,[20] city correctional system,[20] STD or tuberculosis clinic,[20] or a non-medical facility[10] initiated HIV care later than persons diagnosed at a facility with co-located medical care.

There are no statewide studies of delayed initiation of HIV care within the Southern US, a region plagued by poor health indicators and disproportionately affected by the HIV epidemic.[39] We used population-based, state surveillance data for 2015 for NC, the state with the 8th highest number of new HIV diagnoses that year,[37, 97] to estimate the cumulative incidence of

persons initiating HIV care according to time since diagnosis, to examine patient-level

sociodemographic and behavioral characteristics associated with delay in initiating care, and to

assess time to care initiation in relation to characteristics of the facility where HIV was

diagnosed.

4.2   Methods

enhanced HIV/AIDS Reporting System (eHARS)

eHARS is a surveillance system developed by the CDC to enable states to collect and

update sociodemographic and clinical data on persons living with HIV. The NC Division of

Public Health's Communicable Disease Branch maintains the NC eHARS. According to NC

General Statute 130A, all clinicians or persons in charge of laboratories are required to report a

HIV diagnosis to the local health director/health department within 24 hours.[76] Laboratory

results from tests to determine the absolute and relative counts for the T-helper (CD4) subset of

lymphocytes and all results from tests to determine HIV VL are also required to be reported

(10A NCAC 41A.0101 section b4).[77] The Branch uses eHARS to maintain statistics on all

persons either diagnosed with HIV in NC or diagnosed with HIV in another state and currently

residing in NC. eHARS stores sociodemographic, geographic, and HIV transmission risk data as

well as clinical laboratory testing dates and values.

Study Population

We defined our target study population as all adults (age 18 years and above) newly

diagnosed with HIV in NC between January 1 and December 31, 2015, and believed to be alive

and residing in NC as of the end of 2015. According to the 2015 NC HIV/STD Surveillance

Report, 1,345 persons (all ages) were newly diagnosed with HIV in the state during 2015.[42] The

NC Communicable Disease Branch provided an eHARS dataset with data for the 1,272 persons

meeting our inclusion criteria (age ≥18, NC residence through end of 2015). We excluded three

patients missing information on key facility-level variables, leaving 1,269 persons.

eHARS contains the date of each person's initial, Western-blot confirmed HIV diagnosis.

Reporting guidelines specify that the diagnosis date is the date that the specimen for an

individual's first positive HIV test result was drawn.[102] The dataset also included the dates of the

earliest and most recent CD4 counts and VL measurements through June 10, 2016. The earliest

CD4 or VL measurement was treated as the person's date of HIV care initiation. In the final

dataset, 94 patients lacked any CD4 or VL measurement and were treated as having not entered

care as of June 15, 2016 and censored on this date.

Individual-level characteristics

We examined age at initial HIV diagnosis (categorized into approximate quartiles: 17-24

years, 25-30 years, 31-44 years, and 45+ years), sex at birth (male, female), and race/ethnicity

(non-Hispanic white, non-Hispanic black, and Hispanic/other). Due to small counts, persons with

HIV identifying as American Indian/Alaskan Native, Asian, Native Hawaiian/Pacific Islander,

and multi-race were included in the Hispanic/other category. The following CDC hierarchical

HIV transmission categories were utilized: MSM, IDU (including MSM/IDU), heterosexual, and

unknown.

Facility Characteristics

We examined time to initiation of HIV care in relation to three characteristics of the

facility at which the HIV diagnosis was made: whether HIV medical care was available at the

facility (co-located HIV care), the total number of HIV diagnoses reported from the testing

facility in 2015 (facility diagnosis volume), and the type of facility (e.g., STD clinic).

Testing Facility with Co-located HIV Care

Co-located HIV care was defined as the presence of an onsite HIV medical provider who prescribed ART. Testing facilities in NC with co-located HIV care were identified using the *NC ONE CALL HIV Provider Directory*, which lists all licensed HIV medical providers and associated medical groups in the state by county. *ONE CALL* was developed in 2013 through a partnership between the Division of Infectious Diseases at the University of North Carolina at Chapel Hill School of Medicine and the Communicable Disease Branch of the NC Division of Public Health.[103] By matching the names of testing facilities in the eHARS dataset with the *ONE CALL* provider directory, we coded all eligible persons in terms of whether their initial HIV diagnosis was made at a testing facility with co-located HIV medical care.

Testing Facility HIV Diagnosis Volume

The annual HIV diagnosis volume for each eligible person's testing facility at HIV diagnosis was categorized according to approximate quintiles: 1 HIV diagnosis, 2-3 HIV diagnoses, 4-6 HIV diagnoses, 7-14 HIV diagnoses, and 15+ HIV diagnoses.

Testing Facility Type at Initial HIV Diagnosis

HIV testing facilities are assigned one of twenty-six codes in eHARS according to organizational and institutional characteristics. For our analyses, on the basis of these codes, we created six categories: (1) "Private physician's offices" included licensed medical physicians and medical groups providing general or specialty medical care to ambulatory patients; (2) "STD clinics," typically housed in county health departments, provided testing and treatment, or referrals for treatment, specifically for STDs; (3) "HIV counseling and testing sites," predominantly housed within county health departments or non-profit community organizations, were operated to provide testing for HIV/AIDS and referrals for counseling and treatment;

(4) "Inpatient hospitals" included all NC hospitals providing inpatient medical care;

(5) "Outpatient clinics" were facilities providing general or specialty medical care to ambulatory patients, including hospitals' outpatient services, Departments of Veteran Affairs, and freestanding urgent care and medical centers; and (6) "Other" (or "Non-traditional testing facilities") included all other facilities from which positive tests were reported, such as jails and prisons, blood bank and plasma centers, lab testing facilities, community centers, social service organizations, military processing centers, and university student health centers. Our "Other" facility type included the eHARS "Other" category as well as other facility types with fewer than 50 reported patients.

Time to Initiation of and Delayed Entry into HIV Medical Care

Time to initiation of HIV care was defined as the number of calendar days from the date of HIV diagnosis ('Day 0') to the date of the first CD4 or VL measurement. We estimated the cumulative incidence of care initiation at various time points and, consistent with earlier studies,[10, 16, 20, 61] focused on delayed initiation defined as a first CD4 or VL ≥ three months since the date of HIV diagnosis (or no evidence of care initiation).

Statistical Analysis

All variables other than time to initiation of care were coded as dichotomous, nominal, or ordinal categorical variables. ORs and 95% CIs were calculated using unconditional logistic regression for bivariable associations of delayed entry into HIV care in relation to patient sociodemographic and behavioral characteristics and testing facility characteristics. ORs and 95% CIs were reported for comparability to published studies.[10, 16, 61] We would expect the ORs to approximate relative risk estimates given a delayed initiation prevalence slightly greater than 10%. We tested for collinearity using condition indices, but did not observe any, among patient

and facility characteristics. Effect measure modification of the association between each patient

and facility characteristic and delayed care initiation by each additional patient and facility

characteristic was examined by comparing the AIC values of the reduced (main effects) and full

(main effects + interaction) models, where the model with the smaller AIC value was the best fit.

We then used multivariable unconditional logistic regression with a backward elimination

modeling strategy, with Wald chi-squared test $p < 0.10$ for retention, to identify patient and

facility characteristics independently associated with delayed entry into HIV care. The adjusted

coefficients for facility volume displayed a clear dose-response relationship, so we elected to

retain that variable despite its p-value of 0.25. Thus, all coefficients for patient and facility

characteristics were adjusted simultaneously for the other characteristics in a single

multivariable, logistic regression model that included an interaction term for sex with HIV care

co-location.

The Kaplan-Meier non-parametric product limit estimator was used to estimate the

cumulative incidence of HIV care initiation according to days since HIV diagnosis. Persons

either initiated care or were censored at the end of the date range for the data (June 15, 2016).

The graphs of the cumulative incidence of HIV care initiation were stratified by testing facility

characteristics: HIV care co-location, facility HIV diagnosis volume, and testing facility type.

Facility HIV diagnosis volume was collapsed into low-volume (1-3 HIV diagnoses), medium-

volume (4-14 HIV diagnoses), and high-volume (15+ HIV diagnoses) categories.

Of 1,269 participants, 14.1% (N=179) were diagnosed in a hospital as inpatients, and

approximately 3.0% (N=33) had an initial HIV diagnosis occur in the emergency room (ER).

Because some have argued that CD4/VL testing performed during an acute hospitalization or

emergency room visit may not represent true HIV care initiation,[92] we conducted a sensitivity

analysis that excluded these persons. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC). The IRB at the University of North Carolina at Chapel Hill determined that these analyses of data collected for public health surveillance purposes were exempt from full review (IRB # 14-2675).

4.3 Results

Patient and Facility Descriptive Characteristics

The 1,269 persons newly diagnosed with HIV were largely male (80.2%), self-identified as non-Hispanic black (64.3%), and classified in the MSM transmission category (56.7%) (Table 4). About one in six persons (N=205) were diagnosed at a facility with co-located HIV care. Patients received their HIV diagnosis at an outpatient private physician's office (21.7%), STD clinic (18.4%), HIV counseling and testing site (14.1%), hospital (inpatient, 14.1%), outpatient clinic (9.5%), or at a non-traditional testing facility such as a blood bank, plasma donation center, jail, or prison (22.2%).

Nearly all patients (N=1,175, 92.6%) had evidence of initiation of HIV care (median of 16 days from date of diagnosis, ranging from 0 to a high of 407 for the right-censored distribution, IQR=35.0). Nearly two-thirds (63.8%, N=810) of patients had a care initiation date within one month after diagnosis, 267 (21.0%) initiated care between one and three months after diagnosis, and 98 (7.7%) initiated care after three months.

The 98 patients with a care initiation date over three months after the diagnosis date were similar to the 94 (7.4%) patients with no date of care initiation across all patient and facility characteristics except transmission category (Table 4). Combining these two groups yields an overall percentage with delayed care of 15.1% (N=192). Those with delayed care were more likely to be younger, born male, non-Hispanic black. Delay was more common for persons

diagnosed at a facility without co-located HIV care, or at a facility other than a physician's office, outpatient clinic. The proportion of persons with delayed care initiation was positively correlated with higher facility diagnosis volume.

Patient and facility characteristics were associated with one another. For example, among facilities that reported 4-14 HIV diagnoses in 2015, the percentage with co-located HIV medical care (25.5%, not shown) was more than twice the corresponding percentages among facilities with a lower (9.7%) or higher HIV diagnosis volume (12.4%). Similarly, facilities that reported 15 or more HIV diagnoses in 2015 were predominantly HIV testing and counseling sites (41.6%) and STD clinics (30.5%); only 12.8% of such facilities were hospitals diagnosing inpatients, and none was an outpatient clinic or physician's office. Facility diagnosis volume was also related to the patient age, sex, race/ethnicity, and transmission category, with the highest volume category having proportionately more patients who were age 30 years or younger (55.6%), male (86.4%), non-Hispanic black (71.6%), MSM transmission risk (67.5%), and IDU (6.6%). Patients age 30 years or younger comprised approximately two-thirds of patients diagnosed at STD clinics and at HIV counseling and testing sites, and nearly half of patients at facilities in the "other/non-traditional" category, but were in the minority at other facility types.

Risk Factors for Delayed Initiation of HIV Medical Care

Patient-level

In the adjusted analyses (N=1,269), individuals between the ages of 17 and 24 years at time of HIV diagnosis were more likely to have delayed entry into HIV care (aOR, 2.14; 95% CI, 1.26-3.63), as were persons 25 to 30 years of age (aOR, 1.99; 95% CI, 1.18-3.34), compared to persons 45 years and older (Table 5). Females were less likely to have delayed entry into care than males (OR, 0.59; 95% CI, 0.38-0.92). Although non-Hispanic blacks were more likely to

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have delayed entry into care in the crude analysis, the association was substantially attenuated

after adjustment (aOR, 1.14; 95% CI, 0.72-1.80, versus non-Hispanic whites). Compared to

persons with MSM HIV transmission exposure, persons reporting unknown contact (aOR, 3.56;

95% CI, 2.24-5.66) were more likely to have delayed entry into HIV medical care, as were

persons acquiring HIV through IDU exposure (aOR, 2.73; 95% CI, 1.29-5.76). Associations

between patient-level characteristics and delayed care initiation were similar in the sensitivity

analysis that excluded 212 patients (16.7%) diagnosed in a hospital or ER setting; the largest

difference was an aOR of 3.21 (95% CI, 1.47-7.00) for persons acquiring HIV through IDU

exposure.

Testing Facility Characteristics

The time-to-event analysis suggested that persons diagnosed at a facility with co-located

HIV care initiated care more quickly than persons diagnosed at a facility without co-located HIV

care (Figure 7). When persons diagnosed in the hospital or ER were excluded resulting in 1,057

persons (lower graph), Kaplan-Meier curves were similar, although diagnosis at a facility with

co-located HIV care appeared to be slightly more advantageous in the first week after diagnosis

compared to the original analysis (upper graph). In the original analysis, by one month post-

diagnosis, 70.3% of patients testing positive at a facility with co-located HIV medical care

initiated HIV care, compared to 58.2% of patients diagnosed at a facility without co-located HIV

medical care. However, the relationship between co-located care and delayed care initiation was

substantially modified by sex. Males diagnosed in a facility without co-located HIV medical care

had almost three times the odds of delayed care initiation as males diagnosed in a facility with

co-located care (aOR, 2.94; 1.51-5.74), whereas among females there was no evidence that being

diagnosed at a facility without co-located care increased the odds of delayed care initiation

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compared to diagnosis at a facility with co-located care (aOR, 0.85; 95% CI, 0.28-2.52) (Table 5). Associations were similar when persons with a hospital (inpatient) or ER diagnosis were removed in our sensitivity analysis (aOR for delayed care initiation comparing no co-located to co-located care in males, 2.59; 95% CI, 1.31-5.11; females, 0.80; 95% CI, 0.23-2.77).

Although patients diagnosed at a medium-volume facility (4 to 14 HIV diagnoses) had the quickest entry into HIV medical care initially, by the end of one month patients diagnosed at low-volume facilities (1 to 3 diagnoses per year) were most likely to have initiated care, with patients diagnosed at high-volume facilities (15 or more diagnoses) having the most delay throughout the first three months (Figure 8, Logrank $p<0.0001$). In our sensitivity analysis, diagnosis at a low-volume facility was most advantageous approximately one week after diagnosis as opposed to one month as observed when these persons were included in the main analysis.

The clear monotonic association between testing facility HIV diagnosis volume and delayed entry into HIV care was somewhat muted after adjustment, but was still evident (Table 5). Compared to patients diagnosed at facilities with one diagnosis, patients diagnosed at facilities with 15 or more diagnoses were most likely to have delayed entry into HIV medical care (aOR, 1.76; 95% CI, 0.99-3.11), and patients reported from facilities with 7 to 14 diagnoses had higher odds of delayed care initiation (aOR, 1.74; 95% CI, 0.98-3.09). For each facility volume category, crude and adjusted odds ratios in the sensitivity analysis were similar to those in the original analysis.

Figure 9 shows that the great majority (nearly 80%) of persons whose HIV was diagnosed as hospital inpatients received a CD4 or VL measurement within one week of diagnosis. Patients diagnosed at outpatient clinics and private physician's offices also had high

care initiation; about 70% had received a CD4 or VL measurement by three weeks after diagnosis. The cumulative incidence of care initiation among those diagnosed at STD clinics, HIV counseling and testing sites, and other/non-traditional facilities appeared to plateau at around 65% by approximately two months after HIV diagnosis. Even after adjustment for patient and other facility characteristics, HIV diagnosis at a STD clinic (aOR, 3.64; 95% CI, 1.91-6.96), an HIV counseling and testing site (aOR, 3.12; 95% CI, 1.55-6.30), or other/non-traditional facilities (aOR, 3.12; 1.71-5.70) versus diagnosis at an outpatient clinic or private physician's office remained strongly associated with delayed entry into HIV medical care. These associations were similar when we excluded the 212 persons diagnosed as hospital inpatients or in the ER.

4.4   Discussion

We analyzed surveillance data for all adults diagnosed with HIV in 2015 in NC, a Southern state ranking 8th in HIV diagnoses in 2015.[104] This study is one of few to examine delay in HIV care initiation in this US region,[14] where HIV transmission continues at a high level, and is also the first study to consider testing facility diagnosis volume as a possible factor associated with delayed initiation of HIV care.

Published US estimates of delayed HIV care initiation, defined as three or more months since the date of initial HIV diagnosis, range from 17% to 29%.[7, 9, 10, 16, 20, 61] In our study, only 15.1% of newly diagnosed persons had not initiated care within three months (the percentage rose to 16.2% when we exclude persons diagnosed while hospital inpatients or in the ER). On the other hand, even with inclusion of these persons, only 63.8% of newly diagnosed NC residents initiated care within one month, considerably lower than the 2015 national goal of 85%.[100]

Younger age,[62, 105] male gender,[62, 105] minority race,[39, 62, 105] and MSM,[62, 106] are persistent risk factors for HIV infection in the US, particularly in the South. These factors are also associated with delayed entry into HIV care nationally.[61] We found the same in NC during 2015 for younger age, male sex, and non-Hispanic black race/ethnicity, but observed Hispanics and men with MSM transmission risk to have lower proportions with delayed initiation than other groups.

Though identification of personal characteristics associated with delayed HIV care initiation aids understanding of why certain persons may delay entry into care, identification of facility-related factors may be more useful for designing interventions to expedite care initiation. Our finding of more rapid care initiation following diagnosis at a facility with co-located HIV medical care conforms with an earlier report from the ARTAS-II study.[19] Our findings of greater delay following diagnosis at STD clinics, HIV counseling and testing sites, and other facilities that do not provide general medical care also echo reports of delayed HIV care initiation following initial HIV diagnosis at New York City STD/TB clinics and community testing sites.[20]

In NC, timely linkage to care programs involving clinicians, bridge counselors, HIV/STD counselors, and case managers must be strengthened at facilities diagnosing mid-to-large size volumes of patients, particularly STD clinics, HIV counseling and testing sites, and "other" testing facilities (e.g., prisons, jails, correctional centers, plasma donation centers and blood banks, social service organizations, and drug treatment centers). Strategies to improve linkage to care include linkage coordinators familiar with local HIV primary care providers, arranging transportation and possibly accompanying clients to their first medical care appointment, and establishing relationships with case management agencies.[101] Testing at an STD clinic or HIV counseling and testing site may foretell reduced access to subsequent medical care in comparison

to testing in inpatient or outpatient settings with onsite access to HIV providers. Additional assessment of potential patient-level risk factors such as income, poverty status, insurance coverage, educational attainment, geographic descriptive measures, and unmet psychosocial and social service needs is needed to further evaluate why patients may be at risk of delayed entry into HIV care in NC.

The positive association we observed between facility HIV diagnosis volume and delay in care initiation, although weaker after adjustment, has policy implications. For example, monitoring care initiation times for the nine facilities reporting 15 or more HIV diagnoses/year could help to identify barriers affecting a large number of clients and help to target resources. Meanwhile, testing facilities with small patient volumes might benefit from an Internet-based referral system to refer patients to care, which would require moderate resources to institute statewide.

Although our use of surveillance data is a strength in terms of population coverage, it is also a limitation with regards to the range of available variables and reliance on routine data collection, where the investigator has no opportunity to standardize or monitor procedures. For example, the date of initial HIV diagnosis may not always refer to the date when the first positive blood specimen was drawn, may not represent the first diagnosis,[107] or might have been preceded by a positive rapid test that even if not formally diagnostic could nevertheless have prompted initiation of care. Also, our indicator of HIV care initiation – a date of CD4 count or VL measurement– may not reflect effective engagement in HIV primary care,[108] although studies of clinical cohort data suggest reasonably strong agreement between routine HIV care visits and the presence of CD4/VL measures.[109] Analysis of additional CD4 and VL dates not available in our dataset could improve determination of care initiation and retention. In addition, elimination of

persons concurrently diagnosed with HIV and AIDS may have more accurately elucidated the significance of CD4 and VL measurements in the hospital setting, where HIV may be detected in persons seeking evaluation of AIDS symptoms.

All persons in our dataset were believed to have been living in NC as of December 31, 2015, though the 94 persons missing care initiation dates may include persons who died or moved out of the state in 2016. Reliable estimates of delayed care initiation within facility types with small numbers of diagnoses, such as jails, will require accumulating data from multiple years. Also, some facilities assigned to the "other/non-traditional" category might be more properly classified elsewhere, which would provide more accurate assessments of the relationships between facility type and care initiation. Social desirability bias may have influenced self-reported HIV exposure classification. The NC *ONE CALL HIV Provider Directory* developed in 2013 may not contain all active HIV providers in 2015, leading to misclassification in our coding of co-located HIV medical care.

Expanding HIV testing within health care organizations that also provide HIV care facilitates linkage to care following testing. But to identify many people with undiagnosed HIV – including large numbers of young adults, men, ethnic minorities, low income, and rural residents – testing outreach necessarily involves settings without co-located HIV medical care. The ability to invest in additional clinician staffing in such settings will be severely constrained; even facilities diagnosing a dozen HIV patients/year diagnose no cases most weeks. A statewide system that makes use of surveillance data on HIV diagnoses, CD4 counts, and VLs could monitor, facilitate, and assure that persons diagnosed with HIV are in care and virally suppressed. Since each new HIV infection averted will avoid some $300,000 in lifetime health care costs,[110] even a small additional reduction in new HIV infections in NC could offset the cost

of such a system. Further exploration of sociodemographic and behavioral characteristics

associated with delayed care initiation, unmet needs of newly diagnosed persons, and specific

facility referral mechanisms would provide data with which to design such a system. Although

continuing stigma around HIV is a major barrier, consideration should also be given to adapting

wellness strategies used to promote care engagement for other health conditions, especially

strategies that appeal to youth, such as mHealth.[111] Continuing monitoring of surveillance data

linking HIV diagnosis, stage at diagnosis, care initiation, and VLs will be important to achieving

public health goals for HIV clinical care and prevention, as will addressing unmet needs of HIV

patients and persons at elevated HIV risk.

Table 4　　　　HIV medical care initiation by patient and facility characteristics, 2015

	Total* (%)	Care Initiation < 3 months N (%)[†]	Care initiation ≥ 3 months N (%)[†]	No evidence of care initiation N (%)[†]
Total	1269 (100)	1077 (84.9)	98 (7.7)	94 (7.4)
Age (at HIV diagnosis)				
17-24	327 (25.8)	260 (24.1)	33 (33.7)	34 (36.2)
25-30	283 (22.3)	228 (21.2)	26 (26.5)	29 (30.9)
31-44	328 (25.9)	292 (27.1)	22 (22.5)	14 (14.9)
45+	331 (26.1)	297 (27.6)	17 (17.4)	17 (18.1)
Sex				
Female	251 (19.8)	225 (20.9)	12 (12.2)	14 (14.9)
Male	1018 (80.2)	852 (79.1)	86 (87.8)	80 (85.1)
Race/ethnicity				
Non-Hispanic black	816 (64.3)	672 (62.4)	70 (71.4)	74 (78.7)
Hispanic/other	161 (12.7)	147 (13.7)	10 (10.2)	4 (4.3)
Non-Hispanic white	292 (23.0)	258 (24.0)	18 (18.4)	16 (17.0)
Transmission exposure category[‡]				
Unknown	333 (26.2)	269 (25.0)	23 (23.5)	41 (43.6)
Adult IDU	56 (4.4)	44 (4.1)	9 (9.2)	3 (3.2)
Adult Heterosexual	160 (12.6)	147 (13.7)	7 (7.1)	6 (6.4)
Adult MSM	720 (56.7)	617 (57.3)	59 (60.2)	44 (46.8)
Facility HIV Provider Status[§]				
Non co-located HIV medical care	1064 (83.9)	888 (82.5)	86 (87.8)	90 (95.7)
Co-located HIV medical care	205 (16.2)	189 (17.6)	12 (12.2)	4 (4.3)

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Facility HIV diagnosis volume[||]

15+ diagnoses	243 (19.2)	188 (17.5)	27 (27.6)	28 (29.8)
7-14 diagnoses	238 (18.8)	196 (18.2)	21 (21.4)	21 (22.3)
4-6 diagnoses	241 (19.0)	206 (19.1)	17 (17.4)	18 (19.2)
2-3 diagnoses	264 (20.8)	234 (21.7)	18 (18.4)	12 (12.8)
1 diagnosis	283 (22.3)	253 (23.5)	15 (15.3)	15 (16.0)

Facility type at initial diagnosis[¶]

Other/non-traditional facility	282 (22.2)	222 (20.6)	27 (27.6)	33 (35.1)
STD clinic	234 (18.4)	181 (16.8)	29 (29.6)	24 (25.5)
HIV counseling and testing site	179 (14.1)	138 (12.8)	23 (23.5)	18 (19.2)
Inpatient hospital	179 (14.1)	164 (15.2)	6 (6.1)	9 (9.6)
Outpatient clinic	120 (9.5)	114 (10.6)	4 (4.1)	2 (2.1)
Outpatient private physician's office	275 (21.7)	258 (24.0)	9 (9.2)	8 (8.5)

* Column percentages

† Care initiation defined as the number of days between initial HIV diagnosis and first CD4 and/or viral load measure. Delayed initiation defined as care initiation $\geq$ 3 months (90 days).

‡ IDU = injection drug users; MSM = men who have sex with men

§ Co-located HIV medical care defined as a facility with an antiretroviral therapy provider.

|| Facility volume defined as the total number of HIV diagnoses made at a facility in the year 2015.

Table 5   Patient and facility characteristics and delayed entry into HIV medical care, 2015

	N (%)*	Care initiation ≥ 3 months N (%)[†]	OR (95%CI)[‡]	aOR (95% CI)[‡]
Total	1269 (100)	192 (15.1)		
Age (at HIV diagnosis)				
17-24	327 (25.8)	67 (34.9)	2.25 (1.44-3.51)	2.14 (1.26-3.63)
25-30	283 (22.3)	55 (28.7)	2.11 (1.33-3.34)	1.99 (1.18-3.34)
31-44	328 (25.9)	36 (18.8)	1.08 (0.66-1.77)	1.06 (0.62-1.80)
45+	331 (26.1)	34 (17.7)	1.0	1.0
Sex				
Female	251 (19.8)	26 (13.5)	0.59 (0.38-0.92)	
Male	1018 (80.2)	166 (86.5)	1.0	
Race/ethnicity				
Non-Hispanic black	816 (64.3)	144 (75.0)	1.63 (1.09-2.43)	1.14 (0.72-1.80)
Hispanic/other	161 (12.7)	14 (7.3)	0.72 (0.38-1.39)	0.54 (0.27-1.10)
Non-Hispanic white	292 (23.0)	34 (17.7)	1.0	1.0
Transmission exposure category[§]				
Unknown	333 (26.2)	64 (33.3)	1.43 (1.01-2.01)	3.56 (2.24-5.66)
Adult IDU	56 (4.4)	12 (6.3)	1.63 (0.84-3.20)	2.73 (1.29-5.76)
Adult Heterosexual	160 (12.6)	13 (6.8)	0.53 (0.29-0.97)	1.23 (0.60-2.53)
Adult MSM	720 (56.7)	103 (53.7)	1.0	1.0

Facility HIV Provider Status[||]

Non co-located HIV medical care	1064 (83.9)	176 (91.7)	2.34 (1.37-4.00)	
Co-located HIV medical care	205 (16.2)	16 (8.3)	1.0	

Facility HIV Provider Status, by Sex[||]

Female				
Non co-located HIV medical care	204 (81.3)	21 (80.8)	0.96 (0.34-2.70)	0.85 (0.28-2.52)
Co-located HIV medical care	47 (18.7)	5 (19.2)	1.0	1.0
Male				
Non co-located HIV medical care	860 (84.5)	155 (93.4)	2.94 (1.55-5.55)	2.94 (1.51-5.74)
Co-located HIV medical care	158 (15.5)	11 (6.6)	1.0	1.0

Facility HIV diagnosis volume[¶]

15+ diagnoses	243 (19.2)	55 (28.7)	2.47 (1.52-4.00)	1.76 (0.99-3.11)
7-14 diagnoses	238 (18.8)	42 (21.9)	1.81 (1.09-2.99)	1.74 (0.98-3.09)
4-6 diagnoses	241 (19.0)	35 (18.2)	1.43 (0.85-2.41)	1.43 (0.81-2.51)
2-3 diagnoses	264 (20.8)	30 (15.6)	1.08 (0.63-1.85)	1.15 (0.65-2.03)
1 diagnosis	283 (22.3)	30 (15.6)	1.0	1.0

Facility type at initial diagnosis

Other/non-traditional facility	282 (22.2)	60 (31.3)	4.10 (2.33-7.24)	3.12 (1.71-5.70)
STD clinic	234 (18.4)	53 (27.6)	4.44 (2.49-7.92)	3.64 (1.91-6.96)
HIV counseling and testing site	179 (14.1)	41 (21.4)	4.51 (2.47-8.23)	3.12 (1.55-6.30)
Inpatient hospital	179 (14.1)	15 (7.8)	1.39 (0.68-2.86)	0.99 (0.46-2.13)
Outpatient clinic	120 (9.5)	6 (3.1)	0.80 (0.31-2.08)	0.62 (0.23-1.68)
Outpatient private physician's office	275 (21.7)	17 (8.9)	1.0	1.0

* Column percentages

† Care initiation defined as the number of months between initial HIV diagnosis and first CD4 and/or viral load measure. Delayed initiation defined as care initiation ≥ 3 months.

‡ OR = odds ratio, aOR = adjusted odds ratio, 95% CI = 95% confidence intervals for risk factors remaining in final multivariable, logistic model; backward elimination criteria (p = 0.10 for retention)

§ IDU = injection drug users; MSM = men who have sex with men

‖ Co-located HIV medical care defined as a facility with an antiretroviral therapy provider.

¶ Facility volume defined as the total number of HIV diagnoses made at a facility in the year 2015.

Figure 7   Time to HIV medical care initiation by HIV medical care co-location, 2015
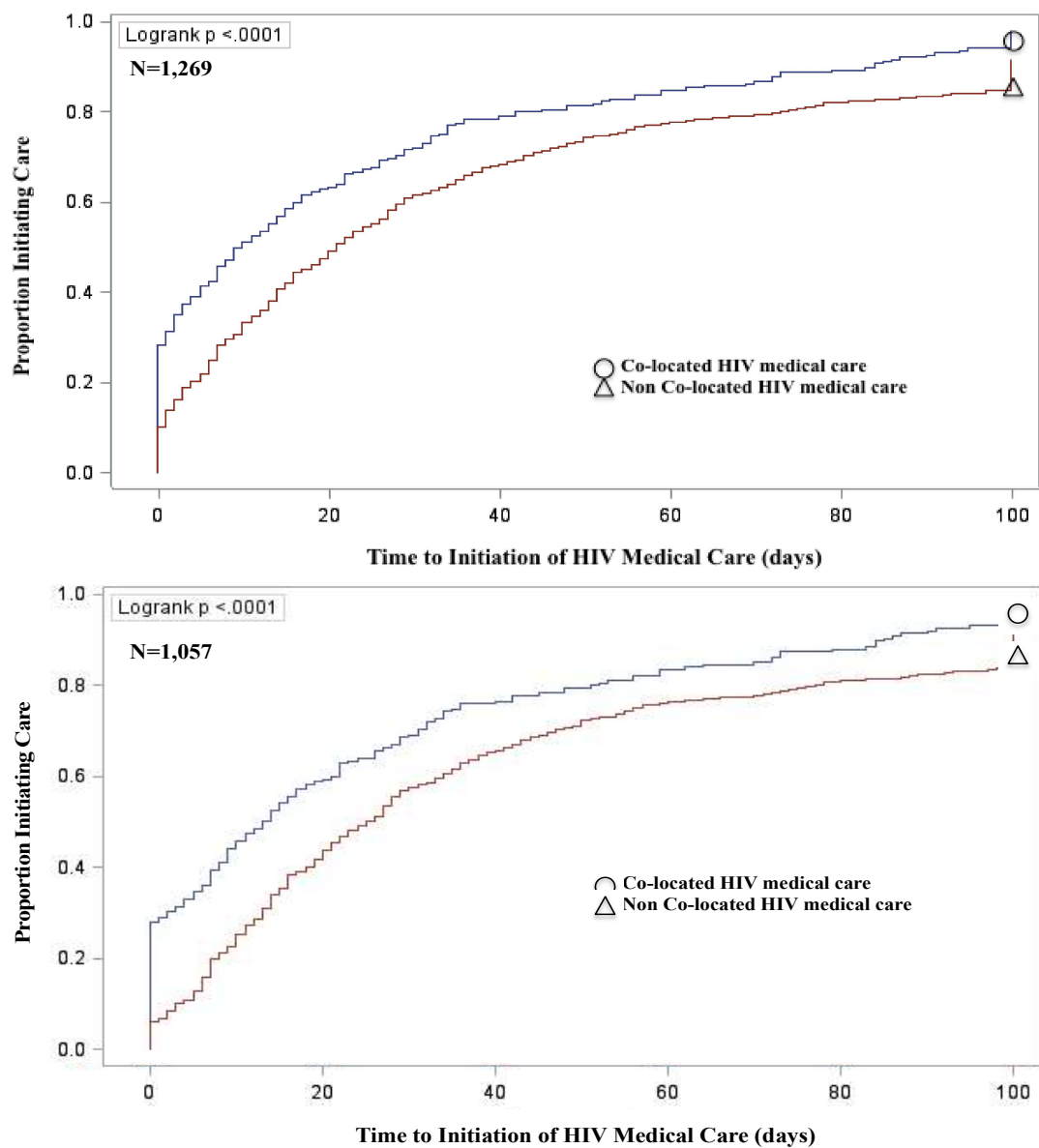
Figure 8   Time to HIV medical care initiation by testing facility HIV diagnosis volume, 2015
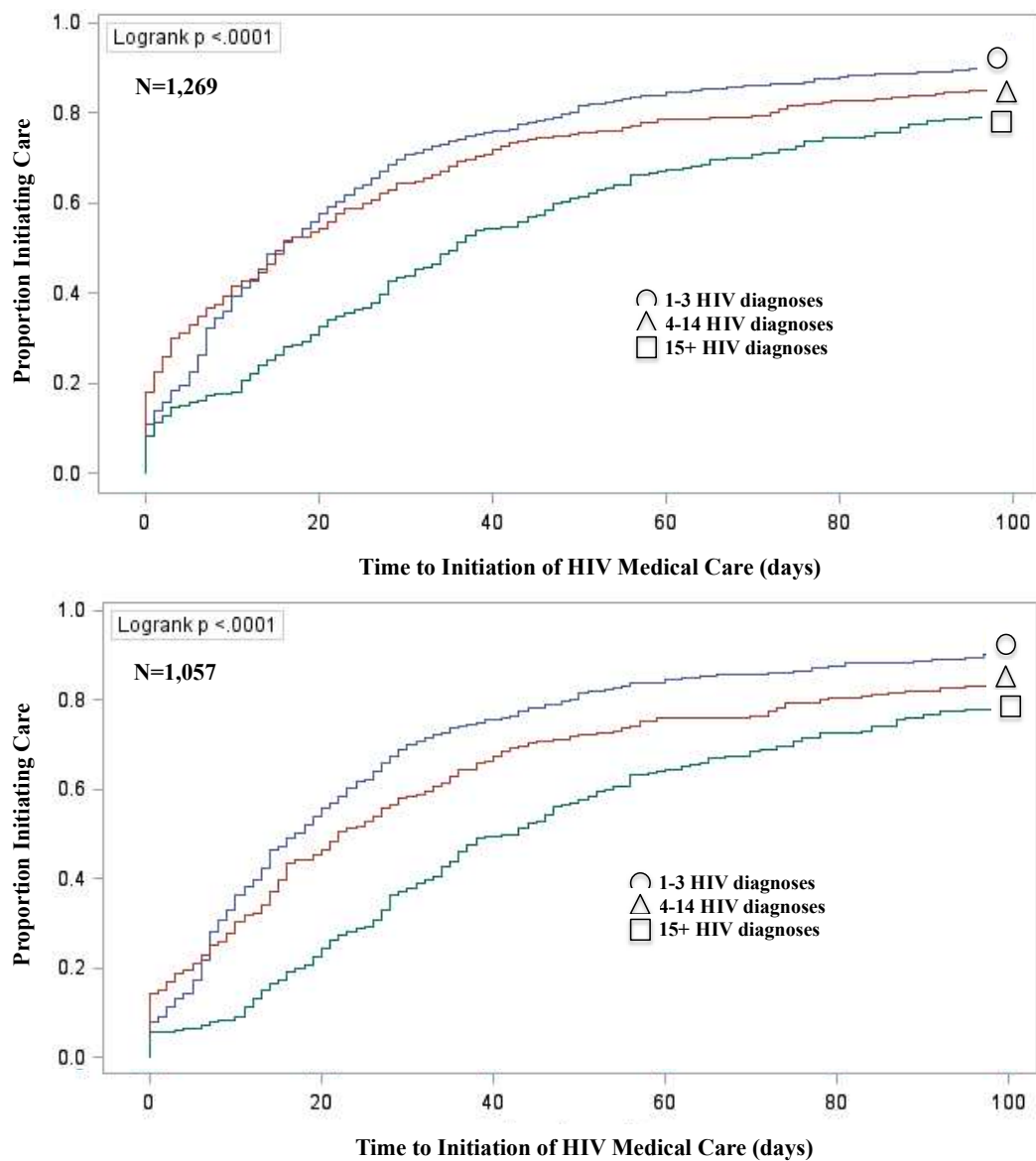
Figure 9   Time to HIV medical care initiation by testing facility type, 2015

Time to Initiation of HIV Medical Care (days)

Time to Initiation of HIV Medical Care (days)
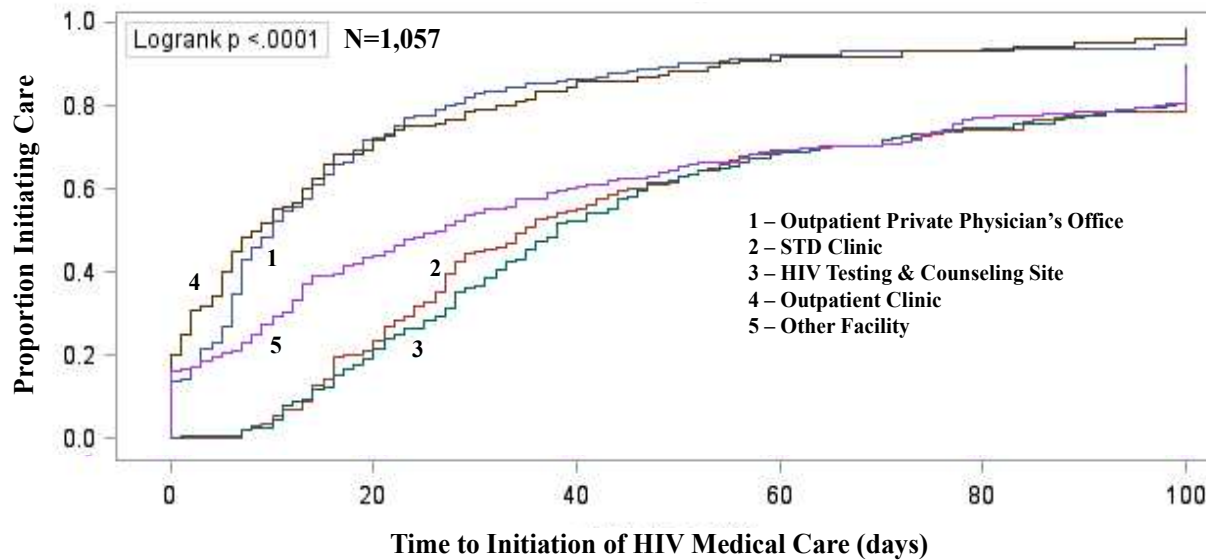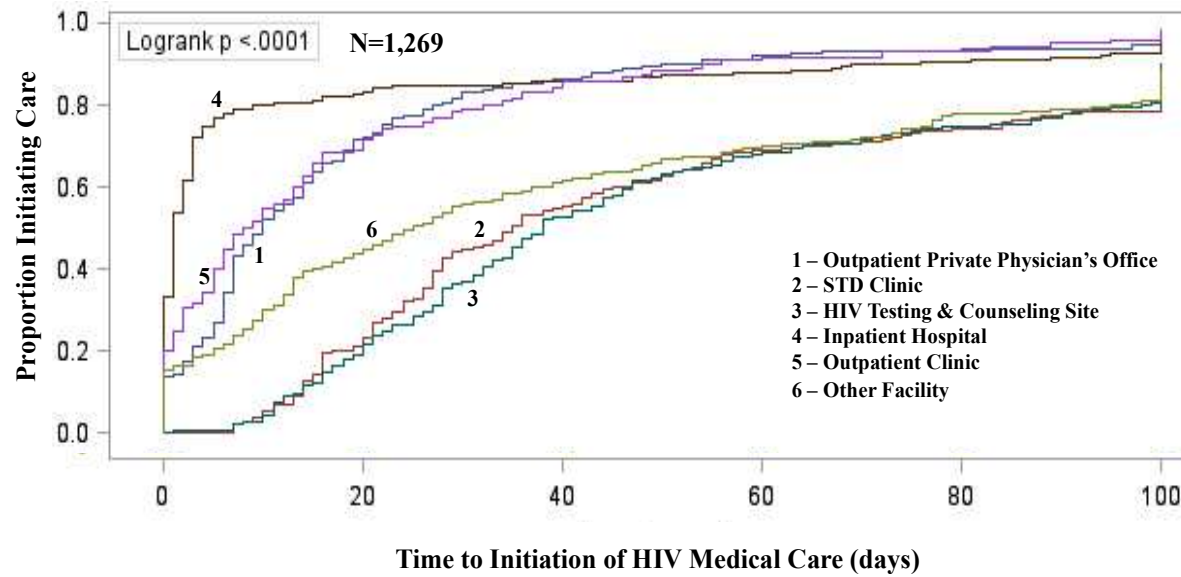
CHAPTER FIVE: DEPRESSION, ART ADHERENCE, AND RECEIPT OF CASE MANAGEMENT SERVICES BY ADULTS WITH HIV IN NORTH CAROLINA, MEDICAL MONITORING PROJECT, 2009-2013

5.1   Background

As recently emphasized in the *US NHAS: Updated to 2020*, prompt diagnosis of HIV infection, timely linkage to and retention in care, ART adherence, and resources for unmet needs are important for effective HIV treatment and prevention. Primary NHAS goals include increasing the percentage of persons with HIV who are retained in HIV medical care to at least 90%, and increasing the percentage who are virally suppressed to at least 80%.[50]

Depression, the most prevalent psychiatric disorder among persons with HIV other than substance use disorders, has important implications for patient retention, quality of life, and HIV transmission.[26] Depression prevalence among persons with HIV engaged in HIV care is 20%-30%,[66] at least twice the depression prevalence in the general US population.[68, 112] Depression and depressive symptoms are associated with poorer ART adherence,[25, 29] which is associated in turn with virological failure[23, 30] and poorer immunological outcomes,[30] increasing the likelihood of poor health and HIV transmission.[113]

One approach both to facilitating treatment of depression and to improving ART adherence is the provision of case management services,[70] which have been used to decrease unmet need for supportive services and to improve HIV medical care among persons with HIV.[114, 115] Most studies assessing the effectiveness of case management for persons with HIV have described the ability of these services to increase linkage to care,[12, 19, 35, 73] ART uptake,[72] and virologic suppression,[32] and to decrease unmet need for emotional counseling.[72] Few studies

have examined the relationship between case management services and current depression or depressive symptoms among persons with HIV.[116] In addition, the role of case management services in facilitating ART adherence has not been well established.[117, 118]

In NC, case management services are offered to clients based on apparent need and availability of services. The services may be provided through the RW HIV/AIDS Program, which provides funding for state and local programs to assist low-income persons with HIV through medical case management, oral health management, home health care, transportation assistance, hospice care, and the ADAP.[119] Public health officials continue to see increases in the HIV burden among low-income residents in Southern states, where financial strain, psychosocial trauma, substance use, and long travel distance to providers are correlated with a high prevalence of mental health illnesses.[120] Improved understanding of the relationships between case management service provision and both depression and ART adherence is needed, particularly among persons residing in regions with barriers to medical care access.

We used 2009-2013 data from the MMP, a national survey of persons with HIV receiving medical care, to assess the prevalence and correlates of case management services, current depression, and ART adherence in NC.[121] We also examined the associations between case management utilization and both depression and ART adherence in this setting, a southeastern state with one of the highest burdens of HIV in the country.[104]

5.2   Methods

Medical Monitoring Project (MMP)

MMP is a supplemental HIV surveillance system that uses a three-stage probability proportional to size sampling design to obtain nationally representative, annual cross-sectional samples of HIV-infected adults receiving outpatient medical care for HIV in the US. The multi-

stage sampling schema and weighting procedures have been described in detail previously.[78-80] NC, considered a primary sampling unit, is one of 16 states sampled annually. For each of the five cycles of data we analyzed (annual cross-sections in 2009-2013), MMP first sampled outpatient facilities in NC, and then HIV-infected adults aged 18 years or older who had at least one medical care visit in a participating facility between January and April of the cycle year. Data were collected via face-to-face interviews between June of the cycle year and May of the subsequent year (e.g., 2009 cycle collection = June 2009 – May 2010). The overall response rates for 2009-2013, combining facilities and patients and adjusting for unknown eligibility, were 39.4%, 30.4%, 26.3%, 30.9%, and 48.5%, respectively. The resulting interview data included a total of 910 HIV-infected respondents – 602 males (67.2%), 297 females (31.3%), 10 transgender persons (1.3%), and 1 intersex person (0.1%).

The first half of the twelve-section MMP questionnaire asked participants about demographic characteristics (including age, education status, and sexual orientation), personal experiences regarding access to HIV care, and related barriers (e.g., HIV testing and care experiences, met and unmet needs, stigma and discrimination, etc.). The second half of the questionnaire included questions on sexual behaviors, substance abuse, transmission risk factors, partners' behaviors, gynecological and reproductive history, health conditions and preventive therapy, HIV prevention activities, and depression.

Case Management Utilization, Depression, and ART Adherence

Case management utilization was assessed based on responses to the MMP question, "During the past 12 months, did you get case management services?" The questionnaire did not provide a specific definition for case management services or assess the reasons for receiving these services.

Depression was identified from responses on the PHQ-8.[84] The PHQ-8 assigns a score for the number of days in the previous two weeks that the respondent experienced each of the eight criteria for depression from the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition*.[93] A 9th criterion assesses suicidal or self-injurious ideation. MMP omitted this question because interviewers were not trained mental health providers. Studies have shown that exclusion of the 9th item does not have considerable effects on scoring because self-injurious ideation is uncommon in the general population and in primary care settings.[94, 122-126] Original validation studies have shown that the PHQ-8 is comparable to the PHQ-9, and identical scoring thresholds for measuring current depression can be used for both questionnaires.[94]

We defined depression as probable current depression (*major* or *other*) based on Kroenke and Spitzer's 2002 algorithm of experiencing at least two depressive symptoms for ''more than half the days'' in the preceding two weeks, with at least one symptom being depressed mood or anhedonia. This diagnostic algorithm yields comparable judgments to a total PHQ-8 score of $\geq$ 10,[84, 94] which we also examined in sensitivity analyses.

ART adherence was defined as 100% ART dose adherence in the past three days, an AIDS Clinical Trials Group measure.[95] At the time of interview, participants were asked, "In the past three days, were you 100% dose adherent to your ART medicine?" ART dose was defined as either a single tablet or multiple tablets taken concurrently. If the respondent missed part of a dose, he or she was instructed to report this as a missed dose. HIV-infected participants were recorded as either 100% ART dose adherent or not 100% ART dose adherent in the past 72 hours on the basis of this question. In sensitivity analyses, we also analyzed ART schedule adherence, which was based on the MMP question, "In the past three days, were you 100% schedule adherent to your ART medicine?"

<u>Additional Measures</u>

Various characteristics were considered as potential correlates and/or effect measure modifiers of the associations between utilization of case management services in the previous twelve months and 1) probable current depression, and 2) 100% ART dose adherence in the past three days. Sociodemographic factors included age (18-29, 30-39, 40-49, $\geq$ 50 years), gender (men, women, transgender/intersex), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic/Latino, other), sexual orientation (heterosexual, homosexual, bisexual, other/unclassified), education (< high school, high school or equivalent, > high school), annual household income ($0-$19,999, $20,000-$39,999, $40,000-$74,999, $\geq$ $75,000), federal poverty level (living at or below, versus above, the poverty level, defined per 2012 standards using household income and size),[96] and health insurance (public or private, RW/ADAP only, uninsured). Because NC has many rural areas requiring long travel distances to visit medical providers, we examined the need for transportation assistance services in the previous twelve months (yes/no). Behavioral factors of interest included alcohol consumption in the previous twelve months (yes/no) and current smoking status (yes/no).

<u>Analytical Methods</u>

MMP respondents with missing or incomplete data on case management utilization, depression, or ART adherence were excluded from analyses using those variables. Patients not taking ART were excluded from the denominator for adherence percentages. The distributions of sociodemographic and behavioral variables, utilization of case management services in the previous twelve months, probable current depression, and 100% ART dose adherence in the past three days were summarized with unweighted counts and weighted percentages. All variables were coded as dichotomous, nominal, or ordinal categorical. Bivariable associations of

sociodemographic and behavioral characteristics with 1) case management utilization in the previous twelve months, 2) probable current depression, and 3) 100% ART dose adherence in the past three days were examined with Rao-Scott chi-square statistics that accounted for the survey design, and prevalence ratios (PRs) with 95% confidence intervals (CIs) obtained from weighted Poisson models with robust variance estimation.

We estimated the association between case management utilization in the past twelve months and: 1) probable current depression and 2) 100% ART dose adherence, using weighted multivariable Poisson models with robust variance to account for violations of the distribution assumptions. Since associations in our cross-sectional data could reflect (1) targeting of case management services with respect to prior (unmeasured) depression and ART adherence status, as well as (2) any effects of past-year case management services on current depression and ART adherence status, our interest in estimating these associations was not to infer causality. Rather, our intent was to assess current unmet need for depression management and ART adherence support according to prior case management utilization, such that targets for future investigation and intervention could be identified.

In model development, we identified potential confounders of the associations between case management and both depression and ART dose adherence based on a literature review and directed acyclic graphs.[127] We assessed effect measure modification for each predictor variable in the models using a product interaction term and an adjusted Wald test with a 0.15 significance level. We assessed collinearity among variables using variation inflation factors; none was noted. Analyses were performed using Stata version 14 (StataCorp, College Station, TX) and SAS 9.4 (SAS Institute Inc., Cary, NC). Except where noted, all analyses incorporated the MMP-

provided sample design and weights, to account for clustering, unequal selection, and nonresponse.

<u>Ethics Statement</u>

The CDC determined that MMP is a public health surveillance activity.[85] MMP itself is therefore not subject to human subjects regulations including federal IRB review.[86] Funding for the NC MMP was provided by a cooperative agreement (PS09-937) from the CDC. The IRB at the University of North Carolina at Chapel Hill determined that these analyses were exempt from full review (IRB # 14-2675).

5.3   Results

<u>Patient Characteristics</u>

HIV-infected adults receiving care in NC during 2009-2013 were predominantly age 40 years and older (74.8%), men (67.2%), non-Hispanic black (61.6%), and heterosexual (59.3%) (Table 6). Slightly more than half (54.6%) had at least a high school education. A majority (62.6%) reported a yearly household income less than $20,000; 45.5% were living at or below the poverty level.[96] Most (75.0%) reported having public or private health insurance coverage in the previous twelve months; 22.3% reported having only RW/ADAP coverage, and 2.7% (n=25) reported having no coverage. About one-fourth needed transportation assistance. A majority of patients used alcohol in the previous twelve months (64.0%); a large minority were current smokers (43.7%). Just over half of patients (53.2%) reported using case management services in the previous twelve months. Approximately one in five patients (21.7%) experienced probable current depression, and 87.0% of patients receiving ART reported being 100% ART dose adherent in the past three days. A total of 8.6% of participants were not receiving ART.

Factors associated with Case Management Utilization

Women were more likely to utilize case management services in the previous twelve months than were men (PR, 1.15; 95% CI, 1.01-1.31), as were patients with less than a high school education (PR, 1.43; 95% CI, 1.21-1.69, versus those with more education). Respondents living at or below the poverty level were more likely to receive case management services (PR, 1.42; 95% CI, 1.22-1.66, versus those living above the poverty line). Patients who received assistance from RW/ADAP (versus private or public insurance), needed transportation assistance in the previous twelve months, or reported current smoking status were all more likely to have received case management services in the previous twelve months.

Factors associated with Probable Current Depression

Women were more likely to be currently depressed (PR, 1.44; 95% CI, 1.17-1.77, versus men), as were those living at or below the poverty level (PR, 1.59; 95% CI, 1.15-2.19, versus those living above the poverty level) (see Table 7). The prevalence of depression was also greater for those who needed transportation assistance (PR, 1.66; 95% CI, 1.25-2.19), as well as current smokers (PR, 1.40; 95% CI, 1.07-1.85, versus non-smokers). Persons who received case management services in the previous twelve months were 41% more likely to be depressed (PR, 1.41; 95% CI, 1.09-1.83, versus persons who did not). We found no associations between probable current depression and age, race/ethnicity, sexual orientation, education, income, health insurance status, or alcohol use (past twelve months).

Factors associated with 100% ART Dose Adherence

Women were less likely to report 100% ART dose adherence in the past three days (PR, 0.92; 95% CI, 0.86-0.98, versus men), as were non-Hispanic blacks (PR, 0.92; 95% CI, 0.88-0.96, versus non-Hispanic whites) (see Table 8). Respondents with less than a high school

education were 10% less likely (PR, 0.90; 95% CI, 0.83-0.98) to be adherent compared to

individuals with at least a high school education. Persons living at or below the poverty level

were 7% less likely (PR, 0.93; 95% CI, 0.87-0.99) to be adherent compared to persons living

above the poverty level. Current smokers were less likely to be adherent compared to non-

smokers (PR, 0.91; 95% CI, 0.85-0.98). Patients reporting probable current depression were less

likely to be adherent than those not experiencing probable current depression (PR, 0.92; 95% CI,

0.86-0.99). We found no associations between 100% ART dose adherence in the past three days

and age, sexual orientation, income, health insurance status, need for transportation assistance

(past twelve months), or alcohol use (past twelve months).

Multivariable associations

Poverty level was found to be a significant effect measure modifier of the association

between case management utilization in the previous twelve months and probable current

depression (Wald *p*-value = 0.02; N=58 respondents were missing data on poverty). After

adjustment for gender, sexual orientation, education, annual household income, health insurance

status, and need for transportation assistance, utilization of case management services in the

previous twelve months was associated with probable current depression among persons living

above the poverty level (aPR, 2.05; 95% CI, 1.25-3.36), but not among those living at or below

the poverty level (aPR, 1.01; 95% CI, 0.72-1.43) (N=842; 10 participants were missing data on

case management utilization and/or probable current depression) (see Table 9). Similar

associations were obtained in sensitivity analyses where depression was defined as a PHQ-8

score ≥ 10 (aPR, 2.05; 95% CI, 1.31-3.20 for above poverty level; aPR, 0.91; 95% CI, 0.64-1.30

for at or below poverty level).

Adjusted for gender, race/ethnicity, education, annual household income, poverty level, health insurance status, need for transportation assistance (past twelve months), and probable current depression, 100% ART dose adherence did not differ between those who did or did not receive case management services in the past twelve months (aPR, 1.00; 95% CI, 0.95-1.05), nor did 100% ART schedule adherence (aPR, 1.01; 95% CI, 0.95-1.08) (N=812; 21 participants were missing data on case management utilization and/or ART adherence, and 77 were not taking ART).

5.4   Discussion

The Southern region of the US has disproportionately high HIV infection rates[105] and greater political, societal, and structural barriers to optimal clinical outcomes and prevention of HIV transmission.[62] This study is one of the first to report prevalence estimates of case management utilization, current depression, and ART adherence using representative data on persons with HIV receiving HIV care in a Southern state.

Among persons receiving HIV care in our setting, 53.2% reported receiving case management services in the past twelve months. It is difficult to place this estimate in context, since the only available national estimate – 56.5% – was reported from the 1996-1997 HIV Cost and Services Utilization Survey and pertained to a shorter six-month period prior to interview.[72] The probable current depression prevalence for persons with HIV in care in NC based on 2009-2013 MMP data was 21.7%, which is somewhat lower than the 25.6% reported from national 2009 MMP data.[68] Both estimates are about twice their corresponding estimates among the general US population.[112]

As is regularly observed,[68, 128-130] women were more likely than men to suffer from probable current depression. Persons with HIV in care with a need for transportation assistance

were more likely to be depressed, consistent with prior studies of the relationship between mental illness and needs for supportive services.[131, 132] We found no differences in depression in relation to sexual orientation. One study reported that gay, HIV-infected men living in non-metropolitan areas were more likely to suffer from depression, which was largely driven by social constraints.[133] We likely underestimated the proportion of persons with HIV in care who are MSM due to low patient response rates.

Among patients with incomes at or below the poverty level, both receipt of case management services and depression prevalence were higher than among patients above the poverty level, but there was no association between case management and depression. By contrast, among patients with household incomes above the poverty level, receipt of case management services and current depression were positively associated. We speculate that the association among patients above the poverty level reflects the targeting of case management services to persons suffering from depression, whereas among those at or below the poverty line, case management services would be indicated for many reasons besides depression. In NC, persons with HIV living in poverty utilize case management services for access to medical care, food, job resources, shelter, and transportation. However, 32.3% of patients above the poverty level had yearly household incomes of $20,000 or less, so an array of unmet needs may be common for a sizeable minority of that group as well.

The prevalence of self-reported 100% ART dose adherence in the past three days among persons receiving care in NC was high (87.0%), and similar to the 86.0% prevalence reported using national MMP data from the 2009-2010 cycle.[134] Non-Hispanic blacks, women, and persons living at or below the poverty level were less likely to be 100% ART dose adherent, as also seen in the national MMP data.[134] The 100% ART dose adherence prevalence estimates

were similar for respondents who received case management and those who did not (aPR, 1.00; 95% CI, 0.95-1.05). It is possible that appropriately targeted case management services boosted adherence among persons who would otherwise have been non-adherent, but our cross-sectional design precludes estimation of such an effect. An important qualifier is that 8.6% of patients were not taking ART, conceivably because they did not perceive a need to initiate ART, were judged likely to have poor adherence, or were not treatment-eligible on the basis of clinical guidelines.

The high prevalence of depression, even among those receiving case management services, warrants public health attention and suggests the need for additional resources for case managers, or more support from providers and mental health professionals. In a previous study, a sample of HIV/AIDS case managers across NC participating in a three-month intensive case management training and adherence program reported client-level challenges to adherence such as depression, which were often associated with geographic barriers (e.g., rural residents with transportation needs) and social isolation. Several case managers felt they were not knowledgeable about adherence coordination and counseling or ART medication.[74] Meeting the mental health needs of persons with HIV requires accessible and effective mental health resources, working in coordination with case managers.

A limitation of our study is its cross-sectional design, in which history of case management utilization, probable current depression status, and ART adherence were ascertained simultaneously. As noted above, if case management was targeted to the subset of persons above the poverty level that was depressed, their depression prevalence may have declined from even higher levels but still be higher than among patients to whom case management was not provided. Among persons living at or below the poverty level, an even higher percentage of

patients receiving case management might have been depressed without it. However, the cross-sectional design does not allow us to disentangle the extent to which effect estimates reflect case management targeting versus case management effects. Direct assessment of the effectiveness of case management to facilitate depression treatment and ART adherence will require prospective measurement of all three factors and appropriate analytical methods to account for time-varying relationships, repeated intra-individual measures, and bidirectional causality.

Another limitation of our study is that information was self-reported and therefore subject to potential social desirability and recall biases, particularly in the case of ART adherence reporting. Self-reported adherence is known to overestimate adherence and is the least accurate of all measures, however, it is commonly used in HIV clinical care for efficiency.[135] In addition, we did not consider geographical data with respect to the participants' residences. With inconsistent quality and accessibility of health care services in the South, location information may shed light on particular barriers faced by individuals in certain geographic regions within NC.[39]

Optimal HIV clinical and prevention outcomes require identifying HIV-positive persons, linking them to and retaining them in care, prescribing appropriate ART, maintaining adherence, and achieving and maintaining viral suppression. These processes, in turn, require addressing unmet needs and psychological wellbeing, monitoring their impacts on ART adherence, and ensuring the effectiveness of mental health and other medical services. Case management and mental health agencies must be adequately funded, monitored, and evaluated to ensure that persons with HIV in-care are receiving assistance to improve HIV-related health outcomes in cost-effective ways.

Table 6   Sociodemographic and behavioral characteristics of participants in the North
               Carolina Medical Monitoring Project, 2009-2013

	Unweighted N	Weighted %*	95% CI§
Total N	910		
Age			
18-29	52	6.1	(4.1-8.1)
30-39	164	19.1	(15.4-22.7)
40-49	307	34.1	(31.0-37.2)
≥ 50	387	40.7	(36.1-45.2)
Gender			
Men	602	67.2	(63.8-70.7)
Women	297	31.3	(28.0-34.6)
Transgender	10	1.3	(0.48-2.29)
Intersex	1	0.1	(0.00-0.38)
Race/ethnicity			
Non-Hispanic white	267	29.4	(23.4-35.5)
Non-Hispanic black	561	61.6	(54.5-68.7)
Hispanic or Latino	25	2.9	(1.7-4.1)
Other	57	6.1	(4.2-8.1)
Sexual orientation			
Heterosexual	548	59.3	(54.0-64.7)
Homosexual	283	31.6	(26.4-36.8)
Bisexual	71	8.0	(6.1-9.7)
Other/unclassified	8	1.1	(0.3-1.9)
Education			
> High school	501	54.6	(48.6-60.6)
High school or equivalent	237	26.7	(21.5-31.9)
< High school	172	18.7	(15.4-22.0)
Income (annual household)†			
$0 - $19,999	538	62.6	(57.7-67.4)
$20,000 - $39,999	174	21.3	(18.6-24.1)
$40,000 - $74,999	94	11.1	(8.3-14.0)
$\geq$ $75,000	44	5.0	(3.2-6.8)

Poverty level[†]

Above poverty level	457	54.5	(50.2-58.9)
At or below poverty level	393	45.5	(41.1-49.8)

Health insurance (past 12 months)[†]

Yes (Public or Private)	691	75.0	(70.9-79.0)
Uninsured (Ryan White/ADAP only)	192	22.3	(18.7-25.9)
Uninsured	25	2.7	(1.5-3.9)

Needed transportation (past 12 months)

No	671	74.3	(71.0-77.6)
Yes	239	25.7	(22.4-29.0)

Alcohol use (past 12 months)[†]

No	334	36.0	(31.9-40.1)
Yes	572	64.0	(60.0-68.1)

Current smoker[†]

No	507	56.3	(51.8-60.8)
Yes	399	43.7	(39.2-48.2)

Case management services (past 12 months)[†]

No	433	46.8	(41.4-52.2)
Yes	474	53.2	(47.8-58.6)

100% ART dose adherence (past 3 days)[†‡]

Yes, 100% ART dose adherent	709	79.6	(77.0-82.2)
No, not 100% ART dose adherent	106	11.9	(9.2-14.5)
Not taking ART	77	8.6	(6.1-11.0)

Probable current depression[†]

No	706	78.3	(75.2-81.4)
Yes	197	21.7	(18.6-24.8)

* Percentages are weighted to account for probability of selection and nonresponse
† Frequencies do not add up to total sample size (n = 910) due to missing data
‡ ART = antiretroviral therapy

Table 7   Probable current depression by sociodemographic and behavioral characteristics, North Carolina Medical Monitoring Project, 2009-2013

	Probable Current Depression		PR (95% CI)[†]	X^2 p-value[§]
	N	%*		
Total (N=900)	195	21.5		
Age				
18-29	8	13.3	1.0	
30-39	39	23.0	1.72 (0.70-4.26)	0.27
40-49	73	24.4	1.83 (0.86-3.91)	
≥ 50	75	19.7	1.48 (0.69-3.17)	
Gender				
Men	115	19.1	1.0	< 0.01
Women	80	27.6	1.44 (1.17-1.77)	
Transgender/Intersex	0	-	-	
Race/ethnicity				
Non-Hispanic white	63	23.2	1.0	
Non-Hispanic black	113	20.3	0.87 (0.65-1.18)	0.76
Hispanic or Latino	6	24.7	1.07 (0.52-2.18)	
Other	13	23.9	1.03 (0.58-1.82)	
Sexual orientation				
Heterosexual	124	22.8	1.0	
Homosexual	51	17.8	0.78 (0.62-0.98)	0.08
Bisexual/Other/unclassified	20	26.2	1.15 (0.79-1.68)	

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Education

> High school	98	19.8	1.0	
High school or equivalent	57	23.9	1.21 (0.95-1.54)	0.39
< High school	40	23.1	1.17 (0.78-1.74)	

Income (annual household)‡

$0 - $19,999	131	24.6	1.0	
$20,000 - $39,999	31	16.7	0.68 (0.42-1.08)	
$40,000 - $74,999	11	14.1	0.57 (0.31-1.03)	0.07
≥ $75,000	7	16.5	0.67 (0.34-1.34)	

Poverty level‡

Above poverty level	76	16.8	1.0	
At or below poverty level	104	26.7	1.59 (1.15-2.19)	< 0.01

Health insurance (past 12 months)‡

Yes (Public or Private)	151	21.8	1.0	
Uninsured (Ryan White/ADAP only)	37	20.3	0.93 (0.66-1.31)	0.90
Uninsured	6	20.0	0.92 (0.42-2.00)	

Needed transportation assistance (past 12 months)

No	124	18.4	1.0	
Yes	71	30.5	1.66 (1.25-2.19)	< 0.01

Alcohol use (past 12 months)‡

No	78	23.2	1.0	
Yes	117	20.6	0.89 (0.71-1.11)	0.30

Current smoker[‡]

No	92	18.2	1.0	
Yes	102	25.6	1.40 (1.07-1.85)	0.01

Case management services (past 12 months)

No	77	17.6	1.0	
Yes	118	24.9	1.41 (1.09-1.83)	< 0.01

* Percentages are weighted to account for probability of selection and nonresponse

† PR = crude estimate of prevalence ratio (PR) and 95% confidence interval (CI) from Poisson regression

‡ Frequencies do not add up to total depression sample size (N=195) due to missing data

§ P-value from Rao-Scott chi square statistic

Table 8   100% ART adherence in the past three days by sociodemographic and behavioral characteristics, North Carolina Medical Monitoring Project, 2009-2013

	100% ART Dose Adherence		PR (95% CI)[†]	X^2 p-value[§]
	N	%*		
Total (N=812)	706	87.0		
Age				
18-29	35	86.5	1.0	
30-39	124	87.1	1.01 (0.87-1.16)	0.35
40-49	228	84.2	0.97 (0.85-1.12)	
≥ 50	319	89.3	1.03 (0.90-1.18)	
Gender				
Men	487	89.3	1.0	
Women	212	82.4	0.92 (0.86-0.98)	0.02
Transgender/Intersex	7	71.1	0.80 (0.49-1.29)	
Race/ethnicity				
Non-Hispanic white	230	92.3	1.0	
Non-Hispanic black	420	84.6	0.92 (0.88-0.96)	< 0.01
Hispanic or Latino	20	94.7	1.03 (0.92-1.15)	
Other	36	79.6	0.86 (0.75-1.00)	
Sexual orientation				
Heterosexual	415	85.5	1.0	
Homosexual	232	89.2	1.04 (0.99-1.10)	0.25
Bisexual/Other/unclassified	59	88.6	1.04 (0.95-1.13)	

Education

> High school	407	89.4	1.0	
High school or equivalent	178	86.3	0.97 (0.91-1.02)	< 0.01
< High school	121	80.5	0.90 (0.83-0.98)	

Income (yearly household)‡

$0 - $19,999	409	85.3	1.0	
$20,000 - $39,999	134	85.6	1.00 (0.92-1.09)	
$40,000 - $74,999	79	94.8	1.11 (1.03-1.19)	0.10
≥ $75,000	37	91.7	1.08 (0.97-1.19)	

Poverty level‡

Above poverty level	375	89.6	1.0	
At or below poverty level	284	83.2	0.93 (0.87-0.99)	0.02

Health insurance (past 12 months)

Yes (Public or Private)	536	87.0	1.0	
Ryan White/ADAP only	163	86.8	1.00 (0.94-1.06)	0.99
Uninsured	7	86.1	0.99 (0.78-1.25)	

Needed transportation assistance (past 12 months)

No	531	88.0	1.0	
Yes	175	84.0	0.95 (0.88-1.04)	0.25

Alcohol use (past 12 months)‡

No	262	85.9	1.0	
Yes	442	87.6	1.02 (0.97-1.08)	0.47

Current smoker‡

No	413	90.4	1.0	
Yes	291	82.4	0.91 (0.85-0.98)	0.01

Probable current depression‡

No	563	88.6	1.0	
Yes	140	81.6	0.92 (0.86-0.99)	0.01

* Percentages are weighted to account for probability of selection and nonresponse; ART = antiretroviral therapy

† PR = crude estimate of prevalence ratio (PR) and 95% confidence interval (CI) from Poisson regression

‡ Frequencies do not add up to total 100% ART dose adherence sample size (N=706) due to missing data

§ P-value from Rao-Scott chi square statistic

Table 9   Associations between utilization of case management services and probable current depression, and 100% ART dose adherence, North Carolina Medical Monitoring Project, 2009-2013

Total (N=842)	Probable Current Depression		Prevalence *	PR	aPR
	Yes (N)	No (N)	%	(95% CI)	(95% CI)‡
Case management utilization (past 12 months)					
At or below poverty level					
Utilized case management	63	173	27.0	1.02 (0.73-1.44)	1.01 (0.72-1.43)
Did not utilize case management	41	112	26.4	1.0	1.0
Above poverty level					
Utilized case management	45	150	23.0	1.90 (1.26-2.87)	2.05 (1.25-3.36)
Did not utilize case management	31	227	12.1	1.0	1.0
	100% ART Dose Adherence†		Prevalence *	PR	aPR
Total (N=812)	Yes (N)	No (N)	%	(95% CI)	(95% CI)§
Case management utilization (past 12 months)					
Utilized case management	374	64	85.6	0.97 (0.92-1.02)	1.00 (0.95-1.05)
Did not utilize case management	332	42	88.7	1.0	1.0

* Percentages are weighted to account for probability of selection and nonresponse

† 100% ART dose adherence (past three days); ART = antiretroviral therapy

‡ Adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) calculated using multivariable Poisson models adjusted for gender, sexual orientation, education, income, health insurance, need for transportation; analyses weighted to account for complex sample design

§ Adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) calculated using multivariable Poisson models adjusted for gender, race/ethnicity, education, income, poverty, health insurance, need for transportation, probable current depression; analyses weighted to account for complex sample design

CHAPTER SIX: DISCUSSION

6.1 Overview

According to the CDC, more than 1.2 million people in the US are currently living with HIV infection, and approximately 13% are unaware of their status.[37] Incident cases declined 19% from 2005 to 2014, and testing rates increased.[37] However, as of December 2016, MSM,[37, 50, 104] black and Latino men and women,[37, 50, 104] injection drug users,[37, 50] youth aged 13-24,[37, 50, 104] and transgender women are most affected by HIV.[37, 50] In addition, HIV remains concentrated among persons living in the South.[37, 50, 104] Particular challenges such as long travel distances to medical care,[13, 136] poor healthcare infrastructures,[62] stigma,[62] states' refusals to expand insurance coverage,[62] disproportionate incarceration of black men,[137, 138] poverty,[137, 138] and racial discrimination[137, 138] drive HIV transmission in this region.

As outlined in "The NHAS: Updated to 2020," improvements are needed along the HIV care continuum.[50] The continuum models the various HIV medical care stages an HIV-infected person needs to traverse from initial HIV diagnosis to maintenance of HIV viral suppression.[21] Beginning with testing and timely initiation of HIV medical care, by measuring the proportions of individuals engaged at each step, researchers and policy makers are able to identify gaps in care continuity and examine barriers to optimal care. In Southern states, patient and HIV testing facility characteristics associated with delayed care initiation are poorly described. This dissertation uses statewide surveillance data to assess time to initiation of HIV care in NC.

Case management has been used as a strategy to decrease unmet need for supportive services and improve HIV medical care among HIV-infected persons.[114, 115] However, few

studies have examined case management utilization in relation to mental health and its implications for ART adherence, necessary for viral suppression. This dissertation uses statewide data for NC to evaluate the receipt of case management support services for persons engaged in HIV care, and the relation of these services to patient quality of life and ART adherence.

6.2   Summary of Findings

Using surveillance data from eHARS for all adults diagnosed with HIV in NC and from the NC portion of MMP that surveys persons in HIV care in 26 project areas, our study examined two stages along the HIV care continuum. We first assessed time to care initiation and proportions of patients first accessing care within one month and three months from initial HIV diagnosis for persons newly diagnosed in 2015. We also examined patient and testing facility characteristics associated with delay in care initiation. Among all newly diagnosed persons (N=1,269), 63.8% initiated care within one month after diagnosis and 84.9% within three months. The median time to care initiation among the 92.6% of persons with evidence of care initiation was 16 days. Even if patients with no date of CD4 or viral load measurement in eHARS had in fact not accessed care by June 15, 2016, the estimate of 15.1% not initiating care within three months of diagnosis was somewhat lower than prevalence estimates of 17%-29% reported in previous literature,[10, 16, 20, 61] but the one-month incidence of entry into care (63.8%) was considerably below the national goal of 85%.[100]

After adjustment for patient and facility characteristics, age 18-30 years (48% of patients) and male sex at birth (80% of patients) were associated with delayed initiation of HIV medical care. Non-Hispanic black ethnicity (about two-thirds of HIV infected persons in NC) was also associated with delayed care initiation, though the association was stronger before adjustment for facility type.

Initial diagnosis at a facility with co-located HIV medical care was associated with shorter time to care initiation among men, though not among women. Persons diagnosed at facilities reporting larger numbers of HIV diagnoses were more likely to have delayed care initiation. Persons diagnosed as hospital inpatients had the shortest intervals to first CD4 or viral load measurements, although additional investigation is needed to determine whether in the inpatient hospital context these tests do indeed indicate the initiation of continuing HIV care. Stratified analysis according to whether or not AIDS is diagnosed concurrently with HIV would also be informative. Compared to patients diagnosed at a hospital, outpatient clinic, or private physician's office, patients initially diagnosed at a STD clinic, an HIV counseling and testing site, or a facility in the "other" category (e.g., blood banks, jails, prisons) were significantly more likely to have delayed care initiation. These findings are consistent with a national study that observed delayed entry into care following initial HIV diagnosis at a STD clinic or a community testing site.[20]

The statewide coverage of the eHARS database was a major strength of our study, but it also had several limitations: coverage was very incomplete prior to 2015, so data before that year are of limited utility. Surveillance data collects limited patient-level information, recording of the date of initial HIV diagnosis may not be fully standardized, date of first CD4 count or viral load measurement may not represent actual initiation of HIV care, and surveillance data may not have the same quality as data collected through a specific study (assuming adequate funding and quality control).

Further along the continuum, patients who have initiated HIV medical care may need support services to facilitate their remaining in care and adhering to ART in order to achieve the best clinical outcomes, extend survival, and minimize further HIV transmission. We used five

years of data (2009-2013) from the MMP survey of HIV-infected persons in HIV medical care in NC to estimate prevalence of case management utilization in the previous twelve months, probable current depression, and ART adherence, and to examine associations of case management utilization with current depression and ART adherence.

Just over half of patients (53.2%) reported receiving case management services in the previous twelve months, 21.7% experienced probable current depression, and 87.0% were 100% ART dose adherent in the past three days. These prevalence estimates were similar to case management utilization (56.5%)[72] and 100% ART dose adherence estimates (86.0%)[134] previously reported using national survey data of HIV-infected persons in care, though the national estimate for case management refers to a shorter recall interval (past six months) some two decades ago.

Our probable current depression prevalence estimate of 21.7% was slightly lower than the 25.6% estimate reported from the national 2009 MMP data.[68] Women, persons living at or below the poverty level, respondents reporting the need for transportation assistance in the previous twelve months, and participants reporting current smoking were more likely to experience probable current depression. After adjustment for sociodemographic and behavioral characteristics, utilization of case management services in the previous twelve months was positively associated with probable current depression among persons living above the poverty level (aPR, 2.05; 95% CI, 1.25-3.36), whereas no association was observed among persons living at or below the poverty level (PR, 1.01; 95% CI, 0.72-1.43).

Women, non-Hispanic blacks, respondents with less than a high school education, persons living at or below the poverty level, current smokers, and those experiencing probable current depression were less likely to be 100% ART dose adherent in the past three days. After

adjustment for gender, race/ethnicity, education, income, poverty level, probable current depression, need for transportation assistance in the past twelve months, and insurance coverage, there was no association between 100% ART dose adherence and receipt of case management services in the previous twelve months (aPR, 1.00, 95% CI, 0.95-1.05 for 100% ART dose adherence). Because of the cross-sectional design of the study, however, it is possible that case management services improved adherence in persons who would otherwise have been non-adherent, resulting in there being no cross-sectional association between current adherence and history of case management services. In addition, the self-reported data were subject to potential social desirability and recall biases.

6.3   Public Health Significance

Scientific breakthroughs during the latter half of the 20th century – discovery of retroviruses, development of highly sensitive and specific biochemical antibody and antigen tests, development of highly effective ART with tolerable side effect profiles, and the demonstration that viral suppression dramatically reduces infectiousness – have given us the ability to control the HIV epidemic, preventing its further spread and enabling infected persons to live a full life. Parallel advances in societal acceptance of the need to address HIV as a public health problem have begun to create the opportunity to tackle this major pandemic. Realizing this opportunity requires closing the gaps in the HIV care continuum, from identifying all cases of HIV to ensuring viral suppression in those found to be infected.

This dissertation has focused on the middle components of the care continuum: entry into HIV care and ART adherence among persons in care. Using NC data from two national surveillance systems – eHARS and MMP – we have assessed (1) timeliness of HIV care initiation in relation to patient and testing facility characteristics at initial HIV diagnosis, and (2)

indicators of effectiveness of HIV care among those already in care. Our findings for initiation of care indicate the need for substantial improvement in order to reach the "NHAS: Updated to 2020" goal of 85% of newly-diagnosed patients initiating care within one month.[100] By contrast, our findings for effectiveness of care show ART adherence in the NC MMP at about the same level as that in the national MMP. Given the various challenges HIV patients must navigate (rural distances, transportation, insurance, stigma, etc.), NC providers and the NC public may be reassured that patients in care are adherent as patients elsewhere in the country. But it is essential to remember that the MMP years in this study include only patients who are in care and have therefore surmounted these obstacles at least to some extent. A fuller analysis needs to account for infected persons not in care, which will become possible with versions of the MMP soon to become available.

In general, patient needs for transportation and social services, as well as for care of medical conditions in addition to HIV, must be met through medical and support services to reduce HIV comorbidities such as depression and improve ART adherence rates. This study provides evidence that persons in care in NC have received support services appropriate for their needs. Case management services were received by a significant proportion (53.2%) of HIV-infected persons covered by the MMP, especially women and persons with one or more of the following characteristics: less than a high school education, lower household income, RW/ADAP coverage only, need for transportation assistance, and current smokers. As expected, persons below the poverty level were both more likely to utilize case management services and to be currently depressed. Contrary to expectations, though, among persons above the poverty line, prevalence of current depression was significantly greater among those who reported having received case management services. However, that finding could reflect targeting of case

management services to persons suffering from depression or having other challenges that increase the risk of depression. The cross-sectional study design unfortunately made it impossible to distinguish among these possibilities.

Similarly, though no difference in 100% ART dose adherence prevalence estimates was observed between respondents who did and respondents who did not receive case management services, it is possible that ARV adherence would be lower without case management. The overall prevalence of 100% ART dose adherence in the past three days, 87.0%, was nearly identical to the 86% adherence prevalence reported from national 2009 MMP data.[134]

6.4   Future Research Directions

In NC, younger adults, males, and non-Hispanic blacks were more likely to have delayed entry into care after their initial HIV diagnosis, but additional, unmeasured patient characteristics may be more strongly associated with delayed entry into care for NC adults. Information on factors such as unmet needs for other medical services, stigma, insurance limitations, income shortages, and travel distance to HIV medical care may provide better indications of how to improve linkage to care programs. Researchers have previously reported that uninsured, HIV-infected persons established in care in Philadelphia travelled further distances than persons with public insurance, which could pose a barrier to care continuity.[13] An analysis using state-specific MMP data of persons established in care, which captures much of these data, would prove useful.

As infectious disease physicians and facilities become more available throughout NC, an updated analysis of the association between HIV medical care colocation and delayed entry into HIV medical care is warranted. Our HIV medical care colocation estimate likely underestimates the true number of sites with on-site HIV medical providers. Although the *NC ONE CALL HIV*

Provider Directory is no longer updated, the names of facilities reporting new HIV cases are collected in the NC eHARS data. These names can be used to develop an updated, more accurate count of facilities with on-site HIV medical providers.

STD clinics, HIV counseling and testing sites, and facilities other than hospitals, outpatient clinics, and private physician's offices were significantly associated with delayed initiation of care in NC. Further assessment of the latter facilities, including blood banks and prisons, is needed to identify barriers to care linkage among patients diagnosed in these facilities. Interventions to facilitate care initiation should be targeted to patients at high volume STD clinics and HIV counseling and testing sites. Lastly, analysis of eHARS laboratory data on multiple viral load measures would help determine which people with an initial measurement have truly entered HIV care and could also assess retention in care, which is essential to reduce transmission and improve clinical outcomes.

Our assessment of the utilization of case management services in the previous twelve months and associations with 1) probable current depression, and 2) 100% ART dose adherence was limited by the use of cross-sectional data. Thus, we were unable to exclude the possibility that higher current depression prevalence in association with receipt of case management in persons above the poverty level reflected targeting of case management. Similarly we could not assess whether 100% ART dose adherence was lower before case management provision. For the few participants in the MMP data reporting a need for case management services in the previous twelve months and an inability to receive these services, reasons for not receiving services were reported. In future research, reasons for case management utilization should also be reported to effectively evaluate the provision of services to HIV-infected clients. In addition, longitudinal data on recent utilization of case management, current depression, ART adherence, and viral load

assessed at least every six months would provide a better opportunity to evaluate the impacts of case management services for HIV patients in NC. Of course, such intensive data collection would be considerably more costly and logistically challenging.

North Carolina collects various data from HIV-infected persons using multiple data sources, including the North Carolina Electronic Disease Surveillance System, care system, eHARS, and MMP. The NC-LINK: Systems Linkage and Access to HIV Care in North Carolina project was funded from a HRSA Ryan White Special Projects of National Significance grant provided to the NC DHHS, Communicable Disease Branch.[139] The project has a goal of increasing testing efforts, clinical lab reporting, and linkage to care rates, while improving coordination among HIV clinicians, counselors, and bridge counselors through the integration of NC data sources into one system called NC ECHO (Engagement in Care for HIV Outreach).[139] Analysis of this complete dataset would provide a new opportunity for continuous monitoring of the HIV care continuum in NC, with regular reporting of indicators at each stage. Maintaining a focus on all steps of the continuum – including a means of monitoring and minimizing the prevalence of undetected HIV infections – will facilitate realizing the opportunity that is now at hand to bring the HIV epidemic under control and to eventually eliminate it.

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