HIV TESTING AND LINKAGE TO CARE IN NORTH CAROLINA:
EARLY DIAGNOSIS, LATE DIAGNOSIS, AND DELAYED PRESENTATION TO CARE

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ABSTRACT

SANDRA McCOY: HIV Testing and Linkage to Care in North Carolina: Early Diagnosis, Late Diagnosis, and Delayed Presentation to Care
(Under the direction of William C. Miller)

Persons with unrecognized HIV infection forgo timely clinical intervention and may unknowingly transmit HIV to partners. In North Carolina (NC), unrecognized infection and late diagnosis are common. To understand more about the individual and structural factors associated with HIV diagnosis and presentation to care, this dissertation examined three sources of data from HIV-positive patients in NC. We analyzed data from 75 patients with acute HIV infection identified through the Screening and Tracing Active Transmission (STAT) program to understand more about motivations for testing during early infection. We found that nearly one-third of patients had a sexually transmitted co-infection at the time of HIV diagnosis. The prevalence of co-infection was highest in women compared to heterosexual men (PR=0.67, 95% CI 0.31, 1.45) and men who have sex with men (PR=0.34, 95% CI 0.15, 0.76). To understand the effect of perceived social support on late presentation to medical care, we examined data from the University of North Carolina Infectious Disease Clinic Clinical and Socio-Demographic Survey. We analyzed data from 216 HIV positive patients and quantified the four functional domains of social support with a modified Medical Outcomes Study Social Support Scale. We found the median delay between diagnosis and entry to primary care was 5.9 months. Only positive social interaction support was associated with delayed presentation in adjusted models. The effect of low perceived positive social interaction on delayed presentation differed by history of a drinking problem (history of alcoholism HR=0.71, 95% confidence interval (CI): 0.40, 1.28;
no alcoholism HR=1.43, 95% CI: 0.88, 2.34). Finally, we conducted a qualitative interview study of 24 HIV positive patients entering care at the UNC ID clinic with moderate to advanced immunosuppression to describe attitudes and beliefs about HIV testing and care. The primary barrier to HIV testing prior to diagnosis was perception of risk; consequently, most participants were diagnosed after the onset of clinical symptoms. While patients were anxious to initiate care rapidly after diagnosis, some felt frustrated by the passive process of connecting to specialty care. The first visit with an HIV care provider was identified as critical in the coping process.
For the people living with HIV who courageously agreed to share their stories with me.
ACKNOWLEDGEMENTS

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<td>AHI</td>
<td>Acute HIV Infection</td>
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<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
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<td>ANOVA</td>
<td>Analysis of Variance</td>
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<tr>
<td>ARS</td>
<td>Acute Retroviral Syndrome</td>
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<tr>
<td>ARV</td>
<td>Antiretroviral</td>
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<td>CD4</td>
<td>Cluster of Differentiation 4</td>
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<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
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<tr>
<td>CFA</td>
<td>Confirmatory Factor Analysis</td>
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<td>CFI</td>
<td>Comparative Fit Index</td>
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<td>CI</td>
<td>Confidence Interval</td>
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<td>CSDS</td>
<td>Clinical and Socio-Demographic Survey</td>
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<td>CTS</td>
<td>Counseling and Testing Site</td>
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<tr>
<td>DHHS</td>
<td>Department of Health and Human Services</td>
</tr>
<tr>
<td>DIS</td>
<td>Disease Investigation Specialist</td>
</tr>
<tr>
<td>ED</td>
<td>Emergency Department</td>
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<tr>
<td>EIA</td>
<td>Enzyme Immunoassay</td>
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<tr>
<td>EMM</td>
<td>Effect Measure Modification</td>
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<tr>
<td>HAART</td>
<td>Highly-Active Antiretroviral Therapy</td>
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<td>HARS</td>
<td>HIV/AIDS Reporting System</td>
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<tr>
<td>HBM</td>
<td>Health Belief Model</td>
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<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>HR</td>
<td>Hazard Ratio</td>
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<td>HRQOL</td>
<td>Health Related Quality of Life</td>
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<td>HSV</td>
<td>Herpes Simplex Virus</td>
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ID  Infectious Disease
IMB  Information-Motivation-Behavioral Skills Model
LR  Likelihood Ratio
ml  Milliliter
mm  Millimeter
MOS  Medical Outcomes Study
MSM  Man who Has Sex with Men
NAAT  Nucleic Acid Amplification Test
NC  North Carolina
OR  Odds Ratio
PCR  Polymerase Chain Reaction
PHA  Proportional Hazards Assumption
PR  Prevalence Ratio
RMSEA  Root Mean Square Error of Approximation
RNA  Ribonucelic Acid
SAS©  Statistical Analysis Software, Cary, NC
SD  Standard Deviation
SSS  Social Support Survey
STAT  Screening and Tracing Active Transmission Program
STD/STI  Sexually Transmitted Disease/Infection
TLI  Tucker-Lewis Index
UNC-CH  University of North Carolina Chapel Hill
US  United States
VCT  Voluntary Counseling and Testing
CHAPTER ONE: SPECIFIC AIMS

Highly active antiretroviral therapy has been the cornerstone of HIV care in the United States since its widespread adoption in the late 1990's. However, its benefit is best realized in conjunction with timely access to medical care. Early presentation for medical care among HIV infected persons can improve the length and quality of life by providing access to antiretroviral drugs and prophylactic treatment for opportunistic infections.\(^1\) Further, HIV testing and counseling and knowledge of one's serostatus has been shown to reduce high-risk behavior, thereby reducing transmission to others.\(^2\),\(^3\) Early entry into care can also optimize personal and healthcare system planning.\(^4\),\(^5\) Despite these benefits, many adults enter care late in the course of HIV infection, countering the benefits of timely access to HIV services and missing opportunities for risk reduction.\(^6\)-\(^8\) Consequently, linking HIV positive persons to high-quality care and prevention services has been identified as a priority of the U.S. Centers for Disease Control and Prevention (CDC).\(^9\)

The process of an HIV-infected individual presenting to primary care can be divided into two meaningful time periods: 1) the time between acquisition of infection and testing; and 2) the time between testing and presentation to care. The time between HIV acquisition and testing is a function of risk perception, access to testing services and testing history, demographic factors, health insurance, education, and prison status.\(^6\),\(^7\),\(^10\)-\(^16\) However, some individuals are diagnosed with HIV in the first few weeks of infection, known as the acute phase, and their reasons for testing are less well understood. For some, co-infection with sexually transmitted infections (STI) may prompt HIV testing during the acute phase.
Although the synergistic relationship between HIV and STIs with respect to transmission and acquisition is well-described, the possible impact of concurrent STIs on HIV testing warrants greater attention.\textsuperscript{17, 18}

Factors affecting the time period between HIV diagnosis and presentation to care are less well characterized. Demographics, health insurance status, injection drug use, and testing and counseling history are associated with delayed presentation, but the role of psychosocial factors, such as perceived social support, on care-seeking behavior has not been rigorously evaluated.\textsuperscript{11, 14, 19, 20} Social support consists of factors such as belonging to a social network, perceived satisfaction with support, emotional support, information, and tangible assistance.\textsuperscript{21} Social support improves coping with HIV, quality of life, and has been demonstrated to improve adherence among patients on highly active antiretroviral therapy (HAART).\textsuperscript{22-26} Given the positive role of social support on adherence, it is feasible that HIV positive individuals with higher levels of perceived social support may seek medical care earlier than those with less perceived social support.

In this dissertation, we examined the structural and individual factors that influence HIV testing and care-seeking behavior in North Carolina. We undertook a multidimensional approach, relying on data from diverse sources and utilizing different methods of data collection. We relied on acute HIV surveillance data, psychosocial factors from clinic interviews, and in-depth qualitative data. This multifaceted approach provides new knowledge about HIV testing and care-seeking that is directly applicable to North Carolina.

**Specific Aim 1.** a. Describe the prevalence and types of sexually transmitted infections (STI) among individuals acutely infected with HIV at the time of testing in North Carolina.

**Hypothesis:** STIs are common among individuals with acute HIV.
b. Evaluate variation in the time from HIV acquisition to testing among individuals with acute HIV infection by the presence of STI at the time of HIV testing and testing site type.

Hypotheses:

1. Persons diagnosed with acute HIV and a concurrent STI will be diagnosed earlier than those without a concurrent STI.
2. Persons diagnosed with acute HIV at STD testing sites will be diagnosed earlier than those diagnosed at non-STD testing site types.

c. Determine differences in median serum viral load (copies/ml) by the presence of STIs at the time of HIV testing and testing site type.

Hypothesis: Among persons with acute HIV infection, the HIV viral load will be higher in persons with an STI than in persons without an STI.

Overview: We utilized information on patients with acute HIV infection identified through the North Carolina Screening and Tracing Active Transmission (STAT) Program to determine the prevalence of STI co-infection and factors associated with co-infection. We determined the effect of STI co-infection and testing site type on the time between HIV acquisition and HIV testing. We also evaluated differences in baseline serum HIV RNA, and examined factors associated with testing before and after peak HIV viremia.

Specific Aim 2. Describe the effect of perceived social support on late presentation to medical care among HIV positive persons receiving care at the UNC Infectious Disease (ID) Clinic.
**Hypothesis:** The presence of a strong social support system will reduce the time between testing HIV positive and initial presentation to HIV care.

**Overview:** Using the Clinical and Socio-Demographic Survey from the Center for AIDS Research Clinical Core at UNC, we examined the effect of social support on the time from the first positive HIV test to the initial presentation for primary medical care. We conducted a validation substudy to examine the reliability of self-reported first positive HIV test by comparing to state HIV/AIDS morbidity records. Social support was quantified with the modified Medical Outcomes Study (MOS) Social Support Survey Scale and entered into a Cox proportional hazards model.27

**Specific Aim 3.** Describe attitudes and beliefs about HIV testing and care among HIV infected persons attending the UNC ID clinic who presented with clinically advanced illness.

**Overview:** We conducted semi-structured qualitative interviews of HIV-infected persons who presented to care with moderate to advanced immunosuppression, defined as an indication for HAART therapy (CD4+ T-lymphocyte cell count <350 cells/mm$^3$ 28). Data collection was guided by the achievement of theme saturation and consisted of 24 interviews. The conceptual framework and interview instrument was developed with constructs from the Health Belief Model (HBM) and the Information-Motivation-Behavioral skills (IMB) model.29, 30
CHAPTER TWO: BACKGROUND AND SIGNIFICANCE

Epidemiology of HIV/AIDS in the Southern United States

The southern region of the U.S. includes 16 states and the District of Columbia and represented 36% of the U.S. population in 2005. By the end of 2005, 40% of the 425,910 persons living with AIDS in the U.S. resided in the southern U.S., and from 2001 to 2005, the number of deaths from AIDS increased in the region, while other regions of the U.S. experienced declines. An analysis of AIDS case reports since 1981 found that being a southern state was independently associated with a 4.3% higher AIDS growth rate compared to other states.

The reasons for the HIV/AIDS burden in the U.S. South are multidimensional and complex. The South performs poorly on a variety of health indicators including death rate (the states with the 11 highest death rates are located in the South), diabetes rate, heart disease, and stroke. The South also has high rates of the uninsured, which increased from 18.2 percent in 2004 to 18.6 percent in 2005. The South has the highest proportion of people living below the poverty line – 14%, compared to 11% in the Northeast and Midwest and 13% in the West. In addition, the high proportion of the population living in rural areas may undermine an already weak health infrastructure by adding additional obstacles to HIV care such as transportation issues and lack of specialty health care providers.

There are other important factors that influence the HIV/AIDS epidemic in the South. The demographic makeup includes a large proportion of the U.S. African American population, a group that is disproportionately affected by the epidemic. High rates of
sexually transmitted diseases play a role by increasing the likelihood of HIV acquisition, transmission, or both. Social factors also play a role facilitating the spread of HIV in the South. Incarceration, stigma, trust in providers, marriage rates, and non-injecting drug use have been shown to be associated with the epidemic. Further, examination of sexual network patterns has suggested that levels of disassortative mixing and concurrent relationships may be higher in the South.

Thus, these factors demonstrate the need to improve our understanding of the epidemiology of the HIV/AIDS epidemic in the South with the goal to reduce new infections and ensure high-quality care for persons living with HIV/AIDS.

Unrecognized HIV Infection

HIV counseling and testing has been the predominant HIV prevention paradigm since the 1980s. Each year, approximately 16 to 22 million people are tested for HIV, a number that has remained the same for the past decade. This translates to roughly 38% of the population having ever had an HIV test in their lifetime. However, there is room for substantial improvement: it is estimated that approximately 25% of all adults living with HIV/AIDS in the U.S. do not know their status.

Unrecognized HIV infection has important public health consequences. In addition to limiting the benefits of early medical care including antiretroviral therapy and prophylaxis for opportunistic infections, persons with unrecognized infection may unknowingly transmit HIV to partners. The prevalence of unrecognized infection varies by group. A national study of young men who have sex with men (MSM) found that 77% of those with HIV infection were unaware of their infection, ranging from 91% of black MSM to 60% of white MSM. Most with unrecognized infection perceived themselves to be at low risk for being infected. An inner city emergency department found 29% of all HIV infections to be unrecognized and among STD clinics, approximately 40% of infections were unrecognized. These results
underscore the barrier that unrecognized infection, and consequently, late diagnosis, poses to HIV prevention and care efforts.

HIV testing recommendations in the past have focused on targeted testing to high-risk groups or areas of high HIV prevalence. However, as the HIV/AIDS epidemic in the United States evolved to include greater numbers of women, minorities, and heterosexuals, persons <20 years, and those who reside outside of major metropolitan areas, targeted testing became less effective. Several studies demonstrated these gaps in HIV prevention efforts. An anonymous HIV serosurvey of 52,260 patients found that those who were not voluntarily tested were more likely to be HIV infected than those who were tested, regardless of demographic characteristics, risk group, or STD diagnoses. Similarly, among young MSM, 72% of those with unrecognized HIV infection had a regular source of health care, suggesting missed opportunities for diagnosis. Of those with HIV infection in a large health care plan, 21% denied having risk factors in the five years prior to diagnosis. Some argued that time restraints precluded incorporation of the traditional HIV counseling and testing model into routine medical care, resulting in missed opportunities to identify those with unrecognized infection.

In response to the changing epidemiology of HIV in the United States, the Centers for Disease Control and Prevention (CDC) launched the Advancing HIV Prevention Initiative in 2003. The Initiative promoted the adoption of simpler testing procedures without pretest counseling and the expansion of testing recommendations to include those with risk factors in low prevalence clinical settings. The Initiative was followed in 2006 by revised testing recommendations for the adoption of routine, voluntary HIV screening for patients in all health care settings. An explicit goal of the new screening guidelines is to foster earlier detection of HIV infection and identify those with unrecognized infection. It is expected that the incorporation of HIV testing into routine medical care will increase the numbers of people tested, de-stigmatize the testing process, and improve access to HIV care after diagnosis.
The availability of over the counter home based HIV testing kits may remove some barriers to HIV testing. Since 1996, home-based specimen collection kits have been available (Home Access HIV-1 Test System) but users are required to call a toll-free number for results after mailing in dried blood spots. In 2005, the FDA began hearings for the first home HIV testing system (OraQuick ADVANCE 1/2). It is unclear if a completely anonymous home based HIV test can increase the number of HIV positive U.S. residents who are aware of their serostatus. Home testers must be able to afford the test (currently US $44) and are likely to be the “worried well,” new couples confirming HIV status, people seeking confirmation of positive tests received elsewhere, and persons with recent high-risk exposures who may be in the window period before antibody detection is possible. In the latter case, false negative results during acute infection may lead to increased transmission during one of the most infectious periods of HIV infection. In addition, monitoring outcomes such as linkage to care will be impossible, and false positive results may cause unnecessary distress. However, home based tests offer convenience, privacy, and the timely receipt of results. While the value of increasing access to HIV testing is unquestioned, the ability of home tests to affect the U.S. HIV epidemic in a meaningful way will be determined in the coming years.

Delays in Presentation for Medical Care

From a clinical perspective, timely access to HIV care can improve the length and quality of life by providing access to antiretroviral drugs and prophylactic treatment for opportunistic infections. Current treatment guidelines recommend the initiation of highly active antiretroviral therapy (HAART) once the CD4+ T-lymphocyte cell count falls below 350 cells/mm$^3$. The CD4 count is an important prognostic marker and is strongly associated with survival. The survival benefit of HAART declines as the baseline CD4+ cell count at the initiation of therapy falls below the treatment threshold of 350 cells/mm$^3$ – individuals
initiating therapy <200 cells/mm$^3$ have at least a three times greater risk of death than those whose levels were above 200 cells/mm$^3$.\textsuperscript{1} Individuals who delay seeking medical care, knowingly or unknowingly, forgo these benefits.

In addition to the clinical benefits of early HIV care, HIV testing and counseling and knowledge of one’s serostatus has been shown to reduce high-risk behavior, thereby reducing transmission to others.\textsuperscript{2,3,58,59} A meta-analysis of 11 studies from 1998-2003 in the U.S. found that the prevalence of unprotected anal or vaginal intercourse was an average of 53% lower in the population aware of their HIV positive status compared to those who were HIV positive but unaware of their status.\textsuperscript{41} Similarly, the transmission rate (number of new infections per year divided by the number of persons living with HIV/AIDS in a year) among those unaware of their HIV infection is more than six times greater than those aware of their status (10.8% vs. 1.7%, respectively).\textsuperscript{60} In additional to the potential for behavior change, the reduction in plasma viral load achieved by antiretroviral therapy may decrease the transmission probability to partners.\textsuperscript{61} Taken together, these studies suggest that prevention counseling and medical care among newly diagnosed individuals can reduce, but not eliminate, transmission to at-risk partners.

Despite these benefits, late entry to care is common among HIV infected adults. In the United States, 40% of those tested in 2004 were diagnosed with AIDS less than one year after the initial HIV diagnosis, a figure that has remained relatively stable since 1994.\textsuperscript{33,62} Further, Samet et al. estimated that the median delay from HIV acquisition to medical presentation in two clinics in Massachusetts and Rhode Island was eight years. The situation in the South is more concerning. In North Carolina, Gay et al. found that in the University of North Carolina HIV outpatient clinic, 75% of patients had an indication for antiretroviral therapy at their first clinic visit, and 50% had a CD4+ T-cell count less than 200 cells/mm$^3$.\textsuperscript{12} In Birmingham, Alabama, 41% of patients presenting to an HIV/AIDS outpatient clinic had progressed to CDC-defined AIDS.\textsuperscript{63} These findings and the knowledge of the
unique HIV epidemic in the South raise special concerns about access to testing and medical services in the region.\textsuperscript{64}

The process of an HIV-infected individual presenting to primary care can be divided into two meaningful time periods: 1) the time between acquisition of infection and testing; and 2) the time between testing and presentation to care (Figure 2.1).\textsuperscript{7} The summation of the time between HIV acquisition and testing (period $T_3$ in the Figure) and the time period between HIV diagnosis and presentation to care ($T_4$) comprise the overall delay between acquisition and presentation to medical care ($T_5$).

Methodologically, considering the two time periods ($T_3$ and $T_4$) as distinct outcomes with separate, but overlapping “etiologies” is necessary to prevent mixing the effects of “delayed testing” with “delayed care.” Studies that consider only the outcome at the time of entry to care, such as “presentation with an AIDS defining illness”, treat barriers to testing the same as barriers to seeking care. The validity of this assumption has not been resolved. For example, a study in a southern HIV/AIDS clinic found that presentation within six months of diagnosis \textit{and} presentation more than five years after diagnosis were associated with AIDS at the initial clinic visit among whites – this finding suggests that some people test early and then delay care, and that some people test late and only present to care once they experience clinical symptoms.\textsuperscript{63} Studying these two time points as methodologically distinct is therefore necessary to understand the process of awareness, testing, and entering care.

Because the date of HIV acquisition is typically unknown, most efforts to improve patient outcomes after diagnosis have focused on promoting testing programs, increasing the numbers of “early testers”. Although HIV testing and counseling is the cornerstone of HIV prevention efforts, focusing on testing behavior alone will not universally improve access to quality HIV care and positive health outcomes. The time period between acquisition and testing may account for the majority of the medical care delay on a population level, but some individuals delay care even after testing positive. A
comprehensive understanding of both the barriers to testing and seeking care is necessary to optimize health outcomes for newly diagnosed HIV positive individuals.

**Delayed presentation to care due to late diagnosis.** Many people do not present to medical care until they are symptomatic or have an AIDS-defining illness, and only then do they find out they are HIV positive. Other people test positive before the development of symptoms but many years after they acquired the infection. This phenomenon, known as delayed testing, is common in the United States. In the Birmingham clinic, 54% of those who presented for initial care with CDC-defined AIDS had been diagnosed in the year preceding their entry to care.\(^6^3\) Similarly, a study of 7,200 HIV infected persons found that 42% sought testing because of illness.\(^5^2\) Delayed testers miss out of the benefits of early medical care and may unknowingly transmit the infection to others.

Factors associated with less HIV testing include age, being non-White, having less education, living in a non-metropolitan area or the Midwest, using recreational drugs, and being exposed to HIV through heterosexual contact.\(^6^2, 6^5, 6^6\) Experiencing symptoms is an important determinant of testing behavior - most people who delay testing (65%) eventually receive HIV testing because of illness.\(^6^2\) In addition, accurately perceiving HIV risk can act as a facilitator or barrier to HIV testing – either by increasing awareness and thus the likelihood of testing or by increasing fear of testing positive.\(^6^5-6^7\) For example, in New England, only 66% of HIV positive participants were aware of their HIV risk before testing, and of those unaware of their risk, 42% were eventually tested by either a physician recommendation or hospitalization.\(^7\) Structural level factors are also related to testing such as contact with the health care system and incarceration.\(^6^8\)

Delayed testing poses a significant barrier to HIV prevention efforts, and many are hopeful that the new CDC testing guidelines will have an impact on reducing the numbers of individuals who first test positive late in the course of disease.
Delayed presentation to care due to delay after diagnosis. Less common than late testing is the phenomenon of delaying the initiation of medical care after testing positive. Median delays from HIV diagnosis to presentation for care range from 30 days to over a year. A study of HIV-infected women in New York City found that roughly one quarter delayed more than six months after diagnosis to see a physician. Delayed initiation of care may become more of a problem as new HIV testing guidelines recommending routine HIV screening in all health care settings take effect. Screening for HIV without successful linkage into HIV care undermines the positive benefit of the screening program, as the maximum advantage of HAART and prophylaxis for opportunistic infections is realized when the patient enters care early in the course of disease. Even recently infected patients for whom treatment is not recommended can benefit from risk-reduction counseling, social services, and case management.

Race is often found to be associated with delay seeking medical care after HIV diagnosis. African Americans and Hispanics tend to delay longer or in greater numbers than Whites, although no effect of race was found in 2 studies. One study found that Hispanics enrolled into care earlier than Whites, with no difference between Whites and African Americans observed. In addition to race, sex is also associated with delayed care. Men have been found to delay care longer than women after diagnosis in some studies, but not all. Intravenous drug use has been associated with delay after diagnosis in most but not all studies.

The data on insurance status and delayed medical care after diagnosis are mixed. Having any insurance has been shown to decrease the likelihood of delay in some studies. However, health insurance at the time of diagnosis was not found to have an effect on care delay in a study of 2 urban hospitals in New England as well as among clients to California’s Early Intervention Program. Turner et al. found that that Medicaid was associated with shorter delays after diagnosis. In contrast, a study of HIV positive patients
from STD clinics nationwide found that none of the patients who had delayed care for at least six months cited lack of money as a primary reason for not making a clinic visit.59

The site of the HIV test or the counseling, notification, or referral method may be associated with delays. Turner et al. found that delays were equally as common among private testing sites, clinics, anonymous testing sites, and hospitals, but testing at “other” testing sites improved linkage to care.20 The authors postulate the “other” sites may be research studies or other programs. Samet et al. reported that not being notified of HIV status in person (e.g. mail or telephone) was associated with a 2.5 years longer delay before entering care.19 Longer delays have been reported for individuals referred from prison, another HIV/AIDS organization, or from family or friends.14, 72 Additional factors, such as competing care giving responsibilities, HIV risk awareness at testing, and having a usual source of care may also be important issues.19, 20, 72, 73 A qualitative study of women found that the main barriers to seeking care were psychological and not socioeconomic, and that the trauma of discovering one’s HIV status often led to a state of denial about their status or the seriousness of their disease.69

There is little information about the effect of social support on delays seeking medical care, and the inconsistency of measurement precludes any definitive conclusions. Samet et al. found that not having a living mother and not having a spouse or partner was associated with delay after diagnosis.19 In the California study, family size of 2 or more was associated with shorter delays (124 vs. 142 days, respectively), although this finding was not confirmed in the multivariable analysis.72 In an urban hospital, perceived support was not correlated with the time since diagnosis, although the time since diagnosis was self-reported and the sample size was only 114 patients.74 More research is needed to understand the role that support from others may play in the decision making-process to seek HIV care.

Although these findings provide important preliminary insight into individuals who delay medical care, many other factors that may be associated with delay have not been
examined. For example, mistrust of the medical establishment, religion/spirituality, financial resources, and transportation may be important influences. To date, only a handful of studies have been explicitly designed to improve our understanding of delayed medical care by interviewing patients for the reasons they delay medical care in their own words. What can be concluded is that HIV testing services perform a critical public health function by linking newly diagnosed patients into care, and the success of this linking function requires rigorous evaluation to determine if improvement is needed.

**Theoretical Considerations about Access to HIV Care**

We can anticipate that antiretroviral drugs will continue to improve and the life expectancy of those diagnosed with HIV will extend past 24 years in the future.\(^7\) Despite these advances, we still do not have an adequate understanding of the process of testing positive and seeking medical care from the patient’s perspective. Unfortunately, most of the HIV/AIDS research in this area has focused on describing characteristics of individuals who present late in the disease course from ubiquitous patient databases – limiting the findings to basic demographics correlated with delayed care. Causal inference requires more in-depth information from that which can be found in medical records, highlighting the need for focused, in-depth studies on the linkage process from testing site to health care provider. In addition, looking to research on other chronic diseases and theories of access to medical care may provide valuable insight as HIV/AIDS is increasingly considered a chronic medical condition.

An ecological perspective of HIV care suggests that we consider individual characteristics and contextual factors such as the availability of services and the policy environment in which individuals seek medical care. Aday and Andersen published a framework for the study of access to medical care in 1974 which illustrates the multiple levels of influence on access to care (Figure 2.2).\(^6\) Characteristics of the health care
delivery system include the volume and distribution of resources as well as the structural organization and method of entry. Characteristics of the population at risk include predisposing characteristics which influence utilization of services (e.g. demographics, beliefs, attitudes, and values), enabling factors which relate to the means of an individual to seek care, and the need component, which refers to illness level. The utilization of health services and consumer satisfaction constructs reflect the outcomes of movement through the health care system.

In the context of HIV testing and care, most research on delayed testing and entry to care has focused on identifying characteristics of the population at risk, with a tendency to identify immutable factors that are associated with delay (e.g., age, race, sex). There are other unknown descriptors of the population at risk, such as barriers to care, views about personal susceptibility and severity of the disease, and beliefs about the benefits of medical care that have yet to be described. At the next level of the framework, evaluation of the impact of health insurance and socioeconomic status begins to address structural factors that influence care seeking ("Characteristics of the Health Care Delivery System," Figure 2.2). However, there remains much to be evaluated in terms of the availability of services, the ease at which persons utilize the services, the barriers to utilizing services, and the personal belief systems which influence the decision-making process. We do not have a comprehensive understanding of the barriers and facilitators to seeking HIV testing and medical care, and improving our knowledge can only help to improve the delivery of HIV/AIDS health care services in the U.S.

The breast cancer model of care can be viewed as similar to that of HIV/AIDS – women are screened for abnormalities and referred to specialty care when necessary. Women who delay screening or medical care frequently present to care in the advanced stage of disease. Lannin et al. examined factors associated with a late tumor stage at the initial breast cancer diagnosis in eastern North Carolina. Factors associated with advanced
disease stage at presentation included being African American, low income, lacking private health insurance, and never having been married. In addition to these findings, they examined the role of culturally derived folk beliefs, religious beliefs, and fatalism on delayed medical care.

Formative research from qualitative interviews with women in the same study highlighted the importance of understanding the cultural belief system with which patients understand their disease and negotiate the health care system. Almost all of the women believed at some point during their diagnosis period that their lumps were a result of “bad blood” and impurities in the body which were best left alone if they were asymptomatic. Many women thought that surgery and other medical care would exacerbate the problem. Medical decisions were made cautiously, juxtaposing an indigenous model of disease with the biomedical model of their caregivers.

As a result of measuring folk beliefs in their study, the effect of race on presentation with advanced stage disease diminished from OR=3.0 to 1.2 when socioeconomics and cultural beliefs were added to the model. These findings illustrate that although many of the demographic factors associated with delayed diagnosis or delayed medical care are similar for breast cancer and HIV/AIDS, a deeper understanding of the attitudes, beliefs, and knowledge are necessary to accurately interpret the findings.

Health Behavior Models. One relevant model to consider is the Health Belief Model (HBM). The HBM was developed in the early 1950’s to explore the reasons that many people did not participate in programs by the U.S. Public Health Service to prevent and detect disease. The model consists of five main dimensions which explain preventative health behavior (Table 2.1). Perceived susceptibility refers to beliefs that a person is susceptible to a condition. Perceived severity refers to beliefs that the condition has serious consequences. Perceived benefits and barriers refer to the costs and benefits of taking action for a
particular condition. Cues to action are factors that stimulate a person to action, such as health promotional materials or television advertisements.\textsuperscript{79} The Health Belief Model has been used in previous HIV research examining the barriers to condom use, medication adherence, and predictors of HIV testing.\textsuperscript{80-82}

Table 2.1 also presents the potential HIV care factors that relate to each construct in the HBM. For example, perceived susceptibility is related to awareness of HIV risk and how this influences HIV testing – awareness of risk is generally a precursor to seeking HIV testing. Further, belief in a folk model of disease may influence if a person who has tested HIV positive believes that he/she is at risk for symptoms or complications as the disease progresses. The HBM is a useful theoretical model which extends beyond simply assessing individual barriers to seeking care by understanding additional societal, contextual, and cultural factors which influence the utilization of health care services.

A second model relevant to this work is the Information-Motivation-Behavioral Skills (IMB) Model.\textsuperscript{30} This model was developed to facilitate the development of interventions to reduce HIV/AIDS risk behavior. The model postulates three determinants of risk reduction: 1) basic \textit{information} about HIV transmission and prevention, 2) \textit{motivation} to act on one’s knowledge about HIV transmission and prevention, and 3) \textit{behavioral skills} for performing specific HIV preventative acts.\textsuperscript{30} The model is novel in that information and motivation are independent, such that highly knowledgeable individuals may not be motivated to change their HIV risk behavior, and highly motivated individuals may not be necessarily well informed about HIV transmission and prevention. The IMB model is directly applicable to the decision to be tested for HIV as well as health seeking behavior after an HIV diagnosis.

In summary, the availability of thoughtful theoretical models and related work in other fields warrants increased attention to the issue of delayed medical care, with a goal to elucidate meaningful factors beyond demographics that are associated with delayed care.
**Acute HIV and Sexually Transmitted Infections (STI)**

Acute HIV-1 infection is the interval in the HIV disease course when the virus can be detected in the blood serum and plasma before the body has created antibodies against the virus. During the acute phase the virus rapidly and widely disseminates to cellular reservoirs throughout the body, typically lasting approximately 4-6 weeks after the initial exposure to the HIV virus. During this period, infected persons experience a dramatic increase in plasma viral load and viral shedding from the genital tract. Over time, the body’s virus-specific immune responses are mounted, resulting in reduction of plasma viral load and shedding, and the beginning of the long clinical latency period.

The period of acute HIV infection has been identified as a key intervention period to interrupt transmission. Because viral load is a predictor of the probability of sexual transmission of HIV, the peak viremia characteristic of the acute phase dramatically increases the likelihood of sexual transmission during this period. The average probability of male to female transmission of HIV-1 in a single unprotected coital act has been estimated to be between 1 in 2000 to 1 in 328 coital acts during established (non-acute) HIV infection. However, during acute infection, the probability of transmission has been estimated to be approximately 1 in 200 coital acts. Population modeling has indicated that this short state of hyper-infectiousness may disproportionately contribute to the propagation of the epidemic.

Understanding the testing behavior of those with acute HIV is important as this is the earliest possible time point for clinical and public health benefit. Individuals who are treated with antiretroviral medications (ARV) during acute infection may experience clinical benefit. Individuals who begin ARV therapy during acute infection appear to have a lower viral set point, which is correlated with survival. They may also have a lesser degree of viral diversification, which could make these individuals less susceptible to developing resistance to antiretroviral drugs. Further, early treatment may reduce the levels of latently HIV-
infected CD4+ T-lymphocytes and preserve host HIV-specific immune function.\textsuperscript{97-100} Regardless of the outcome of the current debate on when best to start treatment, individuals with acute HIV can benefit from the case management and social support services of routine medical care.

In addition to the potential for individual clinical benefits of early diagnosis and treatment, the public health implications of acute HIV are tremendous. In addition to the ability to generate accurate incidence rates of HIV infection, acute HIV detection offers new insights into the real-time dynamics of an epidemic. Detection of acute infections can be used to identify outbreaks of disease or sexual networks at high risk.\textsuperscript{101, 102} Further, the identification of geographic regions of high HIV transmission can allow for more effective targeting of limited public health resources to the areas of highest risk. Detection of acutely infected persons also provides the opportunity for more effective partner notification, counseling, and testing services.\textsuperscript{89, 103} North Carolina has established itself as a leader in detecting acute HIV via a novel pooling strategy utilized at all publicly funded testing sites.\textsuperscript{103}

**Detection of Acute HIV Infection.** Although the detection of HIV during the acute phase could be viewed as a chance occurrence, there are some factors that might influence testing during this brief but critical time period. Roughly half of all people with acute HIV will develop symptoms of acute retroviral syndrome, a nonspecific flu-like illness including fever, rash, fatigue, nausea and vomiting, and night sweats.\textsuperscript{103-105} The symptoms may be severe enough to prompt medical care, and often astute physicians will consider HIV testing. Anecdotal evidence in North Carolina suggests that health promotion materials about acute HIV infection have led to several individuals with acute HIV infection requesting acute (RNA) testing on their own behalf after experiencing symptoms (unpublished data). In North Carolina, most individuals with acute HIV requested an HIV test directly (64%), whereas
other common reasons for testing included STD related testing, provider referral, and testing for drug treatment related reasons (McCoy SI, unpublished data).

In terms of demographics, individuals with acute HIV tend to parallel the HIV infected population. In North Carolina, 73% of men with acute HIV reported a history of sex with men, 22% of all acutely infected persons were recently released from prison, and 22% had engaged in transactional sex.\textsuperscript{103} In San Francisco and Los Angeles, acute or primary infection was associated with MSM and having a known HIV positive partner.\textsuperscript{105, 106} Co-infection with sexually transmitted infections is also common in individuals with acute infection.\textsuperscript{103, 104} Little is known about the testing frequency, cues for testing, and risk awareness of those with acute HIV. Since these individuals represent the earliest possible time point for entry to the medical system and public health intervention, a thorough understanding of the testing behavior during this time is warranted.

While the role of acute HIV in the HIV epidemic has garnered recent attention, little attention has been given to how sexually transmitted infections (STIs) may interact with acute HIV. STIs have a well-established synergistic relationship with chronic HIV infection. Co-infection with HIV and an STI can increase the probability of HIV transmission to an uninfected partner by increasing HIV concentrations in genital lesions, semen, or both.\textsuperscript{90, 107} STI infection can also increase the likelihood of HIV acquisition by reducing physical and mechanical barriers, increasing the concentration of HIV receptor cells, and, in the case of women, changing the vaginal environment to favor HIV infection.\textsuperscript{17, 108-110} In the case of acute HIV, STI co-infection appears to be common. A study in a Malawi sexually transmitted disease (STD) clinic found that 17 of 23 persons with acute HIV infection had an STD detected.\textsuperscript{104} In North Carolina, eight of 23 (35%) persons identified in the first year of the Screening and Tracing Active Transmission (STAT) program had symptoms consistent with an STD.\textsuperscript{103} No additional studies have described the prevalence of STIs among individuals with acute HIV in the United States.
In addition to understanding the types and prevalence of STIs most commonly associated with acute HIV, an improved understanding of the way that STI co-infection impacts testing behavior is also necessary. Individuals with symptomatic STIs may seek medical care at STD clinics and consequently be tested for HIV earlier than those without STD co-infection. Further, STD clinics may be more likely to incorporate routine HIV testing and therefore identify individuals earlier in the course of HIV infection than other types of testing sites. Understanding how STIs impact testing behavior may have important implications for testing protocols as well as the adoption and design of RNA testing programs to detect acute HIV (e.g., targeted testing, pooling algorithms).

Social Support and Health

Social support is a combination of the different types of support received from friends, family, and acquaintances. Social support can be defined as the existence or quantity of social relationships and the resources provided by other persons.\textsuperscript{21, 111} Social support can be subdivided into structural aspects of support and functional aspects of support. Structural aspects of support include an objective assessment of the size, type, contact, and density of social networks and ties.\textsuperscript{112} Functional support assesses whether the interpersonal relationships fulfill particular functions, such as provide affection, a sense of belonging, or material aid (Table 2.2).\textsuperscript{111} Functional support can be subdivided into four support components – emotional, informational, tangible, and belonging (or appraisal). Emotional support includes expressions of comfort and sharing. Informational support consists of sharing advice, information, and guidance. Tangible support includes the provision of material aid, such as transportation, money, or childcare. Finally, belonging support includes belonging to a social network with which to engage in social activities.\textsuperscript{112} Together, structural and functional support describe the types of resources we receive from other people.
Social relationships have a well-established relationship to health. Most studies that evaluate the role of either structural or functional support find that the level of support is inversely related to all-cause mortality.\textsuperscript{112} The impact of social support on specific conditions is less clear, although the findings are compelling. In one study of Mexican Americans, mortality following myocardial infarction was 3.4 times more likely among those with low levels of social support compared to those with higher levels of social support, even after controlling for a battery of cardiovascular disease risk factors.\textsuperscript{113} This finding has been validated by at least one other study.\textsuperscript{112} A landmark study of weekly group therapy and breast cancer survival in 1989 showed a significant effect on survival, although treatment improvements since then may have diminished the effect.\textsuperscript{114-116}

The mechanism by which social support exerts its effect on health is not clear. Social support could act as a main effect and have a causal effect on health outcomes through psychological-physiological pathways which influence immune or neuroendocrine functioning.\textsuperscript{111} Social support could also act as a main effect by influencing the adoption of healthy (or unhealthy) behaviors (e.g. smoking, seatbelt use, medical care seeking). Alternatively, social support may act as a “buffer” between stress and negative health outcomes.\textsuperscript{117} The buffering hypothesis posits that social support reduces the perception that an event is stressful and/or facilitates healthful behaviors after the event.\textsuperscript{117} While the mechanism of social support’s action on health may be unknown, the field of social support and HIV/AIDS has been inadequately explored.

**Social Support and HIV/AIDS.** The relationship of social support on HIV/AIDS outcomes has not been well explored and therefore no firm conclusions are possible. There is, however, some evidence that social support may have an influence on positive health outcomes for individuals with HIV/AIDS.
Social support may improve positive coping with an HIV diagnosis. Coping includes all individual efforts to mediate stressful situations and the negative emotions that arise with these situations. Social support may affect coping by the evaluation of an event or stimuli as stressful and then individual coping with the event if it is deemed to be stressful. One study of social support and coping among HIV positive gay or bisexual men found that men with higher levels of perceived social support reported greater use of positive action coping (e.g., ‘formed a plan of action’) and seeking social support. Men with lower levels of social support reported more self-destructive coping (e.g., ‘reducing tension by drinking’).

Social support has been found to improve adherence in most studies. Adherence to ARVs optimizes treatment benefit, as even small declines in adherence have been shown to have effects on plasma HIV-1 RNA suppression and the development of drug resistant mutations. In general, most studies that evaluate some type of social support find it to be associated with improved adherence. Kalichman et al. found that individuals with less social support were more likely to be nonadherent in the past two days compared to those with higher levels of support (OR=2.0), but this effect disappeared in the multivariable analysis when education and health literacy were included - suggesting the possible overlap of these two constructs. A study in the southeastern U.S. found that an unmet need for a support group was independently associated with not currently taking any HIV medications, even after adjusting for CD4+ cell count, symptom status, and demographics.

Social support might improve quality of life after an HIV diagnosis. One study in Spain evaluated the role of social support on health related quality of life (HRQOL) and found social support to be positively associated with both the physical and mental health indexes of quality of life on the HRQOL scale.
Social support may also affect the care-seeking behavior of newly diagnosed individuals. As described above, social support can influence health independently of other stressors by influencing the adoption of healthy (or unhealthy) behaviors or activities and adherence to social norms. In addition, social support can influence health indirectly by buffering the pathogenic effects of stressful events through the process of perceiving the event as stressful and/or coping with the stress. Both of these mechanisms could potentially impact the care seeking behavior of newly diagnosed individuals. To date, there is only one paper that has explicitly examined the role of social support on the time to seek medical care after an HIV diagnosis, and it did not find any correlation.

However, there is some evidence from related areas that suggests that social support plays an important role in the acceptance and readiness to address a new HIV diagnosis, which may translate to care-seeking behavior. McClure et al. found that the presence of higher levels of social support was significantly associated with attending at least one clinic visit in the first six months after a patient’s initial appointment. Another study found that HIV infected, pregnant women participating in a qualitative study cited lack of social support as a barrier to seeking adequate prenatal care. Another qualitative study of HIV infected women found that the main barriers to seeking care were psychological and focused on the trauma of discovery, lifestyle circumstances, and limited knowledge about the availability and success of newer treatments. Factors related to financial circumstances or health insurance were cited, but much less commonly than the psychosocial factors, suggesting that supportive services to help women come to terms with their infection may reduce delays to seeking medical care.

The presence of functional social support, especially informational and tangible support, may be instrumental in encouraging newly diagnosed individuals to seek care. For example, a social network may help to overcome the previously identified barriers to care, such as fear of drug side effects, lack of transportation, or a fatalistic attitude. Further,
individuals with larger networks or more familial responsibility may believe that they have ‘someone to live for’ and may be more willing to seek care, even if it falls outside of their traditional belief system. Social support may also help to overcome fears about HIV-related stigma in the healthcare system. Thus, evaluation of the role of social support on HIV care-seeking behavior would bring value to programs who seek to improve linkage to medical services after an HIV diagnosis.

**Bridging Case Management.** If social support is an important determinant of seeking care among HIV positive individuals, “bridging case management” programs – specialized case management interventions designed to link newly diagnosed individuals into routine HIV care – may provide needed support services after an HIV diagnosis. In a multi-site study in four large U.S. cities, more bridging case management participants visited a physician at least twice within 12 months compared to those that received passive referral, the current standard of care (RR=1.41, P<0.01). In California, a similar program identified individuals who were out-of-care and successfully linked 29% to care. These findings suggest that programs to increase social support after diagnosis with particular attention to the emotional, informational, and tangible types of support, may improve the efficiency at which we currently link patients to care.

**Summary**

Ensuring timely access to HIV care remains a challenge in the southeastern U.S. despite the availability of safe and effective antiretroviral therapy and programs to link newly positive persons into care. It is anticipated that findings from this dissertation will have an impact on HIV care in North Carolina by broadening our understanding of the testing and care-seeking behavior among those with HIV.
FIGURE 2.1. Conceptual framework describing the steps between acquiring HIV infection and establishing primary medical care. The specific phases are labeled as time periods 1-6. Adapted from Samet et al. 7
FIGURE 2.2. Conceptual framework describing access to medical care. Reproduced with permission from Wiley-Blackwell Publishing.76
<table>
<thead>
<tr>
<th>CONCEPT</th>
<th>DEFINITION</th>
<th>RELEVANT HIV CARE FACTORS</th>
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| Perceived susceptibility | Beliefs about personal vulnerability to a condition | Awareness of personal HIV risk  
Beliefs in folk/indigenous disease model                                      |
| Perceived severity     | Beliefs about the seriousness of a condition and its consequences | Knowledge of HIV/AIDS  
Fatalistic attitude                                                                 |
| Perceived benefits     | Beliefs about the effectiveness of taking action | Confidence in medical establishment  
Knowledge of ARV benefits  
Control of symptoms                                                             |
| Perceived barriers     | Beliefs about the negative material and psychological costs of taking action | Distrust of medical establishment  
Health insurance/financial concerns  
Transportation  
Availability and knowledge of testing/care facilities  
Stigma  
Lack of perceived social support  
Fear of side effects of treatment  
Fear of testing positive |
| Cues to action        | Stimulus to trigger the decision-making process   | Presence of symptoms  
Health promotion materials  
Concurrent sexually transmitted disease                                              |
<table>
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<tr>
<th>TYPE OF SUPPORT</th>
<th>DEFINITION</th>
<th>EXAMPLE</th>
</tr>
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<tbody>
<tr>
<td>Emotional</td>
<td>Expressions of comfort and caring</td>
<td>Someone who makes you feel better because they listen to your problems</td>
</tr>
<tr>
<td>Informational</td>
<td>Provision of advice and guidance</td>
<td>A person who can give you trusted advice and guidance on an issue</td>
</tr>
<tr>
<td>Tangible</td>
<td>Provision of material aid</td>
<td>A family member who could give you a personal financial loan</td>
</tr>
<tr>
<td>Belonging</td>
<td>Shared social activities, sense of social belonging</td>
<td>A friend with whom you enjoy just “hanging out”</td>
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CHAPTER THREE: DESCRIPTION OF DATA SOURCES

The Screening and Tracing Active Transmission Program

Since the advent of the Screening and Tracing Active Transmission (STAT) program in North Carolina in November of 2002, all antibody negative HIV tests performed in publicly funded clinics are tested for viral RNA to detect patients in the acute phase of HIV infection using a novel pooling algorithm.\textsuperscript{103, 130} The STAT program is led by Dr. Peter Leone at the University of North Carolina at Chapel Hill (UNC-CH) in close collaboration with the North Carolina Department of Health and Human Services (NC DHHS).

The STAT program is evidence of one of the many successful partnerships between UNC-CH and the NC DHHS. Since the program’s inception in 2002, the STAT program has successfully tested all antibody negative samples for HIV-1 RNA, over 500,000 tests. Figure 3.1 presents the algorithm of the procedures of the NC DHHS for HIV testing, notification, and surveillance. In the first twelve months of the program, the use of nucleic acid amplification tests increased the rate of HIV identification by 3.9% over standard antibody testing alone, translating to 23 new case-patients and a prevalence of 0.2 per 1,000.\textsuperscript{103}

In addition to the success of the partnership between UNC-CH and the NC DHHS, the STAT program is also successful at linking individuals who are detected with acute HIV-1 infection to medical care. The STAT program provides a complimentary first visit to all acutely infected persons in North Carolina, at which time they receive individualized care guidance from a specialist and are connected with a variety of social services. In the first 3
years of the program, 80% of the reported acute cases were evaluated by an HIV specialist, 65% within 30 days of their first positive test.\textsuperscript{131} Since records were maintained, 88% of all persons with acute HIV infection identified via the STAT system have decided to stay in medical care.\textsuperscript{132}

The University of North Carolina Center for AIDS Research (CFAR) Clinical Cohort

The UNC CFAR is based at UNC-CH and is a collaboration of three productive and successful institutions in the field of HIV research: UNC-Chapel Hill, Research Triangle Institute, and Family Health International. The UNC CFAR is designed to provide infrastructure to support four approaches to understanding and combating the global HIV/AIDS epidemic: clinical, behavioral, and molecular research, and educational outreach. The UNC CFAR provides a variety of epidemiological, statistical, and clinical support services to researchers pursing these goals in the field of HIV/AIDS.\textsuperscript{133}

A major endeavor of the UNC CFAR has been the creation and maintenance of the Clinical and Research Database and the Clinical and Socio-Demographic Survey (CSDS). The UNC CFAR Database includes over 1,700 HIV-infected individuals receiving primary HIV care at the UNC Infectious Diseases Clinic. Data is collected on received clinical care, including laboratory data, medications and illnesses. The CSDS is an in-person interview conducted with HIV-infected patients in the UNC Infectious Diseases Clinic that is designed to collect data not routinely available in medical records, including social, behavioral, and lifestyle characteristics. To date, just over 300 patients have completed the CSDS interview.
FIGURE 3.1. Algorithm of the Procedures of the North Carolina Department of Health and Human Services for HIV Testing, Notification, and Surveillance. Reproduced with permission from the Massachusetts Medical Society. Copyright © 2005 Massachusetts Medical Society. All rights reserved.
CHAPTER FOUR: METHODS

SPECIFIC AIM 1

a. Describe the prevalence and types of sexually transmitted infections (STI) among individuals acutely infected with HIV at the time of testing in North Carolina.

b. Evaluate variation in the time from HIV acquisition to testing among individuals with acute HIV infection by the presence of STIs at the time of HIV testing and testing site type.

c. Determine differences in median serum viral load (copies/ml) by the presence of STIs at the time of HIV testing and testing site type.

Study Design Overview

To understand the overlapping epidemiology of acute HIV and STIs, we conducted a secondary data analysis of data collected as part of the Screening and Tracing Active Transmission Program (STAT) in North Carolina. The STAT study population is an optimal population with which to study acute HIV infection because of its defined geographic area, intensive and thorough interview process, and its rigorous laboratory algorithms to detect acute infection. Our goal was to describe the prevalence and types of STI co-infections and describe the potential effect of co-infection on testing behavior. This study was ruled as exempt by the UNC Institutional Review Board as it is a secondary analysis of existing de-identified data.
Study Population

Identification of Acute HIV-1 Patients. The study population consists of persons who presented for HIV counseling and testing at all publicly funded sites in North Carolina (n~135) between November 1, 2002 and October 31, 2006. All testing was confidential and was linked to patient information with the use of a system of unique identifiers, according to state public health statutes. The routine HIV testing algorithm in North Carolina includes a pooling strategy to detect HIV-1 RNA positive, antibody negative individuals in the acute phase of infection. Serum samples submitted for HIV testing are first tested for HIV-1 antibody, and then all antibody negative samples are screened for HIV-1 RNA by pooling. Antibody indeterminate samples are tested for HIV RNA individually. Standard Vironostika HIV-1 enzyme immunoassay (EIA) and Western Blot analysis kits (Bio-Rad Laboratories) are used for antibody screening. Pools were screened by nucleic acid amplification (NAAT) for HIV-1 RNA with the Procleix HIV-1 assay (GenProbe) and then in July 2005 with the EasyQ HIV-1 quantitative assay (bioMerieux). Individuals for whom HIV-1 RNA is detected but have not yet seroconverted were considered to be acutely infected.

Upon notification of a possible case of acute HIV infection, the NC Department of Health and Human Services (NC DHHS) assigns the case to a team of specially trained disease-intervention specialists (DIS). DIS are located throughout the state and perform the initial interviews, confirmatory testing, and referrals to care within 72 hours of notification. All partners within six months of testing are ascertained at the initial interview; partner notification is then prioritized according to the time of potential exposure. Immediate intervention is required for partners with exposures less than 48 hours from the test date – post-exposure prophylaxis is considered in this situation. Sexual or needle sharing partners with contact less than eight weeks from the initial interview with the index case are notified by DIS and offered testing within 72 hours of the index interview. Partners outside of the 8-week window period are notified after confirmatory testing by the index.
Selection Criteria

Inclusion criteria: All consenting persons who presented for HIV counseling and testing at all publicly funded sites in North Carolina between November 1, 2002, and October 31, 2006 and diagnosed with acute HIV infection were included in the study.

Exclusion criteria: Individuals with acute HIV infection identified as part of the STAT program who were unable to be located by DIS for notification and referral (lost to follow-up) or those who refused DIS field services were excluded from the analysis.

Data Collection

Interviews by DIS and completion of STAT forms. After interviews with the index patient and partners in the exposure window, DIS officers complete a series of forms about acute retroviral symptoms, sexually transmitted diseases, testing history, and sexual behavior with recent partners. Individuals must consent to disclose health information as part of the DIS interview; individuals who do not sign the authorization will not have STAT forms completed. Individuals can consent to the DIS interview but refuse to identify partners for DIS-conducted partner counseling and referral services or choose to conduct partner notification on their own. Completed forms are mailed to the STAT data manager (S. McCoy) for data entry. Forms are routinely audited for complete and valid information. None of the information was identifiable by any of the study investigators; all databases were de-identified and cannot be linked back to individuals.

Conference calls to discuss each STAT case. In addition to the information collected on the required STAT data collection forms, DIS, acute HIV specialists, and other study personnel participate in a weekly conference call to discuss all new cases of acute HIV. Although information from this call is not formally entered into any database, detailed notes are kept
on each case and stored in a secure location available to study investigators. All cases are discussed using a numeric code that cannot be linked back to individuals.

Counseling and Testing Data from the NC DHHS. The NC DHHS routinely shares the counseling and testing data for all HIV tests conducted in public testing sites with STAT personnel at UNC. Clients who presented for HIV testing at publicly funded sites in North Carolina before 2007 were required to sign an informed consent form authorizing the collection of personal information. Information collected as part of counseling and testing included demographics, reason for testing, risk factor information, and testing site. This dataset was merged with the STAT database to match the pre-test counseling information with the information collected by the DIS during notification and referral.

Together, these three sources of information will provide the data to address Aim #1. In the next section, “Measurements and Analysis Plan,” we describe the methods for ascertaining the exposure, outcome, and covariates and the analysis plan for each of the sub-aims of Specific Aim #1. The “Data Management” and “Limitations” sections which follow apply to all of the sub-aims.

Measurements and Analysis Plan – Specific Aim 1a

Specific Aim 1a. Describe the prevalence and types of sexually transmitted infections (STI) among individuals acutely infected with HIV at the time of testing in North Carolina.

Measurements

Outcome: Co-infection with an STI. STI history is captured on the STAT data collection form with the question “Has the patient ever been diagnosed with an STD?” and if yes, the diagnosis and the date (month/year). Dates of diagnosis were compared to the initial test date when acute HIV was diagnosed to determine if the STD diagnosis was made at or near
the same time as HIV testing. If the date of diagnosis of the STD and acute HIV infection were in the same month and year, the potential co-infection was confirmed by chart review by the appropriate regional DIS.

Additional covariates. Additional patient data includes demographic characteristics (e.g., age, sex, race), acute retroviral symptoms, and risk factor information.

- Age was collected as a continuous variable but was categorized in this analysis for presentation of prevalence by age group (≤25 years, 26-35 years, and ≥36 years). Age was entered as a three level categorical variable in all models (Specific Aims #1b-1c).
- Sex was coded as a dichotomous variable (1=Male, 0=Female).
- Race is self-identified on the HIV counseling and testing report form which accompanies all HIV tests sent to the state laboratory. Race was first categorized into “Black,” “White, non-Hispanic,” “White, Hispanic,” “Native American/Alaskan Native,” and “Unknown.” In addition to this classification, race was also be dichotomized into “White, Non-Hispanic” and “Non-White” due to small numbers of people with STI co-infections.
- Acute retroviral symptom information is collected by DIS during the initial interview with the patient and entered onto STAT forms with the onset date. We considered appropriate symptoms (e.g. fever, headache, night sweats, weight loss, body aches) reported during a window period of eight weeks of testing (± four weeks of the test date, inclusive) to be acute retroviral syndrome. The onset of symptoms was considered the earliest date of any symptom onset. Symptoms consistent with acute retroviral syndrome were constructed as two dichotomous variables, one for symptoms at or before testing (present/not present) and one variable for symptoms that developed at any time (present/not present). We also considered a 3-level variable for
symptoms at or before testing, symptoms that developed after testing, and no symptoms.

- We created a three-level gender and risk category of women, heterosexual men, and men who have sex with men (MSM). A man who reports any male partners was classified as MSM, whereas a man with all female partners was classified as heterosexual. We utilized two data sources for this information – the counseling and testing data from pre-test counseling as well as the STAT forms completed by DIS that include the gender of partners.

- Any report of injecting drug use was included as a dichotomous variable (1=Yes, 0=No). This information was abstracted from the STAT forms as well as from the counseling and testing data.

Data Analysis

Frequencies of STI co-infection. We present frequencies of the number of individuals with STI co-infection and the types of infections. We also present the number and percent of individual STIs and determine the prevalence, $\hat{p}$, by computing $A/N$, where $A$ refers to the number of individuals with the outcome (co-infection) and $N$ represents the total number of acute infections. The 95% exact confidence intervals were computed and presented.

Bivariable associations. We also present the prevalence of STI co-infection by age group, race, testing site, gender and risk behavior, and symptoms. To determine factors associated with STI co-infection, we computed the prevalence of co-infection in each stratum and present prevalence ratios (PR) and 95% exact confidence intervals to test associations between co-infection and selected covariates. Statistically significant differences in proportions were determined with Fisher’s exact test.
Measurements and Analysis Plan – Specific Aim 1b

Specific Aim 1b. Evaluate variation in the time from HIV acquisition to testing among individuals with acute HIV infection by the presence of STI at the time of HIV testing and testing site type.

Measurements

Outcome: Time from HIV acquisition to HIV testing. The date of HIV acquisition was estimated using the dates of symptom onset and seroconversion reported by DIS. The date of seroconversion was calculated as the midpoint between the last antibody negative or indeterminate test and the first positive western blot. For individuals with symptoms consistent with acute retroviral syndrome, the date of HIV infection was calculated as 14 days prior to the date of symptom onset. For individuals without symptoms, the time from HIV infection to seroconversion reported in the literature ranged from a median of 46 days on 2nd generation EIA tests among health care workers to over 88 days in plasma donors. Because of this inconsistency, we utilized an average plausible seroconversion interval of 35.5 days with a 2 week window on either side (21.5 to 49.5 days). The rationale for this interval is presented in Table 4.1. As the NC DHHS used a 2nd generation EIA at the time of the study, we computed an average interval between infection and seroconversion of 35.5 days. This interval was consistent with reports from the CDC of median time to seroconversion of 46 days, respectively, but less that that reported by Horsburgh of 72 days.

Exposure: Testing site type. Testing site type is collected on the pre-test counseling and testing report form. Testing sites are collected as:
Preliminary analyses from the first three years of the STAT program (11/1/2002 – 10/31/2005) indicated that 47% of individuals diagnosed with acute HIV infection were tested at STD testing sites, followed by 21% at dedicated HIV CTS sites and 19% at “Other” testing sites. Because few acutely infected individuals tested during prenatal care/obstetric visits, at family planning clinics or were people with tuberculosis, we grouped any testing site other than CTS and STD into an “Other” category.

Additional covariates. Covariates for consideration for this sub-aim include demographic characteristics (e.g., age, sex, race), symptoms, and risk factor information (e.g., MSM, IDU). The coding of these variables was described for Specific Aim 1A.

Data Analysis
Variation in the time from the estimated date of HIV acquisition to testing was evaluated with two proportional hazards models with 1) the presence of an STI co-infection as the exposure and 2) with the testing site type as the exposure.

Proportional hazards regression models the hazard rate, which is based on the number of events per interval of time. Hazard rates are comparable to incidence rates, but conditional on survival in the immediately preceding time interval. The proportional hazards model takes the form of

\[ h_x(t) = h_0(t) \cdot e^{\beta X}, \]
where $X$ is a vector of explanatory variables ($x_1, x_2, \ldots, x_k$), $h_0(t)$ is the baseline hazard (e.g. when all explanatory variables equal 0, $X=0$), and $h_x(t)$ is the hazard at $X=x$. The interpretation of $e^{\beta X}$ in a multivariable model is the hazard ratio comparing those with $x=1$ to those with $x=0$ (the referent category) at all times $t$ adjusted for other variables in the model. A key assumption of the proportional hazards model is that the hazard ratio ($e^{\beta X}$) in the model is assumed to be constant across time. This means that the ratio of the hazard function in the exposed to the hazard function in the unexposed is a fixed constant over time (“hazards are proportional”).

The proportional hazards model was used to examine variation in the time from HIV acquisition to HIV testing by STI co-infection and testing site type. In the bivariate models, the only explanatory variable were the binary exposure of co-infection (1=Yes, 0=No) or site type (‘STD’, ‘non-STD’, or ‘CTS’). The proportional hazards assumption was evaluated for each exposure and covariate graphically with the use of a log(-log(S(t))) curve and was tested by adding an interaction with time to the model (Cox Test). If necessary, the proportional hazards assumption was relaxed using a stratified model or by adding categorical or continuous time interactions. We assessed goodness of fit of the model by examining deviance residuals and influence statistics. Equality of the survival functions between those with and without the exposure was assessed with a Log-Rank Test or Wilcoxon Test, depending on the shape of the survival curves (Wilcoxon gives more weight to early times than late times).

We evaluated effect measure modification (EMM) and confounding for both STI co-infection and testing site type. We then constructed a single, fully adjusted model with both main exposures and all relevant interaction terms and confounders.

**Assessment of Effect Measure Modification.** To assess EMM, we examined the exposure-outcome relationship while adjusting for one covariate at a time in the model. The covariate
was entered into the model individually as a main effect and as an interaction with the main
exposure. The significance of the interaction term was assessed by comparing the likelihood
ratio of the “full” model with the interaction term to the model without the selected interaction
term by the likelihood ratio test (LR). Important interaction terms were included in the
multivariable model along with their corresponding main effect terms.

**Assessment of Confounding.** Potential confounders were considered those covariates that
were not found to be effect measure modifiers and that changed the unadjusted HR by more
than 10% according to the formula \( \ln\left|\frac{HR_{\text{unadjusted}}}{HR_{\text{adjusted}}}\right| \). Potential confounders were
included in the final multivariable model.

**Multivariable associations.** We examined the joint effect of STI co-infection and testing site
type in a multivariable proportional hazards model. Due to the small sample, we were limited
to examining approximately seven explanatory variables in the model.\(^{141}\) We utilized a
backward, manual elimination modeling strategy to assess the joint effects of covariates.
The main exposure, potential confounders, and effect measure modifiers along with the
appropriate interaction terms were added to the model, constituting the fully adjusted model.
EMM was assessed first by examining the LR test result for the model with and without
selected interaction terms. Confounding was examined next – covariates were removed
from the model in order of p-value magnitude if the estimated HR for STI co-infection
changed by more than 10% from the unadjusted association.

The results from Specific Aim 1b are presented in Appendix A.

**Measurements and Analysis Plan – Specific Aim 1c**

**Specific Aim 1c.** Determine differences in median serum viral load (copies/ml) by the
presence of STIs at the time of HIV testing and testing site type.
Measurements

Outcome: Baseline viral load. Quantification of HIV-1 RNA is routinely conducted on the venous blood sample provided at the time of the initial HIV test and on confirmatory samples drawn in the field by DIS. An HIV-1 reverse transcriptase polymerase chain reaction assay (Amplicor HIV-1 Monitor Test, version 1.5, Roche Diagnostic) was used to measure viral load. It is based on reverse transcription (RT) of the target HIV-1 RNA, and polymerase chain reaction (PCR) amplification of the resulting cDNA. The limits of detection of the Amplicor assay are 50 (lower limit) and 750,000 (upper limit) copies per ml.

Additional covariates. Covariates considered in this sub-aim included demographic characteristics, symptoms, and risk factor information. The coding of these variables was described for Specific Aim 1A.

Data Analysis

Differences in the baseline mean log_{10}(HIV-1 RNA) between those with an STI co-infection and those without an STI infection was examined with a one-way analysis of variance (ANOVA). Similarly, we compared the mean log viral load by testing site type using the same method. In addition, we were interested in the relationship between study covariates and viral dynamics in order to understand more about the timing of testing. Towards this end, we examined the viral dynamics among the subset of participants with both initial and confirmatory HIV RNA values using two common epidemiologic models:

1. Logistic regression. We classified patients as having an increasing or decreasing HIV RNA slope. We then used exact logistic regression to assess the relationships between this dichotomous indicator of HIV RNA slope (1=increasing slope, 0=declining slope) and study
covariates. We assumed that a positive HIV RNA slope was indicative of testing before the peak viremia. Logistic regression takes the form

\[ E(Y_i) = \frac{\exp(\beta_0 + \beta_1 X_i)}{1 + \exp(\beta_0 + \beta_1 X_i)} \], where

\( Y_i \) is a binary response variable, \( X_i \) is a known constant from the \( i \)th participant, and \( \beta_0 \) and \( \beta_1 \) are parameters. The results from this approach are presented in Chapter Five.

2. Linear regression. We constructed linear regression models with the change in log_{10}(HIV RNA) as the outcome. Linear regression takes the form \( E(Y_i) = \beta_0 + \beta_1 X_i \), where \( E(Y_i) \) is the expected response at level \( i \) of predictor variable \( X \), \( \beta_0 \) is the intercept parameter, or mean when \( X=0 \). \( \beta_1 \) is the slope of the regression line. A key assumption of the model is that the outcome is normally distributed \( (Y_i \sim N(\beta_0 + \beta_1 X_i, \sigma^2)) \) so the skewed distribution of serum viral load was log transformed. The results from this analysis are presented in Appendix B.

**Data Management**

The data used for this secondary data analysis project were collected as part of the Screening and Tracing Active Transmission Database housed at the UNC Center for AIDS Research. The database was located on a server in a secured access area. Access to the server was restricted to key personnel such as computer support staff and the data manager. All information in the database was de-identified, with linking files kept separately at the NC Department of Health and Human Services. When data analysis files were created these were linked by a nonsense unique record identifier. All analyses were conducted in SAS version 9.1.2 (Cary, NC).

**Sample Size.** Our study represents the first four years of the STAT program; a statewide collaboration to detect acute HIV at all publicly funded HIV testing sites in North Carolina. To
date, no other state in the U.S. has implemented such a program. Information on 75 acute HIV patients identified through the STAT program was available for analysis, a sample size that is unrivaled for acute HIV research in the United States.

Because our sample size was fixed, we solved for the power available for the two sample t-test of the log_{10}(HIV RNA) comparing those with and without STI co-infection and those from STD and non-STD testing sites. The results are presented in Figure 4.1. Graph A in the figure describes the expected power for a two-sample t-test to detect a difference by STI co-infection. Various hypothesized standard deviations of the outcome and effect sizes (differences between the means) are presented for a 0.05 two-sided significance level. We assumed that approximately 30% of our sample will have an STI co-infection, translating to a fixed sample size of 23 and 53. For example, with a pooled standard deviation of 2.0, we had 84% power to detect a difference in mean log_{10} (HIV RNA) of 1.5.

Graph B in the figure describes the expected power for detecting a difference in mean log_{10}(HIV RNA) by testing site type. We knew that 34 people tested at STD clinics and 42 people tested at other types of clinics. Similarly, we found that with a pooled standard deviation of 2.0, we had 89% power to detect a difference in mean log_{10} (HIV RNA) of 1.5.

**Approach to Missing Data.** Individuals who could not be located by DIS for interview were excluded from the analysis. The presence of an STI co-infection is indicated on the conference call and on STAT forms when present, however, we do not have data on four individuals who did not consent to take part in the study and receive counseling (5.1%). Likewise, the absence of STAT forms resulted in missing dates of symptom onset and seroconversion for the same four individuals, the endpoint of the main outcome. These individuals will therefore be excluded from the analysis, leaving 75 cases with which to examine STI co-infection. Testing site type is currently available on all STAT cases in the study period. Viral load values are available for 74 of 75 consenting participants (99%) of the
STAT cases in years 1-4. This small amount of missing data is not expected to bias the results, but will result in a loss of precision.

In proportional hazards regression, we will utilize a complete case analysis approach. This is expected not to bias the data because of the small number of missing data for the main exposure and outcome; however, we can expect a loss in precision of our estimates. Any covariate for which more than 5% of values are missing will be excluded from the analysis.

**Strengths and Limitations**

The primary strength of this study is the reliance on the STAT program, a unique collaboration to routinely detect acute HIV in public health settings. We had access to four years of data from the STAT program, translating to 75 cases of acute HIV for examination. Few studies have access to such a large and rich database about acute HIV infection. However, several factors limit the validity or generalizability of our findings:

**Potential for selection bias.** There are two potential sources of selection bias in this study. First, this analysis only includes cases of acute HIV identified through publicly funded HIV testing sites. While the type and number of public testing sites are diverse, more than half of the HIV tests in the state are conducted in private facilities and not eligible to be included in the STAT program public testing arm. It is possible that individuals who test for HIV at private sites are systematically different that those who test in public sites (e.g., race). This could limit the transferability of our findings beyond the public HIV testing system. Second, the recent revised testing guidelines underscore the recommendation for routine HIV testing of all STD clinic attendees and those seeking treatment for STDs in other clinical settings. This testing practice may bias our findings toward overestimating the prevalence of STI co-infection with acute HIV (e.g., diagnostic bias).
**Algorithm to determine the date of infection.** We used an algorithm to estimate the time of HIV acquisition for the acutely infected study participants. This algorithm is subject to several design flaws. 1) *Symptomatic patients:* Although most studies of acute or primary infection note the onset of symptoms approximately 2 weeks after infection, it is possible that the estimated date of exposure to the virus in these small samples was incorrect. Further, the three studies on which this calculation was based were conducted in only 12, 12, and 10 patients, respectively.\textsuperscript{134-136} In addition, seroconversion times may differ based on route of exposure. 2) *Asymptomatic patients:* There is mixed information about the times from infection to seroconversion among asymptomatic patients, and most available information is from health care exposures. To approach this problem, we utilized multiple sources of information and considered a plausible range of intervals from infection to seroconversion.

**Serum viral load as outcome.** We examined the differences in serum viral load among those with and without STI co-infection and those from different testing site types. Optimally, we would have seminal viral load or viral load from genital secretions to make inferences about transmissibility. Although plasma viral load is correlated with HIV transmission probability, Cohen et al. demonstrated that men co-infected with urethritis had seminal plasma HIV concentrations eight times higher than those without urethritis with no difference in blood plasma RNA.\textsuperscript{61, 107} This finding suggests that even if we find no difference between plasma viral load concentrations in our study population, important differences may remain in the genital tract, which has implications for sexual transmission.

**Possible influence of STI co-infection on seroconversion.** Co-infection with an STI could influence the time to seroconversion, and it is impossible to know this in our study. Since we
are replying on a range of plausible outcomes to determine the date of infection for asymptomatic patients, our results will be biased if co-infection is found to affect the time to seroconversion. If co-infection shortens the pre-seroconversion interval, we will overestimate the date of infection for all asymptomatic individuals who are co-infected. In contrast, we will not rely on the date of seroconversion for symptomatic patients (date of symptom onset is used). Plasma viral load has been shown to be stable with urethritis co-infection although seminal plasma increased, suggesting that STIs might not have any effect on seroconversion.107

**SPECIFIC AIM 2**

Describe the effect of perceived social support on late presentation to medical care among HIV positive persons receiving care at the UNC Infectious Disease (ID) Clinic.

**Study Design Overview**

To determine the effect of perceived social support on HIV care-seeking behavior, we conducted a secondary data analysis of the UNC-CFAR HIV/AIDS Clinical Socio-Demographic Survey (CSDS) and the UNC Center for AIDS Research (CFAR) HIV Clinical and Research Database. The CSDS is a comprehensive in-person interview completed by UNC CFAR HIV Cohort participants. The Clinical and Research Database includes medical record information on patients receiving HIV care at UNC. Detailed data are collected on demographic, social, behavioral, clinical and lifestyle characteristics. This secondary analysis was ruled as exempt by the UNC Institutional Review Board.

To enhance the accuracy of our findings, we conducted a validation sub-study to determine the reliability of the self-reported date of diagnosis contained in the CSDS. We compared the self-reported value to the value reported to the NC Department of Health and
Human Services through routine infectious disease reporting. We also compared these values to the date recorded in the UNC medical record.

**Study Setting**

The parent study for this analysis was conducted in the University of North Carolina at Chapel Hill Infectious Disease Clinic. As a large, university-based medical center, the Clinic follows approximately 1,300 HIV infected patients per year and provides comprehensive HIV primary services including antiretroviral therapy, chemoprophylaxis, health maintenance services, and referrals to specialty care. Patients in the clinic are predominantly from central and eastern North Carolina, although patients from all 100 counties and surrounding states are accepted for care. Overall, approximately one-third of all HIV-infected patients seen at UNC-ID are women, 62% African Americans, 2% Native Americans, and 4% Hispanics/Latinos. Patients are referred to the Clinic from public testing venues, private offices, and inpatient services.

**Study Population**

For this secondary data analysis project we merged the clinical data available in the UNC CFAR Database with the social and behavioral data available in the CSDS. All patients participating in the UNC CFAR Database and the CSDS interview provided written informed consent to participate in these respective studies. The merge of the databases was done among patients who provided written informed consent to participate in both studies. A description of the UNC CFAR CSDS and the UNC CFAR Database is available in Chapter Three of this dissertation.
Selection Criteria

Inclusion criteria: All HIV infected patients participating in the UNC CFAR Clinical and Research Database project and the CSDS who received care at the UNC Infectious Diseases clinic and who met the inclusion criteria were eligible. The inclusion criteria were:

1. At least 18 years of age
2. Provided written informed consent to participate in the UNC CFAR Research and Clinical Database
3. Provided written informed consent to participate in the Clinical Socio-Demographic Survey
4. Date of HIV diagnosis known (either self-reported, in NC DHHS records, or in the UNC medical record, please see description of measurements below)
5. Date of initial entry to HIV care at UNC is known
6. At least 80% of the social support questions were complete in the CSDS interview.

Sampling

To be eligible to participate in the CSDS Interview, patients must have been in care at the UNC Infectious Diseases Clinic, provided written informed consent to participate in the UNC CFAR Research and Clinical Database, were at least 18 years of age, able to speak English, and able to provide written informed consent.

Recruitment

Potential participants were identified and approached for participation by their primary care provider in the UNC Infectious Diseases Clinic on the day of their HIV clinic visit. Primary care providers informed their patients of the study and asked the patient if they were willing and able to speak with study personnel. If the patient agreed then study personnel met with the patient in a private and quiet office in the UNC Infectious Diseases Clinic or the UNC
General Clinical Research Center. Patient information was only collected once the patient agreed to participate and provided written informed consent and HIPPA authorization.

**Data Collection**

Study personnel explained the study and went through the informed consent form and the HIPPA authorization form with the patient. If the patient agreed to participate they were asked to sign the informed consent form and the HIPPA authorization form. A copy of the informed consent form and HIPPA authorization form was given to the participant.

Trained research assistants or study investigators conducted all CSDS in-person interviews. Interviews were conducted in a private and quiet office in the UNC Infectious Diseases Clinic or the UNC General Clinical Research Center. Participants were told that they could decline to respond to any question and could refuse to continue the interview at any time. During the interview all participant responses were entered on paper forms. Patients were given $15 at the completion of the interview for their time. Data from the interviews were entered into a Microsoft ACCESS database which is housed on a secured server.

**Measurements**

**Main Outcome: Time from diagnosis until presentation for care.** The main outcome variable is the time (months) from HIV diagnosis until entry to HIV care. The date of HIV diagnosis was obtained from the NC Department of Health and Human Services HIV/AIDS Reporting System. In cases where a match was not obtained with state records or the NC reporting system date was after the diagnosis date in the medical record, the date of diagnosis from the medical record was used. Five patients only had the self-reported date of diagnosis available. To correctly capture the date of entry to HIV primary care, as opposed to general health care visits, we defined entry to care as the first outpatient visit to the UNC ID clinic for
patients only receiving care at UNC. For patients who received care at other institutions, we defined entry to care as the earliest non-hospitalized date of CD4 T-lymphocyte cell count, HIV RNA, antiretroviral therapy initiation, AIDS-defining clinical condition, or outpatient visit. In cases where a hospitalization was the first HIV–related care, we accepted the date of the first CD4 T-lymphocyte cell count as the entry to care date. Patients with only self-reported dates of entry to care were excluded from the analysis.

Main Exposure: Perceived Social Support. The exposure of interest, perceived social support, was quantified with the Medical Outcomes Study (MOS) Social Support Scale (SSS). The MOS-SSS is a brief, multidimensional, 20-item survey. Two items measure structural support and the remaining 18 items measure four functional dimensions of social support: emotional/informational, tangible, affectionate, and positive social interaction.27 The modified version used in our study contained items to measure structural support and 13 of the 18 items to measure functional support (four of four tangible indicators, three of three affectionate indicators, four of eight emotional/informational indicators, and one of four positive social interaction indicators plus an additional positive social interaction indicator evaluated but not included in the MOS-SSS). The scale was developed for patients in the MOS, a two year study of patients with chronic illnesses (n=2,987). Thirty-nine percent of the sample was male, 20% were non-White, and 68% were married, and there was an average of 13.3 years of education. The structural measures of support were found to be distinct from the functional types, and the scale showed high convergent and discriminate validity of scale items.27 The modified MOS-SSS used in this study is presented in Table 4.2.

Structural social support was quantified with the following two measures of network size and connectedness from the MOS-SSS:

1. “About how many close friends do you have (people you feel at ease with and can talk to about what is on your mind)?”
(2) “About how many close relatives?”

Overall network size was considered the summation of the number of close friends and relatives and considered as a continuous variable as well as categorized into 0-3, 4-7, 8-12, and 13 or more close friends and relatives.

Functional social support was quantified with a score for each dimension of functional social support. Responses to items on the 5-point Likert scale of responses were assigned a numeric value (1: Support type is never present – 5: Support type is always present) and a composite average number was generated for the functional social support dimension. This average was transformed so that the lowest possible score was 20 and the highest possible score was 100. We also computed a composite functional social support score for each participant.

Internal consistency of the scale was measured with Cronbach’s alpha, a value that ranges between 0 and 1 and indicates the level of internal consistency of the scale (whether a single underlying construct is being measured). A widely accepted rule of the thumb is that values of at least 0.7 are required to indicate good internal consistency.\textsuperscript{147} The coefficient alpha was calculated as:

$$\alpha = k \frac{s_T^2 - \sum s_i^2}{k - 1}$$

where $k$ indicates the number of items, $s_T^2$ is the total variance of the sum of the items, and $s_i^2$ is the variance of an individual item.\textsuperscript{147}

As our scale was modified from the original 19 item MOS-SSS scale, we used confirmatory factor analysis (CFA) to determine the validity of the model in our study population. The purpose of CFA is to identify a set of latent factors that account for the variation and covariation of a set of indicators (indicators are the actual questions asked). A
latent factor is unobservable and accounts for the correlations of observed indicators. The researcher determines the latent factors and pattern of indicator and factor loadings in advance and then uses concepts of structural equation modeling to solve the multiple resulting models. The goal is obtain estimates for each parameter that produces a predicted variance-covariance matrix that resembles the sample variance-covariance matrix as closely as possible.

The CFA common factor model for this analysis is presented in Figure 4.2. We had four first-order latent factors corresponding to the four dimensions of functional social support. These latent factors were related to individual indicators (factor loadings). We also had one second order latent factor corresponding to a single, composite measure of functional social support. A fundamental equation of the common factor model is:

\[ Y_j = \lambda_{jm} \eta_m + \delta_j, \text{ where} \]

\( Y_j \) represents the jth indicator (in our example, A-M) obtained from a sample of independent subjects, \( \lambda_{jm} \) represents the factor loading relating indicator j to the mth factor \( \eta_m \), and \( \delta_j \) represents the unique variance (measurement error) for indicator \( Y_j \).

We first evaluated the first order solution to see if the four dimensions of functional social support were valid in our sample. We allowed for the errors of two similarly worded questions to be correlated (“Someone to give you good advice about a crisis” and “Someone who’s advice you want”). We determined model fit based on a CFA model with 332 patient records, 13 indicators, four latent variables (emotional/informational, affectionate, tangible, and positive interaction types of functional social support), and a robust weighted least squares fitting function. We then examined the suitability of the higher-order model with the
single measure of functional social support. CFA analyses were done with Mplus software. The results of the CFA are presented in Chapter Six.

We present medians, means and standard deviations for each level of functional support. The distributions of functional support were skewed so we investigated several methods to model each dimension of functional social support.

1. We created 4-level variables which corresponded to quartiles of each functional social support dimension. Using these variables in proportional hazard models, we found no evidence to suggest that any of the functional social support terms were linear in the hazard. Use of continuous terms for social support was therefore not indicated.

2. To determine if the fit of a linear term could be improved with linear splines, we entered each of the dimensions of functional social support into a proportional hazards model and created three linear spline terms corresponding to knots at the specified percentiles depending on the distribution of each functional support variable. We tested the statistical contribution of the spline terms with the LR test. None of the models with the linear spline terms improved the fit of the model. The creation of spline variables is described in more detail in Table 4.3

3. We examined scatter plots of the survival function estimate and the linear functional support dimension. Based on this graphical display of data, a 3-level or 2-level categorization of each functional social support variable seemed reasonable. The scatter plots for each functional support dimension is presented in Figure 4.3.

Based on these preliminary analyses, the functional support scores were categorized for entry into a proportional hazards model based on levels corresponding to social support being available <70 (“Less than most to all of the time”), and ≥70 (“Most to all of the time”).
**Additional Covariates.** Additional patient data included demographic characteristics (e.g., age, sex, race); clinical factors (e.g., CD4 cell counts, AIDS defining illnesses), and risk factor information (e.g., ever spent time in prison, ever homeless). Age was calculated as the difference between the date of birth and the date of the interview, and classified into \( \leq 30 \), 31-40, and \( \geq 41 \) years. Sex was a dichotomous variable. Race was categorized into “Black,” “White,” and “Other.”

Potential confounders of the relationship between social support and HIV care included substance abuse (alcohol and illegal drugs, dichotomized into “ever had a drinking problem,” or “ever used illegal drugs on a regular basis”) and ever having been homeless or in prison (Yes/No). Substance abuse treatment and mental health history were not available for the analysis. Other variables of interest that were investigated included income, availability of transportation for medical visits, education, transactional sex, and self-identified sexual identity. We also examined the number of biological children as a 3-level variable of no children, one child, and two or more children. The hypothesized causal model is presented in Figure 4.4

**Validation Sub-study.** We conducted a validation sub-study to examine the reliability of the self-reported first positive HIV test by comparing to state HIV/AIDS morbidity records and UNC medical records. In the first phase of the sub-study, we matched all the patients that consented to participate in the CSDS to the NC DHHS HIV/AIDS Reporting System (HARS) using a 4-step algorithm. First, patients were matched deterministically using the first four letters of the last name, first three letters of the first name, month and year of birth, and sex. In the second stage, single matches are removed and the remaining non-matched subjects were matched deterministically by social security number, if available. The remaining non-matched subjects were then manually matched by record lookup using an inexact matching algorithm and rotating the first name, last name, date of birth, and sex though the lookup
system to identify changed names, gender errors, etc. Finally, multiple matches for a single patient were investigated and resolved and all matches were manually reviewed for potential errors. This phase of the analysis was approved by the NC DHHS under statute 10A NCAC 41A.0101, “Reportable Diseases and Conditions.” In the second phase of the analysis, we examined the diagnosis date available in the UNC medical record. The results of the validation sub-study are presented in Appendix C.

For the main analysis, the date of HIV diagnosis was determined with an algorithm to select the earliest of: self-reported diagnosis date, provider report in the UNC medical record, or date of diagnosis recorded in North Carolina HIV/AIDS Reporting System.

Data Management and Data Analysis
To ensure data integrity, the UNC CFAR Clinical and Research Database and the CSDS rely on rigorous data management and quality control procedures that we utilized for this study. In addition to data entry systems that include range checks and assessment of completeness and consistency across items, the UNC CFAR staff engaged in several levels of error detection and correction. Questionable values were flagged for verification against paper records. The UNC CFAR Database and the CSDS are located on a dedicated server in a secured access area where most administrative University servers are housed. Access to the server is restricted to key personnel such as computer support staff. All information in the databases are de-identified, with linking files kept separately under additional security and password protections. Access to any of the data requires passwords that change each 90 days, and again only key personnel have access to these files, including the database manager and SAS programmer. When data analysis files are created these are linked by a unique patient identifier.
**Validation sub-study.** Self-reported dates of diagnosis that were within the same year as the HARS reported date or the date in the UNC medical record were considered concordant, likewise, dates more one year discrepant were considered discordant. We report the percent agreement between the self-reported date of diagnosis and the validated date of diagnosis. For individuals who were missing a self-reported date of diagnosis, a date of diagnosis in the HARS system, or a date of diagnosis in the UNC medical record, we took the earliest of the available dates as the date of diagnosis.

**Descriptive Statistics.** We first performed basic descriptive analyses, including calculating means, standard deviations, and frequencies of the exposure and covariates. A summed measure of structural support was generated, along with summary scores of the four types of functional social support. The mean structural and functional support score is presented and compared to the MOS population for which the scale was validated.

**Bivariable Associations.** Each functional dimension of functional social support was quantified with the modified MOS-SSS Scale and entered into a Cox proportional hazard model as a 3-level variable to determine differences in the time to seeking HIV care. The proportional hazards model is described in the methods for Specific Aim 1.

We began our analysis by modeling each of the four functional social support terms as the main exposure. For all variables, the proportional hazards assumption was evaluated graphically with the use of a log(-log(S(t))) curve and was tested by adding an interaction with time to the model (Cox Test). If necessary, the proportional hazards assumption was relaxed using a stratified model or by adding categorical time interactions or continuous time interactions. We assessed goodness of fit of the models by examining deviance residuals and influence statistics. Equality of the survival functions between the exposure levels was tested with a Log-Rank or Wilcoxon test, depending on the shape of the survival curve. We
present the Kaplan-Meier curves, unadjusted hazard ratios for all four models, and 95% confidence intervals.

Assessment of Effect Measure Modification. To assess effect measure modification (EMM), we examined the exposure-outcome relationship for each of the four dimensions of functional social support while adjusting for one covariate at a time in the model. The covariate was entered into the model individually as a main effect and as an interaction with the main exposure. The significance of the interaction term was assessed by comparing the likelihood ratio of the “full” model with the interaction term to the model without the selected interaction term by the likelihood ratio test (LR). Important interaction terms were included in the multivariable models along with their corresponding main effect term.

Assessment of Confounding. Each covariate in the analysis was examined for confounding of the functional social support measures. Potential confounders were considered those covariates not found to be effect measure modifiers in the bivariate models and that changed any level of the unadjusted HR by more than 10% \( \ln\left(\frac{HR_{\text{unadjusted}}}{HR_{\text{adjusted}}}\right) \). Confounders were included for further assessment in the multivariable models.

Multivariable Associations. We constructed four fully adjusted models and then reduced each model to only the most essential EMMs and confounders with a backwards elimination modeling strategy. In the first step of the analysis, the main exposure, covariates, and interaction terms (based on the assessment of EMM in the bivariate analyses) were added to the model, constituting the fully adjusted model. EMM was assessed first with the LR test. Confounding was examined next – covariates were removed from the model if the estimated social support coefficients changed by more than 10% from the unadjusted association. After a final model was generated for each dimension of functional social support, we
combined the models into a single model with all four measures of functional social support. The model was then reduced to eliminate unnecessary interaction terms and confounders.

**Approach to Missing Data.** Of 336 unique people in the CSDS, four had not completed the MOS-SSS up to the 80% criterion (n=4, three non-completers, one with 11 items missing). These people were excluded from the analysis. After these exclusions, 13 people had missing data in the social support scale. Because each value was required to compute the summary scores, we used several methods to determine the optimal method for handling the missing data:

1. Complete case analysis
2. Single imputation with the mean of other values given by the same person
3. Single imputation with the mean of the values given the study sample
4. Single imputation with the low value (1)
5. Single imputation with the high value (5)
6. Conditional mean imputation with a linear model. Predictive multiple linear regression models were constructed using the subset of the sample with complete data. The outcome was the variable of interest and the predictor variables were all the other variables in the MOS-SSS scale and age, race, and risk factor information.

The results of the missing data analysis are presented in Table 4.4. As the results were consistent across methods of handling missing data, we proceed by singly imputing missing questions with the mean of available values across all participants (option #3).

**Sample Size**

The sample size in this study is fixed so we calculated the power available for the non-parametric log-rank test for equality of the survival curves. We assumed that the hazard ratio was constant over time and that there was no accrual or dropouts (a reasonable assumption
since all participants in the cohort eventually experience the outcome of entering medical care and we will treat time 0, the date of diagnosis, as the same for all patients). We included the proportion of patients not in care at three months as a parameter for our calculations. From preliminary analyses on a subset of the full dataset, we found that we have 78 patients with low functional social support and 261 patients with high functional social support (fixed). The results are presented in Table 4.5. The hazard ratio can be interpreted as the hazard of not being in care in the group with low social support compared to the group with high social support.

For example, when the sample size in group one is 78 and the sample size in group two is 261, the log-rank test for equality of survival curves with a 0.05 two-sided significance level will have approximately 79% power to detect the difference between the survival curves assuming a constant hazard ratio of 2.29. This estimate of power was based on the assumption that 60% of those with low social support will be in care at three months and that 80% of those with high social support will be in care at three months.

**Strengths and Limitations**

**Strength: Timeliness and geographical focus of topic.** Much of the discussion about HIV prevention has shifted to focus on prevention for positives. In line with the goal to target prevention messages to HIV-positive individuals, this dissertation examines factors associated with care-seeking behavior which could translate to reduced transmission either directly via reduced viral load by ARV therapy, or indirectly, by behavior change. Further, 40% of all persons living with AIDS in the U.S. resided in the southern U.S., and from 2001 to 2005, the number of deaths from AIDS increased in the region, while other regions of the U.S. experienced declines. To help to understand these disturbing trends, our study focuses on the care-seeking behavior of individuals in the South, which may be different from the behavior of HIV-positive individuals in other areas of the U.S.
Limitation: Selection bias. Participation in the CSDS is likely biased toward individuals with fewer obligations and who need financial support. The effect of this bias is unknown – persons who decline to participate in the study may have different levels of social support than those who do participate and may also have different care-seeking behaviors.

Limitation: Unmeasured Confounders. Some important confounders are unmeasured in this study such as mental health diagnoses, substance abuse treatment, life stress and coping style and therefore cannot be included in the analysis.

Limitation: Temporality of exposure and outcome. We do not know if the reported levels of social support were present at the time of diagnosis. It is feasible that being diagnosed with HIV impacts the level of social support by increasing access to support providing services (e.g. support groups, case management). The inability to establish temporality restricts our ability to make causal inferences.

SPECIFIC AIM 3
Describe attitudes and beliefs about HIV testing and care among HIV infected persons attending the UNC ID clinic who present with clinically advanced illness.

Study Design Overview
I conducted a qualitative, semi-structured interview study in the UNC outpatient clinic with patients who presented to care late in the course of illness to increase our understanding of the process of testing HIV positive and seeking medical care. I interviewed 24 clinic patients and discussed their experience testing positive, their decision-making process about seeking medical care, and their experience in the clinic once they sought care. Using the
Health Belief and Information-Motivation-Behavioral Skills Model as our conceptual framework, we present barriers and facilitators to testing and seeking care in North Carolina.

**Study Setting**

This study was conducted in the UNC Infectious Disease Clinic.

**Study Population**

I conducted semi-structured, individual qualitative interviews of HIV-infected persons who presented to care at the UNC Infectious Disease Clinic in the previous year with moderate to advanced immunosuppression, defined as an indication for HAART therapy (CD4+ T-lymphocyte cell count <350 cells/mm$^3$).$^{150}$

Patients of the clinic are typically followed every three months for therapeutic, virologic, and immunologic monitoring.$^{28}$ Although the initial clinic visit representing the point of initiation of care would theoretically be ideal for our interview, this visit is time-consuming for the patient and would have resulted in poor response rates. The first clinic visit typically includes a complete medical history, physical examination, laboratory testing, and meetings with social workers and case management services. More appropriately, a follow-up visit offers the opportunity to recruit patients who have had at least one contact with HIV care providers and have returned for continuing care. It is common for patients to have a follow-up visit shortly after their initial visit, usually 2-4 weeks afterward. Returning patients may differ from patients on their first visit in that they may be more reflective of their attitudes and beliefs about medical care and they may have formed new opinions since their first visit.
Selection Criteria

Inclusion criteria: The study population was all HIV positive persons who received care at the UNC Infectious Diseases clinic and who met the inclusion criteria. The inclusion criteria were:

1. At least 18 years of age
2. Provided written informed consent to participate in the study
3. Willing to complete the interview on the same day as the clinic appointment or willing to be contacted by phone to schedule another time to return to the clinic
4. Mentally and physically able to be interviewed, in a conversational style, for up to 1.5 hours (determined by study screener)
5. New to the UNC ID clinic since April 2006
6. Had not received any HIV-related medical care at any other institution
7. CD4+ T-lymphocyte cell count <350 cells/mm³ at the first visit (eligible for HAART).

In this study, we were interested in ‘late testers’ as well as individuals who delayed care after a more distal diagnosis. We expected that individuals who tested late in the course of illness, often prompted by the onset of symptoms, would represent the majority of the study population.

Recruitment

UNC Infectious Disease Outpatient Clinic employs a research screener who meets with all new patients to determine eligibility for the various research protocols. Patients are typically screened on their second or third study visits, when laboratory results are available and the patient has time to discuss participation in research projects. Patients interested in learning more about research studies, including those who consent to participate in the UNC CFAR Clinical and Research Database, will be eligible for the study.
We utilized a two-pronged approach to recruit patients for the study. Eligible patients were approached by the clinic-based research screener to determine interest in study participation. Patients interested in learning more about the study met with the study interviewer (S. McCoy) before or immediately after their regular clinic visit, at their next regularly scheduled clinic visit, or at a separate appointment time selected by the patient. The study interviewer explained the study and obtained written, informed consent at the start of the interview.

**Data Collection**

We conducted in-depth, face-to-face, semi-structured interviews with study participants. All interviews were audio recorded and took place in private interview rooms in the UNC Infectious Disease Outpatient Clinic. Interviews took approximately 45 minutes.

An interview guide approach was used to conduct the interviews. Qualitative interviews using an interview guide use pre-determined issues to be covered in the interview beforehand, however the interviewer is free to change the sequence and the wording in the course of the interview. Interviews are conversational in style but the interview guide format ensures that data collection is somewhat systematic thorough the study. A weakness of this technique is that important topics may be missed due to interviewer inflexibility and that differences in wording from interview to interview may change the meaning and interpretation of the questions. In-person, qualitative interviews were the most appropriate method for our research question because we sought to understand the process, meaning, and context within which HIV positive persons make decisions about health care. In-person interviews, as opposed to focus groups, were best suited to this study due to the sensitive and highly personal nature of the subject area. Interview questions were comprised of three main types of questions. *Main questions* addressed the themes of the
research questions and were intended to be broad in nature. *Follow-up questions* sought additional details, and *probes* encouraged even deeper, more detailed information.\(^{151}\)

Participants were compensated for their time at the end of the interview with a $40 gift card to a local grocery retailer (Food Lion). At the completion of the interview, interview summaries were created to record the non-verbal attributes of the interview, first impressions of the data, and successes or suggested improvements for future interviews.

**Data Management and Data Analysis**

All interviews were digitally taped with consent from the study participants and transcribed verbatim within a week of the interview. Interviews were securely stored on the CFAR server which was backed-up nightly. Interviews did not contain personal identifiers but were identified with a unique study ID in the file name. Consent forms, containing patient identifiers, were be stored in a locked, separate file cabinet accessible only to study staff.

Analysis was ongoing and first involved single-case analysis, including the generation of memos and interview summaries, followed by cross-case analyses to identify emergent themes, barriers, and patterns.\(^{152}\) Atlas/ti qualitative analysis software was used for analysis.\(^{153}\)

*Memo writing.* Memos are brief, unstructured narratives which can assist in the development of new ideas and the identification of themes and patterns which emerge from the data.\(^{152}\) Memos record, reflect, demonstrate, describe and interpret ideas.\(^{154}\) Memos were utilized to record field notes after every interview, after reviewing transcripts, and to record surfacing themes.

*Coding of interviews.* Reviewing transcripts and coding began once data collection commenced. A start list of organizational and deductive, descriptive codes developed from
the Health Belief and Information-Motivation-Behavioral skills (IMB) models was used to begin coding, however, coding was continuous and evolving.\(^{151, 152, 155}\) Interpretive, inductive codes were added to the code list as themes and patterns emerged from the data. Data displays and memo writing facilitated the development of new codes. Codebook evolution was documented by noting the dates and interviews from which new codes emerged.\(^{151}\) The final codebook for analysis is presented in Table 4.6.

**Description of the Study Population.** We first present a description of our study population, including sample size and demographic breakdown (gender, race, and age). We also present information on baseline clinical characteristics of the participants when they first sought medical care (year of diagnosis, CD4 T-cell count and time since diagnosis).

**Single Case Analysis.** The formal qualitative analysis of the data began with data immersion into individual interviews. Interviews were broadly coded for themes, examined for narrative structure, and compared to the conceptual framework. Segments of text were read for multiple dimensions, including the primary message content, attitudes, individual or group-level ideas, and the degree to which the ideas represented factual or hypothetical experience.\(^{151}\)

**Cross-Case Analysis.** Once we completed analysis on 15 interviews, we performed coding sorts to examine each theme in more detail. Coding sorts are collections of similarly coded passages from multiple interviews.\(^{151}\) Detailed memos with emerging themes and concepts were written for each coding sort. The codes used for this analysis included “Facilitators,” “Barriers,” “Susceptibility,” “Cues to Action,” “Starting Care,” “Prior HIV Knowledge,” “Personal Experience,” and “Stigma.”
Data Reduction and Interpretation. Data reduction is the process of reducing the data to its most essential concepts, ideas, and relationships.\textsuperscript{151} We developed a conceptual diagram to graphically illustrate the most important concepts that emerged from the data (presented in Chapter Seven). We also present the main barriers and facilitators to HIV testing and prompt linkage to primary care.

Sample Size
For this study, we employed a small, purposeful sample to understand the reasons that many people do not seek testing and medical care early in the course of illness. Data collection was guided by the achievement of theme saturation – when little new information was being heard from study participants we had likely interviewed enough participants.\textsuperscript{151, 156} Our study consisted of 24 interviews.

Validity Issues, Strengths and Limitations
The goal of this study was to understand the process of seeking HIV testing and medical care with an emphasis on understanding potential barriers and facilitators that may be structural (e.g., insurance status, transportation), psychosocial (e.g. lack of social support, depression), or behavioral (e.g. risk awareness, fear). Towards this end, ensuring valid, credible interpretations of the data was paramount. Common threats to validity in qualitative research are researcher bias, the “lens” through which the researcher views the world, and reflexivity, the concept that the researcher is part of the world that he/she studies.\textsuperscript{152} To ensure the trustworthiness of the data, we utilized several techniques to validate the credibility of our findings.

One such technique was the maintenance of a comprehensive audit trail. An audit trail is a record that allows the researchers and outsiders to track the process that lead to the study’s conclusions.\textsuperscript{151} In this study, the audit trail includes unedited transcripts, tape
recordings, and field notes of interviews, coding lists and codebook evolution memos, data reduction and analysis notes, diagrams, hypotheses, study protocol documents, and instrument development notes. These documents ensure that the findings from the study could be confirmed by other researchers.

As we developed explanations for the actions of the study participants, we actively looked for ‘rival hypotheses’ or negative cases to invalidate our hypotheses. The bias that is introduced by the researcher’s influence over the interpretation of the results was addressed by discussions with study team members, the collection of in-depth data, and by the generation of an accurate representation of the concepts offered by the study participants.

Despite the commitment to ensuring the validity of our findings, one limitation of our study is the ability to apply our findings to other populations. Our study focuses on HIV positive patients who come to the UNC outpatient clinic for primary care, therefore we have limited generalizability of outside of the UNC catchment area. Although UNC patients come from all 100 counties in North Carolina, our findings may not be transferable to clinics with a high proportion of rural residents, or clinics where injecting drug use is more prevalent. We can, however, expect that our findings will be transferable to other HIV/AIDS clinics in the southeastern U.S.

LIMITATIONS

The limitations of the proposed methods for the study aims were presented at the conclusion of each research design section. Here we repeat certain limitations that apply to several or all of the aims.

Limitation: Limited generalizability outside of the Southern U.S.

This dissertation focuses exclusively on patients with HIV in North Carolina. Our findings may not be directly applicable to the national epidemic; however, they are likely relevant for
other areas in the southern U.S. which may have similar rates of poverty, STDs, and proportion of residents living in rural areas.

**Limitation: Causal inference.**
Because of the retrospective nature of all of the data utilized in this proposal, we have limited ability to infer causality to our findings. Both the CSDS questionnaire and the qualitative interviews ask patients to recall their behavior after testing positive. Misclassification of exposures and outcomes may have occurred. Similarly, patients may have reported factors that hindered or helped their successful linkage to care, but it is possible that the importance of reported factors changed over time and the reported factors and actual factors differed.

**Limitation: Limited power to detect differences.**
For Aim 1 and 2, we had low statistical power to detect small differences. This resulted in imprecise estimates. However, although our number of acute HIV cases was small, it is a large number with respect to previous studies of acute HIV patients. Further, our study of social support and entry to care is one of the few studies on the topic and is a valuable contribution to the literature despite any imprecision.

**SUMMARY**
The new testing recommendations issued by the Centers for Disease Control in 2006 aim to incorporate HIV testing into routine medical care. A comprehensive understanding of how, when, and why newly diagnosed individuals enter care is therefore necessary to ensure that the new screening guidelines yield their maximum benefit. Towards this end, we sought to understand the HIV testing and care-seeking behavior of individuals in North Carolina. We undertook a multidimensional approach, relying on data from diverse sources and utilizing
different methods of data collection. This dissertation is innovative in that it relied on intensive interviews with the DIS in the field, psychosocial factors from interviews in the clinic, as well as qualitative interviews with patients. This multifaceted approach expanded our current knowledge about HIV testing and medical care in the region.
TABLE 4.1. Estimates of time periods between HIV infection and detectable HIV antibody on 2nd and 3rd generation EIAs.

<table>
<thead>
<tr>
<th>Window</th>
<th>Description</th>
<th>Reported Estimates</th>
<th>Average Interval</th>
</tr>
</thead>
</table>
| 1      | HIV infection to infectivity         | 10 days\textsuperscript{137, 157}  
           |                        | 2.5 days\textsuperscript{158}  | 6.3 days         |
| 2      | Detectable HIV RNA                   | 11 days\textsuperscript{157}  
           |                        | 9 days\textsuperscript{159}  | 10 days          |
| 3      | Detectable p24 antigen               | 3 days\textsuperscript{137}  
           |                        | 5 days\textsuperscript{157}  | 6 days (Genprobe assay)\textsuperscript{159}  
           |                        | 4.2d (Roche assay)\textsuperscript{159}  
           |                        | 7 days (50 copies/ml)\textsuperscript{139}  
           |                        | 5 days (100 copies/ml)\textsuperscript{139}  | 5.0 days          |
| 4      | Antibody detection via 3\textsuperscript{rd} generation EIA | 5 days\textsuperscript{137}  
           |                        | 6 days\textsuperscript{157}  | 5.4 days         |
| 5      | Antibody detection by 2\textsuperscript{nd} generation EIA | 8.8 days\textsuperscript{139}  | 8.8 days         |

1. Window periods are the time between the previous interval and the next event. For example, window period two represents the time between HIV infectivity to detectable HIV RNA.
FIGURE 4.1. Power estimates for the two sample t-test test of log(HIV RNA). Graph A (top) illustrates the power for detecting a difference between individuals co-infected with an STI and those without co-infection; Graph B (bottom) illustrates the power for detecting a difference between testing site type.
TABLE 4.2. Modified Medical Outcomes Study Social Support Survey

1. About how many close friends do you have (people you feel at ease with and can talk to about what is on your mind)?
   __________ (No. close friends)

2. About how many close relatives.....?
   __________ (No. close relatives)

3. People sometimes look to others for companionship, assistance, or other types of support. How often is each of the following kinds of support available to you if you need it?

<table>
<thead>
<tr>
<th>Support Provided</th>
<th>None of the time</th>
<th>A little of the time</th>
<th>Some of the time</th>
<th>Most of the time</th>
<th>All of the time</th>
<th>Skip=7</th>
<th>Dk=8</th>
<th>RF=9</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Someone to have a good time or hang with</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Someone to do things with and help you get your mind off things</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Someone to help you if you were confined to bed.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Someone to give you good advice about a crisis.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Someone who's advice you want.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. Someone to take you to the doctor if you needed it.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>g. Someone who shows you love and affection.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>h. Someone you can count on to listen when you need to talk.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. Someone who hugs you.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>j. Someone to prepare your meals if you were unable to do it.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>k. Someone to share your most private worries and fears with</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>l. Someone to help with daily chores if you were sick.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>m. Someone to love and make you feel wanted.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7   8   9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
FIGURE 4.2. Common factor model used for confirmatory factor analysis of the modified MOS Social Support Scale.

Legend:

A-M: Observed indicators
δ = Unique variance (measurement error) for each indicator
λ = Factor loadings or regression slopes for predicting the indicator values from the latent factor
η = First-order latent factors (unobserved)
ξ = Second-order latent factor (unobserved)
ζ = Factor errors
φ = Factor covariances
γ = Association of exogenous and endogenous latent factors
TABLE 4.3. Creation of linear spline terms for each dimension of functional social support.

Knots were created at appropriate cutpoints, entered into a proportional hazards model, and tested for statistical contribution to the model with the likelihood ratio test.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Knot 1 (score)</td>
<td>10th percentile (53.3)</td>
<td>10th percentile (50.0)</td>
<td>10th percentile (40.0)</td>
<td>10th percentile (40.0)</td>
</tr>
<tr>
<td>Knot 2 (score)</td>
<td>25th percentile (73.3)</td>
<td>50th percentile (80.0)</td>
<td>50th percentile (85.0)</td>
<td>50th percentile (80.0)</td>
</tr>
<tr>
<td>Knot 3 (score)</td>
<td>50th percentile (93.3)</td>
<td>75th percentile (95.0)</td>
<td>70th percentile (95.0)</td>
<td>75th percentile (90.0)</td>
</tr>
<tr>
<td>LR test of spline terms (p-value)</td>
<td>0.83</td>
<td>0.73</td>
<td>0.89</td>
<td>0.86</td>
</tr>
</tbody>
</table>
FIGURE 4.3. Scatter plots of survival function estimates and functional social support. A: Emotional/informational support; B: Affectionate support; C: Tangible support; D: Positive social interaction support.
FIGURE 4.4. Hypothesized causal diagram of the relationship between social support and delayed HIV care. Dashed lines indicate potential associations that are unmeasured or unknown in the data. The relationship between race and sex and perceived social support has not been described.
TABLE 4.4. Results of analysis strategies for handling missing data in the modified MOS-Social Support Scale. Thirteen of 332 (3.9%) participants completing the CSDS had any missing data in the 13-item functional support scale (9 had one missing value, three had two missing values, and one person had three missing). The mean and standard deviation for each of the functional social support types is presented for each missing data strategy.

<table>
<thead>
<tr>
<th>Functional Support Type</th>
<th>Complete Case Analysis (n=319)</th>
<th>Single Imputation&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Single Imputation&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Positive Interaction</td>
<td>71.8</td>
<td>22.8</td>
<td>71.9</td>
</tr>
<tr>
<td>Tangible</td>
<td>79.7</td>
<td>21.5</td>
<td>79.5</td>
</tr>
<tr>
<td>Emotional/information</td>
<td>78.9</td>
<td>19.3</td>
<td>78.8</td>
</tr>
<tr>
<td>Affection</td>
<td>83.8</td>
<td>21.7</td>
<td>83.5</td>
</tr>
<tr>
<td>Total</td>
<td>79.2</td>
<td>18.0</td>
<td>79.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Functional Support Type</th>
<th>Single Imputation&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Single Imputation&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Conditional mean imputation&lt;sup&gt;5&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Positive Interaction</td>
<td>71.7</td>
<td>22.7</td>
<td>71.9</td>
</tr>
<tr>
<td>Tangible</td>
<td>79.0</td>
<td>21.7</td>
<td>79.8</td>
</tr>
<tr>
<td>Emotional/information</td>
<td>78.7</td>
<td>19.3</td>
<td>78.9</td>
</tr>
<tr>
<td>Affection</td>
<td>83.5</td>
<td>21.9</td>
<td>83.6</td>
</tr>
<tr>
<td>Total</td>
<td>78.8</td>
<td>18.0</td>
<td>79.2</td>
</tr>
</tbody>
</table>

1. Missing values were imputed with the mean of the available data within each respondent.
2. Missing values were imputed with the mean of the same question for the study sample.
3. Missing values were imputed with the lowest value (1).
4. Missing values were imputed with the highest value (5).
5. Predictive multiple linear regression models were constructed for each question on the MOS-SSS using the subset of the sample with complete data. The outcome was the indicator of interest and the predictor variables were all the other variables in the MOS-SSS scale and demographic factors. If a record was missing more than one value in the scale, the model was constructed using only the available indicators. The predicted value for each person was then used in place of the missing value.
TABLE 4.5. Power estimates for the log-rank test for equality of the survival curves comparing the time to entry to medical care by levels of social support.¹

<table>
<thead>
<tr>
<th>Expected Constant Hazard Ratio, HR</th>
<th>HR=4.10</th>
<th>HR=3.10</th>
<th>HR=2.29</th>
<th>HR=1.60</th>
<th>HR=5.63</th>
<th>HR=4.26</th>
<th>HR=3.14</th>
<th>HR=2.19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test significance level, α</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>2-sided test</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>N₁ (Low Social Support)</td>
<td>78</td>
<td>78</td>
<td>78</td>
<td>78</td>
<td>78</td>
<td>78</td>
<td>78</td>
<td>78</td>
</tr>
<tr>
<td>N₂ (High Social Support)</td>
<td>261</td>
<td>261</td>
<td>261</td>
<td>261</td>
<td>261</td>
<td>261</td>
<td>261</td>
<td>261</td>
</tr>
<tr>
<td>% Not in care at 3 mo, Group 1</td>
<td>80</td>
<td>80</td>
<td>80</td>
<td>80</td>
<td>85</td>
<td>85</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>% Not in care at 3 mo, Group 2</td>
<td>40</td>
<td>50</td>
<td>60</td>
<td>70</td>
<td>40</td>
<td>50</td>
<td>60</td>
<td>70</td>
</tr>
<tr>
<td>Power</td>
<td>99</td>
<td>97</td>
<td>79</td>
<td>30</td>
<td>99</td>
<td>99</td>
<td>92</td>
<td>62</td>
</tr>
</tbody>
</table>

¹. Accrual is expected to be 100% at 3 months with no dropouts – all participants eventually experience the outcome.
<table>
<thead>
<tr>
<th>No.</th>
<th>Code Name</th>
<th>Created / Modified</th>
<th>Brief Definition</th>
<th>Full Definition</th>
<th>When to Use</th>
<th>When Not to Use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Level 1 Codes – Organizational</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>L1 Decision to Test</td>
<td>Start List</td>
<td>How individual was tested for HIV</td>
<td>Answers to question: “Tell me about your decision to get tested for HIV.”</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>2</td>
<td>L1 Testing process</td>
<td>Start List</td>
<td>What testing was like</td>
<td>Answers to question: “Tell me about the actual testing process for HIV.”</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>3</td>
<td>L1 Impact of Result</td>
<td>Start List</td>
<td>Finding out you are HIV positive</td>
<td>Answer to question: “How were you affected by learning that you were positive?”</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>4</td>
<td>L1 Knowledge of HIV</td>
<td>Start List</td>
<td>How much known about HIV before diagnosis</td>
<td>Answer to question: “Did you know about HIV when you were first diagnosed?”</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>5</td>
<td>L1 Seeing a Doctor</td>
<td>Start List</td>
<td>Thoughts about seeing a doctor</td>
<td>Answer to question: “Did you think about seeing a doctor after your diagnosis?”</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>6</td>
<td>L1 Medical Care</td>
<td>Start List</td>
<td>Thoughts about seeking care</td>
<td>Answer to question: “What was it like seeking medical care for the first time for HIV?”</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>7</td>
<td>L1 Come Back</td>
<td>Start List</td>
<td>Thoughts about staying in care</td>
<td>Answer to question: “Why did you come back this time?”</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Great quotes</td>
<td>Start List</td>
<td>Great quotes</td>
<td>Vivid, insightful, and/or unusual descriptions of feelings and thoughts</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>No.</td>
<td>Code Name</td>
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<td>Full Definition</td>
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<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>1.</td>
<td>Trauma of discovery</td>
<td>Start List</td>
<td>Reactions to diagnosis</td>
<td>Feelings and thoughts about learning one is HIV positive</td>
<td>If talking about immediate reactions to the diagnosis, use this code; often occurs as shock, sadness, depression, fatalism</td>
<td>Not appropriate for current thoughts and feelings about diagnosis</td>
</tr>
<tr>
<td>2.</td>
<td>Suicide</td>
<td>11/28/07, Interview 1</td>
<td>Subcode of Trauma of Discovery</td>
<td>Suicidal thoughts and feelings about learning one is HIV positive</td>
<td>Use for “pre-existing” suicide as well as suicide thoughts or attempts after diagnosis</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Denial</td>
<td>12/11/07, Interview 2</td>
<td>Subcode of Trauma of Discovery</td>
<td>Refusal to recognize or acknowledge the gravity of the HIV diagnosis</td>
<td>Use this code for patients who seem indifferent about their diagnosis or who refuse to accept the seriousness of the disease</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Fatalism</td>
<td>12/11/07, Interview 2</td>
<td>Subcode of Trauma of Discovery</td>
<td>The acceptance of the HIV diagnosis as inevitable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Depression</td>
<td>12/11/07, Interview 3</td>
<td>Subcode of Trauma of Discovery</td>
<td>References to depression before or after the diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Being overwhelmed</td>
<td>12/11/07, Interview 3</td>
<td>Subcode of Trauma of Discovery</td>
<td>To be presented with an excessive amount of something, usually information</td>
<td>Use this code when patients refer to knowing PLWHA prior to diagnosis</td>
<td>Not applicable to experiences with PLWHA after diagnosis</td>
</tr>
<tr>
<td>7.</td>
<td>Personal experience</td>
<td>Start List</td>
<td>Contact with PLWHA</td>
<td>Narratives about participants’ past experience with HIV positive persons</td>
<td>Use this code when patients refer to knowing PLWHA prior to diagnosis</td>
<td>Not applicable to experiences with PLWHA after diagnosis</td>
</tr>
<tr>
<td>8.</td>
<td>Prior HIV knowledge</td>
<td>Start List</td>
<td>Prior HIV/AIDS knowledge</td>
<td>Knowledge about HIV/AIDS before seeking medical care, including transmission, clinical course, and treatment.</td>
<td>Use to describe all knowledge about HIV/AIDS biology, treatment, or outcomes prior to diagnosis</td>
<td>This code is not appropriate for knowledge obtained about HIV/AIDS after diagnosis</td>
</tr>
<tr>
<td>No.</td>
<td>Code Name</td>
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<td>Full Definition</td>
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</tr>
<tr>
<td>9.</td>
<td>Barriers</td>
<td>Start List</td>
<td>Obstacles to testing and medical care</td>
<td>Self-identified reasons for not seeking testing or medical care after diagnosis</td>
<td>Use for instances when the patient describes obstacles to seeking testing or care, whether self-imposed (perception of risk) or structural (did not know where to seek testing or care).</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>Drugs/Alcohol</td>
<td>12/11/07, Interview 2</td>
<td><strong>Subcode</strong> of Barriers</td>
<td>References to way that drugs or alcohol abuse may impede testing or seeking care</td>
<td>Appropriate for all reasons why the individual sought testing and medical care, including personal (wanted to know) and structural (provider-initiated testing)</td>
<td>This code should not be used to code references to the potential benefits of seeking testing or care – in this case the code ‘Benefits’ is more appropriate.</td>
</tr>
<tr>
<td>11.</td>
<td>Facilitators</td>
<td>Start List</td>
<td>Factors which provoked testing and medical care</td>
<td>Self-identified reasons for seeking testing or medical care after diagnosis</td>
<td>Use this code for all references to individual perceived risk of acquisition; also for references to severity of disease after acquisition.</td>
<td></td>
</tr>
<tr>
<td>12.</td>
<td>Susceptibility</td>
<td>Start List</td>
<td>Vulnerability to HIV/AIDS</td>
<td>Beliefs about perceived susceptibility to HIV disease, whether before testing positive or after testing positive</td>
<td>Use this code when the participant refers to thoughts about the positive aspects of testing and medical care. These thoughts do not necessarily have to be the ones that incited testing or seeking care.</td>
<td>References to actual reasons for seeking testing or medical care should be coded as ‘Facilitators.’</td>
</tr>
<tr>
<td>13.</td>
<td>Benefits</td>
<td>Start List</td>
<td>Advantages to seeking testing and care</td>
<td>Beliefs about the advantages of seeking testing and medical care after diagnosis</td>
<td>Use this code for references about the potential benefits of seeking testing or care, such as an illness, provider-initiated testing, or an incident STI.</td>
<td>Not appropriate for references to benefits or facilitators of testing, this code is reserved for the actual prompt which incited testing or seeking care.</td>
</tr>
<tr>
<td>14.</td>
<td>Cues to action</td>
<td>Start List</td>
<td>Prompts to take action</td>
<td>Stimuli which ultimately resulted in seeking testing or medical care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Code Name</td>
<td>Created / Modified</td>
<td>Brief Definition</td>
<td>Full Definition</td>
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<td>When Not to Use</td>
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<td>----------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>15.</td>
<td>Provider-initiated testing</td>
<td>11/28/07, Interview 1, 3/19/07 modified</td>
<td><strong>Subcode</strong> of Cue to Action. When a patient did not seek testing</td>
<td>Testing events where the patient did not request or seek testing, rather, testing was recommended by a provider</td>
<td>Use this code for testing experiences that did not include client-initiated testing</td>
<td></td>
</tr>
<tr>
<td>16.</td>
<td>Missed opportunities</td>
<td>12/11/07, Interview 3</td>
<td><strong>Subcode</strong> of provider-initiated testing</td>
<td>Missed opportunities for provider-initiated testing</td>
<td>Use for perceived near death experiences as well as major medical episodes experienced by the patient</td>
<td>Not for references to death-related thoughts and planning</td>
</tr>
<tr>
<td>17.</td>
<td>Near death</td>
<td>11/28/07, Interview 1</td>
<td>Near-death experiences</td>
<td>Experiences of the patient that were perceived to be near death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.</td>
<td>Spirituality</td>
<td>11/28/07, Interview 1</td>
<td>The role of God or religion</td>
<td>References to God, religion, or spirituality</td>
<td>Use this code for all references to God, religion, or spirituality, named or implicit</td>
<td></td>
</tr>
<tr>
<td>19.</td>
<td>Punishment</td>
<td>11/28/07, Interview 1</td>
<td><strong>Subcode</strong> of Spirituality</td>
<td>Thoughts that God is punishing the patient by giving them HIV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20.</td>
<td>Confusion</td>
<td>11/28/07, Interview 1</td>
<td>Uncertainty about the HIV diagnosis or meaning</td>
<td>References to confusion about the testing process, results, or meaning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21.</td>
<td>Changes after diagnosis</td>
<td>11/28/07, Interview 1</td>
<td>How an individual's life was altered</td>
<td>References to changes after an HIV diagnosis</td>
<td>References to changes in material possessions, job status, or behavior after diagnosis</td>
<td></td>
</tr>
<tr>
<td>22.</td>
<td>Social support</td>
<td>11/28/07, Interview 1</td>
<td>Resources from other people</td>
<td>References to the existence or quantity of social relationships and the resources provided by other persons.</td>
<td>Can be used for references to <em>structural</em> or <em>functional</em> social support.</td>
<td></td>
</tr>
</tbody>
</table>

**Level 3 Codes – Inductive codes – Emergent Themes and Concepts**
<table>
<thead>
<tr>
<th>No.</th>
<th>Code Name</th>
<th>Created / Modified</th>
<th>Brief Definition</th>
<th>Full Definition</th>
<th>When to Use</th>
<th>When Not to Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>23.</td>
<td>Starting care</td>
<td>11/28/07, Interview 1</td>
<td>Thoughts and feelings about starting HIV care</td>
<td>References to the patient’s thoughts or feelings about starting HIV care</td>
<td>Use for references to fear, stigma, being overwhelmed, or anticipation</td>
<td></td>
</tr>
<tr>
<td>24.</td>
<td>Medical care challenges</td>
<td>11/28/07, Interview 1</td>
<td>Subcode of starting care. Difficult aspects of medical care</td>
<td>References to challenges staying in care, taking ARVs, being overwhelmed, etc.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25.</td>
<td>Staying in care</td>
<td>12/11/07, Interview 2</td>
<td>Subcode of starting care.</td>
<td>References to the challenges of staying in care, or how the person successfully stays in care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26.</td>
<td>Stigma</td>
<td>11/28/07, Interview 1</td>
<td>References to stigma, experienced or perceived</td>
<td>(Unfavorable) attitudes, beliefs, and policies directed toward people perceived to have HIV/AIDS</td>
<td>Use for references to experienced or perceived stigma, including fear of stigma and decisions made with stigma in mind, also for fear of people finding out or talking about someone with HIV</td>
<td></td>
</tr>
<tr>
<td>27.</td>
<td>Disclosure</td>
<td>12/11/07, Interview 2</td>
<td>The act of revealing one’s HIV status to another person</td>
<td>The process of telling someone else, outside of the healthcare system, that you are HIV positive</td>
<td>Use for all references to the process of disclosure, the good and bad outcomes of disclosure, and thoughts about disclosing</td>
<td></td>
</tr>
<tr>
<td>28.</td>
<td>Double-whammy disclosure</td>
<td>12/12/07, Interview 5</td>
<td>Subcode of disclosure</td>
<td>The process of disclosing HIV status and another secret (e.g., being gay, having an affair)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29.</td>
<td>Planning for death</td>
<td>12/11/07, Interview 2</td>
<td>Thoughts about planning after diagnosis</td>
<td>References to planning after diagnosis, including planning for death, preparing estates, finances, or family members</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30.</td>
<td>Hope</td>
<td>12/11/07, Interview 2</td>
<td>To have confidence in the future</td>
<td>The feeling that what is wanted can be had or that events will turn out for the best</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ABSTRACT

Objective: Our objective was to describe the frequency and types of STI co-infections among patients with acute HIV infection (AHI). Methods: We examined surveillance data from publicly-funded HIV testing sites in North Carolina. Antibody negative specimens are retested for HIV RNA using specimen pooling. Demographics, symptoms, and STI infections are collected. We calculated the prevalence of co-infection and determined risk factors for co-infection with prevalence ratios (PR). Results: Between 11/1/2002 and 10/31/2006, 75 clients with AHI were identified. Of these, 23 (31%) had STI co-infections at the time of diagnosis — nine (39%) had gonorrhea and five had trichomoniasis (22%). The prevalence was highest in women (53%) compared to 35% in heterosexual men (PR=0.67, 95% CI 0.31, 1.45) and 18% in men who have sex with men (PR=0.34, 95% CI 0.15, 0.76). The type of co-infection differed by gender with women more likely to be diagnosed with trichomoniasis (p<.01). Non-Whites were 3.9 times as likely to report a co-infection as Whites (95% CI 1.00, 15.10). Conclusions: STI co-infection is common among patients with AHI. Differences in the prevalence of co-infection by gender, risk and race suggest that STIs may have a role in the heterosexual HIV epidemic in North Carolina.
INTRODUCTION

Acute HIV-1 infection (AHI) is the 4-6 week interval in the HIV disease course when the virus can be detected in the blood prior to seroconversion. During this time, the virus is distributed to cellular reservoirs throughout the body and infected persons experience a dramatic increase in plasma viral load and viral shedding from the genital tract. Roughly half to two-thirds of people with AHI will develop symptoms of acute retroviral syndrome about two weeks after infection. The acute phase of infection has been identified as a key intervention period to interrupt HIV transmission because the peak viremia characteristic of AHI may dramatically increase the likelihood of sexual transmission during this time.

Sexually transmitted infections (STIs) have a well-established synergistic relationship with HIV infection. Co-infection with HIV and an STI can increase the probability of HIV transmission to an uninfected partner by increasing HIV concentrations in genital lesions, genital secretions, or both. STI infection can also increase the likelihood of HIV acquisition by interrupting mucosal barriers, increasing the access to and concentration of HIV receptor cells, and, in women, changing the vaginal microflora to favor HIV infection. Among patients with AHI, co-infection with an STI may be common. More than 70% of AHI patients had an STI co-infection in a Malawian sexually transmitted disease (STD) clinic in two separate studies. However, little is known about the frequency of STI and acute HIV infection co-infection outside of the STD clinic setting.

In addition to facilitating HIV transmission, STIs may also influence HIV testing behavior. Symptomatic STIs in recently HIV-infected individuals may provide motivation to seek medical care and to consequently receive HIV counseling and testing services earlier than persons without co-infections, either by provider- or client-initiated testing. However, recently revised testing recommendations only recommend RNA testing in patients with compatible clinical syndromes and recent high-risk behavior. Under these guidelines,
patients who co-acquire HIV and an STI infection may be missed by standard HIV antibody tests when STI symptoms appear, given the short incubation periods of some bacterial STIs. Since individuals with AHI represent the earliest possible time point for entry into the medical system and public health intervention, a thorough understanding of factors relating to testing behavior during AHI is warranted.

To further examine these issues, we conducted a secondary data analysis of 75 AHI patients identified from the statewide Screening and Tracing Active Transmission Program (STAT) in North Carolina (NC) from 2002-2006. Our goals were to describe the prevalence and predictors of acute HIV and STI co-infection in a systematically collected, statewide sample of AHI patients and to examine whether STI co-infection might influence the likelihood of presenting early during AHI.

METHODS

Study Design and Population

Persons with AHI are routinely identified through the STAT Program of the North Carolina Department of Health and Human Services (NC DHHS) and the University of North Carolina at Chapel Hill (UNC). The screening methodology has been previously described. In brief, all clients presenting for confidential HIV counseling and testing at approximately 135 publicly funded sites in NC are included in a testing algorithm to detect HIV-1 RNA positive, antibody negative individuals. Serum samples submitted for HIV testing are first tested for HIV-1 antibody, and then all antibody negative samples are screened for HIV-1 RNA by pooling. Antibody indeterminate samples are tested for HIV RNA individually. Vironostika HIV-1 enzyme immunoassay (EIA) and Western Blot analysis kits (Bio-Rad Laboratories) are used for antibody screening. Pools were screened by nucleic acid amplification (NAAT) for HIV-1 RNA with the Procleix HIV-1 assay (GenProbe) and then in July 2005 with the EasyQ HIV-1 quantitative assay (bioMerieux). Samples in which HIV-1 RNA is detected and
are either EIA negative or EIA positive and Western Blot negative or indeterminate are considered to represent acute infections, and are confirmed by follow-up antibody testing. We included clients with AHI during the first four years of the STAT program, November 1, 2002 through October 31, 2006.

**Follow-up and Confirmatory Testing**

The NC DHHS assigns potential AHI cases to a team of disease intervention specialists (DIS). DIS are located throughout the state and perform initial interviews, confirmatory testing, and referrals to care within 72 hours of notification. After interview with the patient and medical record review, DIS complete standardized case report forms. This information is merged with pretest counseling and testing data from the NC DHHS, including risk factor information and testing site. All data are de-identified.

**HIV-1 RNA Quantification**

Quantification of HIV-1 RNA is routinely conducted for all AHI patients on the initial and confirmatory venous blood samples. An HIV-1 reverse transcriptase polymerase chain reaction assay is used to quantify serum HIV-1 RNA (Amplicor HIV-1 Monitor Test, version 1.5, Roche Diagnostic, limits of detection 50–750,000 copies/milliliter). HIV RNA was not detected in one patient despite having RNA detected initially; this was likely due to specimen degradation secondary to shipping delays. This patient was excluded from viral load analyses.

**Statistical Analysis**

We assigned sexual risk groups according to the gender of partners reported in the previous eight weeks. Men with any male partners were classified as men who have sex with men (MSM) and men with only female partners were classified as heterosexual. All of the women
in the study reported only male partners (classified as heterosexual). We defined STI co-infection as the diagnosis of gonorrhea, chlamydia, trichomoniasis, Human Papillomavirus (HPV), genital herpes, bacterial vaginosis (BV), or syphilis during the same month and year of the initial AHI diagnosis, as the data collection forms only require the month and year of STI diagnoses. STI infections were confirmed by medical record review. For two AHI patients, the date of STI diagnosis was in the month preceding the HIV diagnosis by 13 and 18 days, respectively. We considered these situations to represent STI co-infections.

Information on self-reported STI-compatible symptoms was assessed if present at or within four weeks prior to AHI diagnosis. Similarly, we considered appropriate symptoms reported during a window period of eight weeks of testing (± four weeks of the test date, inclusive) to be acute retroviral syndrome.

We describe the characteristics of the study population and the proportion of AHI patients with an STI at the time of AHI diagnosis. To determine factors associated with STI co-infection, we computed the prevalence of co-infection, prevalence ratios (PR), and 95% exact confidence intervals to test associations between co-infection and selected covariates. Because viral load is associated with the likelihood of sexual transmission of HIV, we examined variations in mean log_{10}(HIV-1 RNA) from initial testing samples with one-way analysis of variances to determine predictors of HIV-1 RNA variation. Similarly, we were interested in the relationship between study covariates and viral dynamics in order to understand more about the timing of testing. Towards this end, among the subset of participants with both initial and confirmatory HIV RNA values, we classified patients as having an increasing or decreasing HIV RNA slope. We then used exact logistic regression to assess the relationships between this dichotomous indicator of HIV RNA slope (outcome) and study covariates. We assumed that a positive HIV RNA slope was indicative of testing before the peak viremia. The statistical significance of covariates entered individually in
models was assessed with an exact probability test of the $\beta$ parameter(s). All analyses were performed with SAS Software (version 9.1.2, SAS Institute, Cary, NC).

**Human Subjects Protection**

Clients who presented for confidential HIV testing in NC were required to sign an informed consent form authorizing the collection of personal information. Patients with AHI signed an additional consent to release information and blood to the STAT program. This analysis was approved by the UNC Institutional Review Board.

**RESULTS**

From November 1, 2002 to October 31, 2006, 79 persons with AHI were detected through the STAT program. Of these, three could not be located for interview and one refused post-test counseling and partner notification services, leaving a sample of 75 patients with AHI for analysis. Seventy-five percent of the study population were male (Table 5.1), and 52% were MSM. The median age was 28 years (range: 16-56). The majority of the population were Black, followed by a quarter White, non-Hispanic. Half of the cases were identified at STD clinics. A majority of persons (n=45, 60%) reported at least one acute retroviral symptom at or before the initial testing date. The most common symptoms were fever (37%), night sweats (24%), fatigue (24%), body aches (21%), and nausea (21%). Of those persons with symptoms, 87% reported two or more symptoms and 58% reported three or more symptoms at or before the initial test. A small number of persons (9) reported symptom onset after the test date.

Nearly one third of patients (n=23, 31%) had an STI at or near the time of the AHI diagnosis, consistent with co-infection. Five (22%) of the 23 participants with STI co-infections had more than one concurrent STI diagnosis at the time of AHI recognition. One person reported three STI co-infections: HPV, genital herpes, and syphilis. Medical record
review confirmed 26 of 29 (90%) individual STI diagnoses from the DIS, which corresponded to 21 (91%) of the 23 patients with co-infections. The most common co-infections were gonorrhea (39%), trichomoniasis (22%), and syphilis (17.4%) (Table 5.2). Co-infections differed substantially by gender – the majority of male co-infections were gonorrhea (54%) whereas among women the most common co-infection was trichomoniasis (50%, Fisher’s exact test, p<.01). An additional five patients (7%) self-reported STI compatible symptoms (e.g. genital discharge or sores, scrotum pain, or burning upon urination) within four weeks before the test date that did not result in an STI diagnosis. These patients were all non-White, predominantly men (80%), and diagnosed with AHI at STD clinics (80%).

We identified a strong interrelationship between gender, race, risk category, and STI co-infection. The prevalence of co-infections was lower in MSM (18%, PR=0.34, 95% CI 0.15, 0.76) and heterosexual men (35%, PR=0.67, 95% CI 0.31, 1.45) than women (53%, Table 5.3). Non-Whites were 3.9 times as likely to report a co-infection as Whites (95% CI 1.00, 15.10). Among MSM, all seven STI co-infections occurred in non-Whites (p=.03); this finding was consistent for heterosexual men as all six co-infections were in non-Whites, although only one White heterosexual man was in the study population. All four syphilis infections were detected in non-White men (3 MSM, one heterosexual). Among women, two of the three White women were co-infected and half (8 of 16) of the non-White women reported an STI co-infection.

The prevalence of STI co-infection was roughly equal among AHI patients detected at HIV counseling and testing (CTS) locations (35%, 95% CI 14.2, 61.7) and STD testing locations (36%, 95% CI 20.8, 53.8). However, AHI patients detected at other types of clinics (e.g., prison/jail, obstetrics/gynecology, outreach testing events) were less likely to have a co-infection identified (18.2%, 95% CI 5.2, 40.3). AHI patients with acute retroviral
symptoms at or before testing were also somewhat less likely to report STI co-infections (PR: 0.61 95% CI 0.31, 1.20), although the estimate is imprecise.

We found little variation in serum viral load at the time of testing (Table 5.4). The overall mean viral load at the time of testing was 5.2 log_{10} copies/ml. MSM had slightly higher mean log_{10}(HIV RNA) at testing compared to both heterosexual men and women (p=.36). Individuals at least 36 years of age had the highest mean HIV RNA (5.48 log_{10} copies/ml) compared to both those ≤25 years (5.0 log_{10} copies/ml) and those 26-35 years (5.1 log_{10} copies/ml). Non-Hispanic Whites had higher mean HIV RNA than non-Whites (p=.22). Individuals with STI co-infections had slightly lower mean HIV RNA at testing (4.9 log_{10} copies/ml) compared to those without co-infections (5.3 log_{10} copies/ml, p=.13).

We used logistic regression to assess the role of demographic and behavioral factors on the slope of log_{10}(HIV RNA) using a subset of 44 clients for which both the initial and confirmatory HIV RNA values were available (Table 5.4). The samples were collected an average of 16 days apart. We hypothesized that some factors would be predictive of an increasing HIV RNA slope, suggesting that the initial HIV test was performed before the peak viremia, whereas other factors may be associated with declining slopes suggesting that the test was performed near or after the HIV RNA peak. Factors associated with increasing HIV RNA slopes were younger age, non-White race, and symptoms at or before testing. In particular, non-Whites were almost twice as likely to have an increasing HIV RNA slope than Whites (OR=1.70, 95% CI 0.31, 11.99), and individuals with symptoms were about three times as likely to have an increasing RNA slope than those without symptoms (OR=2.94, 95% CI 0.67, 15.67). The only factor that was associated with a declining HIV RNA slope was testing location; compared to HIV CTS sites, both STD clinics and other testing sites were associated with a declining HIV RNA slope. Gender, risk behavior and STI co-infection had little relationship with HIV RNA slope.
DISCUSSION

In a large study evaluating STI co-infection during acute HIV infection, we demonstrated that STIs are commonly detected among people who very recently acquired HIV. As we have defined them, co-infections can represent three potential scenarios. First, co-infections may signify infections where HIV and an STI were acquired simultaneously in a co-transmission event. They can also represent prevalent infections present before HIV acquisition. Finally, co-infections can represent incident STI infections obtained after HIV acquisition. We believe that this latter possibility is unlikely, since most of the AHI patients were detected within several weeks of infection. Assuming that co-infection corresponds to the first two situations – co-acquisition events or prevalent STI infections – a causal role for STI infection in facilitating HIV transmission is possible, either by increasing the likelihood of HIV transmission from the source partner or by increasing the susceptibility of the index patient.

Although this study represents one of the largest examinations of persons with AHI, the sample size remains small and does not represent all HIV cases identified in NC. The STAT program routinely tests for HIV RNA in all samples from publicly funded clinics throughout the state but approximately 60% of NC HIV cases are detected outside of the public testing system. If people who test through the publicly-funded system are systematically different than those who test outside of the publicly-funded system, selection bias may be introduced. In addition, our modest sample size results in limited power to detect small differences and a decreased ability to control confounding in multivariable models. Despite these important shortcomings, our study is one of the largest to evaluate STI co-infection in the setting of acute HIV infection.

The high proportion of AHI patients with STI co-infections is surprising as our study was not limited to the STD clinic setting. Although about half of the AHI cases were identified in STD clinics, the proportion with co-infections from STD clinics (35%) was
roughly the same as those cases identified from HIV counseling and testing sites (36%). While the coding of testing site type is variable from county to county and therefore subject to misclassification, our results underscore the importance of STI symptoms as an indicator of AHI risk, even in non-STD clinic settings. Further, since co-infection rates do seem to vary by population and geography, high rates of co-infection in NC may suggest the importance of STIs on HIV transmission in the U.S. South, a region that has been disproportionately impacted by HIV and STIs.\textsuperscript{33, 34, 37, 38, 161}

Our most compelling finding was the variation in the prevalence of STI co-infection by gender, risk category, and race. MSM in our study were less likely to have a co-infection (18%) than heterosexual men (35%) or women (53%), and almost all (91%) co-infections occurred in non-Whites. These findings may help to explain the epidemiology of the NC HIV epidemic where racial disparities are dramatic – the HIV rate for non-Hispanic blacks is more than eight times greater than for non-Hispanic Whites – and heterosexual transmission is nearly as prominent as MSM transmission.\textsuperscript{33, 162} Heterosexual transmission of HIV in NC occurs largely among African-Americans; high rates of STIs in this group would facilitate HIV transmission and may be a necessary component of the HIV epidemic for this population.\textsuperscript{162} Although STIs were present among MSM AHI patients, they may not be necessary to maintain transmission of HIV in the context of higher-risk activities such as unprotected anal sex. These findings imply that the magnitude of the STI cofactor effect may be greater among heterosexuals than MSM in the South.

We hypothesized that STI co-infection may act as a biological cue to seek testing. In our study, 31% of AHI patients had an STI co-infection and 76% of AHI patients had either an STI co-infection or acute retroviral syndrome symptoms at or before testing (not shown), suggesting that these factors may motivate people to seek testing as does partner notification or provider referral. Although STI co-infection did not have an influence on the timing of testing during AHI, we did observe that the presence of acute retroviral symptoms
at or before testing was associated with testing before the peak viremia. We also identified testing location as a potential factor related to the timing of testing. AHI patients identified at CTS sites were more likely to have an increasing HIV RNA slope than those who tested at STD clinics or other types of sites. Individuals who seek testing at HIV CTS sites may differ in several important ways which could explain this result. CTS sites may attract a more risk-aware clientele, which is a key factor associated with testing. In this case, anxiety over the risk of exposure may be a key factor that drives HIV testing shortly after infection. AHI clients who are detected at STD clinics may present later, once acute HIV or STI symptoms appear. Given the inconsistent usage of testing site type across the state, additional examination of reason for testing and presenting location would help to elucidate these issues.

Despite data from our study and others that people with primary infection often present to medical care, the opportunity for diagnosis is frequently missed either by not recognizing acute retroviral syndrome or reliance on antibody testing alone. In the case of STI co-infections, we would expect infected individuals to present to care at symptom onset. However, standard antibody EIAs will often not detect HIV during this time (Figure 5.1). Gonorrhea and trichomoniasis, the most common STIs in our study population, also have two of the shortest incubation periods. It is therefore not unexpected that, in these cases, HIV was only detected with NAAT testing. This is an important limitation of strategies to offer HIV testing services to all STI patients, as HIV will often be missed in settings where testing is limited to standard third-generation EIAs.

We found little variation in viral load at the time of HIV testing. In particular, viral load was not higher among those with STI co-infections. During established HIV infection, both ulcerative and non-ulcerative STIs increase viral shedding from the genital tract, but their impact on blood plasma viral load is less well-defined. Among men-only or predominantly male studies, syphilis, genital ulcer disease, and herpes simplex virus (HSV)
shedding was significantly associated with increased plasma HIV RNA.\textsuperscript{168-171} Among women, plasma HIV RNA levels increased with gonorrhea infection and HSV lesions.\textsuperscript{172} In contrast, a study of men with urethritis found that while seminal plasma HIV levels were higher in the urethritis group than in among controls, plasma levels did not differ at baseline or after therapy.\textsuperscript{107} Given these previous reports, it is possible that systemic effects of STIs differ by gender and STI type and our sample size prohibited further stratification to explore these variations. It is also feasible that during AHI, STI-related plasma HIV RNA increases are overwhelmed in magnitude by the ramp-up viremia. The absence of a measurable effect of STIs on peak viremia could also suggest that STIs impact spread in acute transmission networks principally through susceptibility rather than infectiousness. However, we only had access to blood serum for HIV RNA quantification, whereas semen or genital secretions are preferable for inferences about transmissibility. In addition, our serum samples are often subject to testing and shipping delays, which may bias quantification of HIV RNA downward for both initial and confirmatory samples. Given our findings, further investigation of how STI infection during AHI impacts viral dynamics in the blood and genital tract is an area for future exploration.

The detection of AHI affords a tremendous public health opportunity to interrupt transmission and detect networks at high risk, but recognition requires a unique synergy of clinical suspicion, risk awareness, and appropriate diagnostic tests. We have shown that co-infection with STIs is common in a large sample of AHI patients in NC; antibody testing alone in many of these patients would have missed their HIV infection precisely when they present an increased transmission hazard to sexual partners. The frequency of STI co-infection among women and heterosexual men hints that STIs help to fuel the heterosexual HIV epidemic in the South.
TABLE 5.1. Demographic characteristics of 75 patients with acute HIV infection in North Carolina, November 1, 2002 through October 31, 2006.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Year of identification</strong></td>
<td></td>
</tr>
<tr>
<td>Year 3 (11/2004 – 10/2005)</td>
<td>19 (25.3)</td>
</tr>
<tr>
<td><strong>Gender and risk behavior</strong></td>
<td></td>
</tr>
<tr>
<td>Man who has sex with men</td>
<td>39 (52.0)</td>
</tr>
<tr>
<td>Heterosexual man</td>
<td>17 (22.7)</td>
</tr>
<tr>
<td>Female</td>
<td>19 (25.3)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
</tr>
<tr>
<td>≤ 25</td>
<td>33 (44.0)</td>
</tr>
<tr>
<td>26-35</td>
<td>20 (26.7)</td>
</tr>
<tr>
<td>36-45</td>
<td>12 (16.0)</td>
</tr>
<tr>
<td>≥46</td>
<td>10 (13.3)</td>
</tr>
<tr>
<td><strong>Race or ethnic background</strong></td>
<td></td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>20 (26.7)</td>
</tr>
<tr>
<td>White, Hispanic</td>
<td>4 (5.3)</td>
</tr>
<tr>
<td>Black</td>
<td>49 (65.3)</td>
</tr>
<tr>
<td>Native American/Alaskan Native</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td><strong>Testing Location</strong></td>
<td></td>
</tr>
<tr>
<td>HIV Counseling and testing site</td>
<td>17 (22.7)</td>
</tr>
<tr>
<td>STI Clinic</td>
<td>36 (48.0)</td>
</tr>
<tr>
<td>Other type of clinic</td>
<td>22 (29.3)</td>
</tr>
<tr>
<td><strong>History of injection drug use</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>No</td>
<td>73 (97.3)</td>
</tr>
<tr>
<td><strong>STI co-infection at diagnosis</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>23 (30.7)</td>
</tr>
<tr>
<td>No</td>
<td>52 (69.3)</td>
</tr>
<tr>
<td><strong>Symptoms at or before testing</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>45 (60.0)</td>
</tr>
<tr>
<td>No</td>
<td>30 (40.0)</td>
</tr>
</tbody>
</table>

¹. Percentages may not add to 100% due to rounding.
TABLE 5.2. Types of STI co-infections among 23 patients diagnosed with acute HIV and another STI in North Carolina, November 1, 2002 through October 31, 2006.

<table>
<thead>
<tr>
<th>STI Type¹</th>
<th>N  (%)</th>
<th>Men (n=13)</th>
<th>Women (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonorrhea</td>
<td>9 (39.1)</td>
<td>7 (53.8)</td>
<td>2 (20.0)</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>5 (21.7)</td>
<td>0 (0)</td>
<td>5 (50.0)</td>
</tr>
<tr>
<td>Syphilis</td>
<td>4 (17.4)</td>
<td>4 (30.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Herpes</td>
<td>3 (13.0)</td>
<td>2 (15.4)</td>
<td>1 (10.0)</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>3 (13.0)</td>
<td>1 (7.7)</td>
<td>2 (20.0)</td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td>3 (13.0)</td>
<td>---</td>
<td>3 (30.0)</td>
</tr>
<tr>
<td>Genital ulcer disease, unspecified</td>
<td>1 (4.3)</td>
<td>1 (7.7)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

¹. Five (21.7%) of 23 participants with an STI co-infection had more than one concurrent STI diagnosis.
**TABLE 5.3.** Frequency and prevalence of STI co-infections by demographic factors among 75 patients with acute HIV in North Carolina.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>STI co-infection at diagnosis&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Prevalence (95% CI)</th>
<th>Prevalence Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=23)</td>
<td>No (n=52)</td>
<td></td>
</tr>
<tr>
<td>Gender and risk behavior</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Man who has sex with men</td>
<td>7</td>
<td>32</td>
<td>18.0% (7.5, 33.5)</td>
</tr>
<tr>
<td>Heterosexual man</td>
<td>6</td>
<td>11</td>
<td>35.3% (14.2, 61.7)</td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td>9</td>
<td>52.6% (28.9, 75.6)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 25</td>
<td>13</td>
<td>20</td>
<td>39.4% (22.9, 57.9)</td>
</tr>
<tr>
<td>26-35</td>
<td>4</td>
<td>16</td>
<td>20.0% (5.7, 43.7)</td>
</tr>
<tr>
<td>≥36</td>
<td>6</td>
<td>16</td>
<td>27.3% (10.7, 50.3)</td>
</tr>
<tr>
<td>Race or ethnic background</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>2</td>
<td>18</td>
<td>10.0% (1.2, 31.7)</td>
</tr>
<tr>
<td>Non-White</td>
<td>21</td>
<td>33</td>
<td>38.9% (25.9, 53.1)</td>
</tr>
<tr>
<td>Testing Location</td>
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<tr>
<td>HIV Counseling and Testing</td>
<td>6</td>
<td>11</td>
<td>35.3% (14.2, 61.7)</td>
</tr>
<tr>
<td>STI Clinic</td>
<td>13</td>
<td>23</td>
<td>36.1% (20.8, 53.8)</td>
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<tr>
<td>Other type of clinic</td>
<td>4</td>
<td>18</td>
<td>18.2% (5.2, 40.3)</td>
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<tr>
<td>History of injection drug use</td>
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<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>1</td>
<td>1</td>
<td>50.0% (1.3, 98.7)</td>
</tr>
<tr>
<td>No</td>
<td>22</td>
<td>51</td>
<td>30.1% (19.9, 42.0)</td>
</tr>
<tr>
<td>Symptoms at or before testing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11</td>
<td>34</td>
<td>24.4% (12.9, 39.5)</td>
</tr>
<tr>
<td>No</td>
<td>12</td>
<td>18</td>
<td>40.0% (22.7, 59.4)</td>
</tr>
</tbody>
</table>

1. Numbers may not add to 75 due to missing data.
TABLE 5.4. Mean serum viral load (log_{10}copies/ml) at the time of testing and logistic regression models of HIV RNA slope among patients with acute HIV in North Carolina.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean HIV RNA (log_{10} copies/ml, n=74)</th>
<th>p-value¹</th>
<th>Logistic Models of HIV RNA slope²</th>
<th>Mean change³</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender and risk behavior</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Man who has sex with men</td>
<td>5.4 (5.0, 5.7)</td>
<td>0.36</td>
<td>-0.46</td>
<td>1.20 (0.29, 4.93)</td>
<td>0.96</td>
<td></td>
</tr>
<tr>
<td>Heterosexual man</td>
<td>4.9 (4.3, 5.6)</td>
<td></td>
<td>-0.24</td>
<td>1.20 (0.23, 6.39)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>5.1 (4.6, 5.6)</td>
<td></td>
<td>-0.47</td>
<td>Referent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 25</td>
<td>5.0 (4.7, 5.4)</td>
<td>0.29</td>
<td>-0.05</td>
<td>3.33 (0.53, 20.91)</td>
<td>0.26</td>
<td></td>
</tr>
<tr>
<td>26-35</td>
<td>5.1 (4.6, 5.7)</td>
<td></td>
<td>-0.68</td>
<td>1.25 (0.19, 8.44)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 36</td>
<td>5.5 (5.0, 5.9)</td>
<td></td>
<td>-0.71</td>
<td>Referent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race or ethnic background</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>5.4 (5.0, 5.9)</td>
<td>0.22</td>
<td>-0.87</td>
<td>Referent</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>Non-White</td>
<td>5.1 (4.8, 5.4)</td>
<td></td>
<td>-0.22</td>
<td>1.72 (0.38, 7.85)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testing Location</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV Counseling and Testing</td>
<td>5.0 (4.5, 5.5)</td>
<td>0.57</td>
<td>0.61</td>
<td>Referent</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>STI Clinic</td>
<td>5.3 (4.9, 5.7)</td>
<td></td>
<td>-0.72</td>
<td>0.19 (0.04, 0.94)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other type of clinic</td>
<td>5.1 (4.7, 5.6)</td>
<td></td>
<td>-0.81</td>
<td>0.36 (0.07, 1.88)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STI co-infection at diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4.9 (4.4, 5.4)</td>
<td>0.13</td>
<td>-0.33</td>
<td>1.30 (0.36, 4.72)</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>5.3 (5.0, 5.6)</td>
<td></td>
<td>-0.45</td>
<td>Referent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms at or before testing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5.3 (5.0, 5.6)</td>
<td>0.41</td>
<td>-0.18</td>
<td>3.02 (0.78, 11.66)</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>5.1 (4.6, 5.5)</td>
<td></td>
<td>-0.78</td>
<td>Referent</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. P-values from one way analysis of variance (ANOVA)
2. 44 patients with AHI had both initial and confirmatory values available for analysis. Seventeen patients (38.6%) had increasing viral loads between the initial and confirmatory samples. Bivariate models were constructed with the difference between the log-transformed initial and confirmatory viral load values as the response variable (1=increasing slope, 0=decreasing slope).
3. Mean change in HIV RNA (log_{10} copies/ml) from the initial and confirmatory specimens
FIGURE 5.1. Potential impact of STI co-infection on the detection of HIV infection. At the time of symptom onset of several common STIs, HIV would be missed by standard 2nd and 3rd generation EIAs. The horizontal timeline represents the time elapsed after co-acquisition of HIV and a concurrent STI. Vertical boxes represent the approximate times when HIV could be detected by RNA, 4th generation antigen/antibody enzyme immunoassays (EIA), and 3rd generation EIA tests. Horizontal bars below the timeline illustrate the approximate incubation periods for common STIs.134-136, 139, 166, 173
CHAPTER SIX: Social Support and Delays Seeking Care after HIV Diagnosis, North Carolina, 2000-2006

ABSTRACT

Background: Many adults enter primary care late in the course of HIV infection, countering the clinical benefits of timely HIV services and missing opportunities for risk reduction. Our objective was to determine if perceived social support was associated with delay entering care after an HIV diagnosis. Methods: Two hundred sixteen patients receiving primary care at a large, university-based HIV outpatient clinic in North Carolina were included in the study. Dimensions of functional social support (emotional/informational, tangible, affectionate and positive social interaction) were quantified with a modified Medical Outcomes Study Social Support Scale and included in proportional hazard models to determine their effect on delays seeking care. Results: The median delay between diagnosis and entry to primary care was 5.9 months. Levels of social support were high but only positive social interaction was associated with delayed presentation in adjusted models. The effect of low perceived positive social interaction on the time to initiation of primary care differed by history of alcoholism (no history of alcoholism, hazard ratio (HR): 1.43, 95% confidence interval (CI): 0.88, 2.34; history of alcoholism, HR: 0.71, 95% CI: 0.40, 1.28). Conclusions: Ensuring timely access to HIV care remains a challenge in the southeastern United States. Affectionate, tangible, and emotional/informational social support were not associated with the time from diagnosis to care. The presence of positive social interaction may be an important factor influencing care seeking behavior after diagnosis.
INTRODUCTION

Early presentation for medical care among HIV infected persons can improve the length and quality of life by providing access to antiretroviral drugs and prophylactic treatment for opportunistic infections. Further, HIV testing and counseling and knowledge of one’s serostatus has been shown to reduce high-risk behavior, thereby reducing transmission to others. Despite these benefits, many adults enter care late in the course of HIV infection, countering the benefits of timely access to HIV services and missing opportunities for risk reduction. Consequently, linking HIV positive persons to high-quality care and prevention services has been identified as a priority of the U.S. Centers for Disease Control and Prevention (CDC).

The process of an HIV-infected individual presenting to primary care can be divided into two meaningful time periods: 1) the time between acquisition of infection and testing; and 2) the time between testing and presentation to care. Delayed testing is common in the United States - 40% of those tested in 2004 were diagnosed with AIDS less than one year after the initial HIV diagnosis, a figure that has remained relatively stable since 1994. In contrast, delayed initiation of medical care after diagnosis is less well-characterized. Median reported delays from HIV diagnosis to presentation for care range from 30 days to over a year. Demographics, health insurance status, injection drug use, and the testing and counseling history are associated with delayed presentation, but the role of psychosocial factors, such as perceived social support, on care-seeking behavior have not been thoroughly evaluated.

Social support can be subdivided into structural and functional aspects of support. Structural support includes the size, type, contact, and density of social networks and ties. Functional support represents the capacity of relationships to fulfill particular functions, such as providing affection, a sense of belonging, or material aid. Together, structural and functional support describes the types of resources we receive from other people.
support can influence health directly by influencing the adoption of healthy (or unhealthy) behaviors and adherence to social norms.\textsuperscript{111} It can also influence health indirectly by buffering the pathogenic effects of stressful events through the processes of stress perception and coping.\textsuperscript{117} Social support may improve coping with HIV and quality of life, improve adherence among patients on highly active antiretroviral therapy (HAART), and improve patient retention in care.\textsuperscript{22-26, 126} Therefore, HIV positive individuals with higher levels of perceived social support may seek medical care earlier than those with less perceived social support. Towards this end, our objective was to describe levels of support available to patients in a Southeastern HIV clinic and determine if social support was associated with delays between HIV diagnosis and presentation for care.

METHODS

Study Population

The source population for the study was the University of North Carolina at Chapel Hill Infectious Disease (UNC ID) Clinic. As a large, university-based medical center, the Clinic follows approximately 1,300 HIV infected patients per year and provides comprehensive HIV primary care services. Patients in the clinic are predominantly from central and eastern North Carolina, although patients from all 100 counties and surrounding states are accepted for care.\textsuperscript{145} For this study, we conducted a secondary data analysis of the UNC Clinical and Socio-Demographic Survey, originally designed to collect sociodemographic and behavioral data not available in medical records. The primary goal of the analysis was to describe the effect of social support on the time between HIV diagnosis and presentation for HIV care.

Recruitment and Data Collection

Patients receiving care at the UNC Infectious Diseases Clinic who are at least 18 years of age, English speaking, and able to provide written informed consent were eligible to
complete the survey. Potential participants were identified and approached for participation by trained research assistants in the clinic. Consenting patients were interviewed in a quiet and private room, typically after their clinic visit. Data from the interviews were entered into a Microsoft Access database housed on a secured server.

**Measurements**

The main outcome variable is the time (months) from HIV diagnosis until entry to HIV care. The date of HIV diagnosis was obtained from the NC Department of Health and Human Services HIV/AIDS Reporting System. In cases where a match was not obtained with state records (n=36) or the NC reporting system date was after the diagnosis date in the medical record (n=115), the date of diagnosis from the medical record was used. In five cases, only the self-reported date of diagnosis was available. To correctly capture the date of entry to HIV primary care, as opposed to general health care visits, we defined entry to care as the first outpatient visit to the UNC ID clinic for patients who only received care at UNC. For patients who received care at other institutions, we defined entry to care as the earliest non-hospitalized date of CD4 T-lymphocyte cell count, HIV RNA, antiretroviral therapy initiation, AIDS-defining clinical condition, or outpatient visit. In cases where a hospitalization was the first HIV–related care, we accepted the date of the first CD4 T-lymphocyte cell count as the entry to care date. Patients with only self-reported dates of entry to care were excluded from the analysis.

As the aim of our study was to determine factors associated with the time between diagnosis and care, we excluded patients whose clinical presentation prompted testing and entry to care. These people represent those who significantly delayed testing and the onset of symptoms instigated rapid linkage to primary care. Methodologically, considering delayed testing and delayed presentation to care as distinct outcomes, with overlapping etiologies, is necessary to prevent mixing the effects of late testing with delayed care. We assumed that
patients with less than three weeks between diagnosis and entry to care with an AIDS defining illness before, at, or 45 days after diagnosis represented people who were diagnosed due to AIDS related illnesses, and they were excluded from Cox proportional hazards models (n=18). We reviewed medical records of patients with less than three weeks between diagnosis and entry to care and CD4 cell counts ≤200 cells/mm$^3$ without AIDS defining illnesses; those diagnosed as inpatients or diagnosed because of illness were excluded (n=6). We evaluated the time from diagnosis to entry to care for 10 years after diagnosis; patients not in care at this time were censored.

The exposure of interest, perceived social support, was quantified with a modified version of the Medical Outcomes Study Social Support Scale (MOS-SSS). The MOS-SSS is a brief, multidimensional, 20-item survey. Two items measure structural support and the remaining 18 items measure four functional dimensions of social support: emotional/informational, tangible, affectionate, and positive social interaction.$^{27}$ The modified version used in our study contained items to measure structural support and 13 of the 18 items to measure functional support (four of four tangible indicators, three of three affectionate indicators, four of eight emotional/informational indicators, and one of four positive social interaction indicators plus an additional positive social interaction indicator evaluated but not included in the MOS-SSS). We included participants who completed at least 80% of the MOS-SSS.

Consistent with the methods for the original MOS-SSS, structural social support is measured by overall network size, or the summation of the number of close friends and relatives. Responses to each functional support indicator on the 5-point Likert scale of responses are assigned numeric values (1: Support type is never present – 5: Support type is always present) and a composite average number is generated for each participant representing the four dimensions of functional social support. This average is transformed so that the scores range from 20 to 100.
Confirmatory Factor Analysis

As our scale was modified from the original 19 item MOS-SSS scale, we used confirmatory factor analysis (CFA) to determine the validity of the model in our overall study population, before exclusions. We evaluated model fit based on a CFA model with 332 patient records, 13 indicators, four latent variables (emotional/informational, affectionate, tangible, and positive interaction domains of functional social support), and a robust weighted least squares fitting function. CFA analyses were done with Mplus software.\textsuperscript{149}

Statistical Analysis

Eight participants had missing data in the social support scale. We compared the results of complete case analysis, mean imputation, imputing the high and low values, and conditional mean imputation and found little difference in the resulting scores. For the analyses presented here, we imputed missing values with the mean of known values for the variable.

We first performed basic descriptive analyses, including calculating means, standard deviations, medians, and frequencies of the exposure and covariates. In bivariable analyses, we examined the effect of social support on the time to seeking HIV care using Cox proportional hazards regression. We excluded factors from Cox models that violated the assumption of temporality, for example, events or measurements that took place after HIV diagnosis (e.g. number of times moved since diagnosis, CD4 cell count at entry). We assumed that other factors could be assumed to be valid at the time of diagnosis despite being measured after care was initiated, such as income, ever being homeless, or ever spending time in prison. The proportional hazards assumption was evaluated for all exposures and covariates graphically with the use of a log(-log(S(t))) curve and was tested by adding an interaction with time to the model (Cox test). If necessary, the proportional hazards assumption was relaxed with a stratified mode or with categorical or continuous
interactions with time. Equality of survival functions was tested with the log-rank test. We present hazard ratios (HR) and 95% confidence intervals (CI).

In multivariable analysis, we used a manual, backward, change-in-estimate model building strategy. Measurements or events that took place after HIV diagnosis were excluded from Cox models. Potential effect measure modification was assessed by fitting appropriate product interaction terms and comparing models with and without the interaction terms with the likelihood ratio test. Potential confounding variables were assessed by examination of the change in social support estimate; we set a cutpoint of a 10% change in the parameter estimate or more to classify confounding. We first constructed multivariable models for each of our four functional support domains, and then created a single multivariable model with all four levels of social support and relevant confounding and modifying covariates.

Human Subjects Protection

All participants in the study provided written informed consent to participate in the interview and HIPAA authorization to access medical information. This study was approved by the UNC Institutional Review Board.

RESULTS

From July 2000 to June 2006, 216 patients completed the interview and met the criteria for inclusion in the analysis. Women comprised 40% of the population, heterosexual men represented about 26% of the population, and men who have sex with men (MSM) were 33% of the population (Table 6.1). Seventy percent of the population was Black; the median age was 36 years at diagnosis and 43 years at the time of interview. At entry to care, the median CD4 T-lymphocyte cell count was 346 cells/mm³ (range: 4-1,428). Ever having spent time in prison was common (30.2%), as was ever having been homeless or
living on the streets (28.7%), ever having a drinking problem (34.7%), ever having used illegal drugs on a regular basis (70.1%), and ever having sex for drugs or money (27.4%). Most (67.4%) patients reported having a main partner or spouse and less than two sexual partners in the previous year (72.7%).

**Confirmatory Factor Analysis**

The validity of the four factor functional social support model in our sample was evaluated with confirmatory factor analysis. The overall goodness-of-fit indices suggested that the four factor CFA model fit the data reasonably well: $\chi^2(30)=108.1$, $p<.01$, root mean square error of approximation (RMSEA) 0.089, comparative fit index (CFI) 0.969, and Tucker-Lewis Index (TLI) 0.992. All freely estimated parameters were statistically significant; standardized factor loadings ranged from (0.56-0.97), and indicator reliability ranged from 0.32 to 0.92 with eight indicators having reliabilities greater than 0.7. All indicator reliability estimates were significant ($p<.01$). We allowed for correlated errors between two similarly worded emotional/informational indicators. The reliability of the four latent variables was 0.72 for emotional/informational support, 0.83 for positive social interaction, 0.86 for tangible support and 0.90 for affectionate support. Cronbach’s alpha indicated that the scale was internally consistent (0.93). Higher order factor analysis did not support the creation of a single construct for functional social support.

**Social Support**

The clinic population had high levels of social support. The median network size of close friends and relatives (structural social support) was six people (range: 0-1,030). Functional support scores were skewed and clustered near levels corresponding to the level of support being present “most to all of the time.” Levels of affectionate support were the highest (median score=93.3, mean=83.7), followed by tangible support (median=85.0, mean=79.8),
emotional/information support (median=80.0, mean=78.8) and positive social interaction (median=80.0, mean=71.5, Table 6.2). Although the median network size was the same for patients with and without a spouse or main partner, those with a spouse or main partner reported higher median levels of affectionate support (p<.01), positive social interaction (p=.08), and emotional/information support (p=.02).

**Delays between Diagnosis and HIV Care**

The median delay between diagnosis and entry to care was 5.9 months (inter-quartile range: 1.8 to 38.3 months). Although 57% of patients initiated care within the year after diagnosis, only 12.5% of patients initiated care in the second year. Overall, 69% were in care by two years post diagnosis, 74% were in care by three years, and 79% by four years (Figure 6.1). Thirty-eight patients (17.6%) delayed entering HIV care for five or more years.

Twenty-eight patients (13%) had an AIDS defining illness at or before entering HIV care. Of these patients, *Pneumocystis carinii* pneumonia was the most common diagnosis (39%) followed by candidiasis (18%). Half of patients entered care within a month following an AIDS defining illness diagnosis; however, seven of the 28 patients (25%) with an AIDS defining illness at or before HIV diagnosis delayed HIV care longer than one year.

In unadjusted analyses, the time to presentation varied little by functional social support (Figure 6.2). Across all four domains of functional social support, those with levels of support available “less than most of the time” had shorter median times to care than those with the level of support available “most to all of the time,” although these results were not statistically significant. In multivariable analyses, tangible, emotional/informational, and affectionate support remained unassociated with the time between diagnosis and entry to care (Table 6.3). The effect of positive social interaction on the outcome differed by a history of alcoholism. In those who had ever had a drinking problem, those with lower levels of positive social interaction had about 0.7 times the hazard of entering care over time.
compared to those with the highest levels of positive social interaction. However, those without a history of a drinking problem and who had positive social interactions present less than “most of the time” had about 1.4 times the hazard of entering care over time than those with positive social interactions present “most to all of the time” (HR: 1.43, 95% CI: 0.88, 2.34).

DISCUSSION

Successful efforts to reduce HIV-related morbidity and mortality and improve quality of life are contingent on the timely receipt of primary care services. Although highly active antiretroviral therapy has been the cornerstone of HIV care in the United States since its widespread adoption in the late 1990’s, the survival benefit of HAART is strongly related to baseline immunosuppression. In addition to clinical services, patients in care benefit from a host of social services which can improve the maintenance of care and adherance to therapy, as well as prevention programs to reduce the frequency of transmission to partners. Despite these benefits, prompt linkage to primary care is not always possible. Recently diagnosed individuals must cope with discovering their status, notify at-risk partners, contemplate disclosure to friends and family members, confront fears about morbidity and mortality, and initiate, establish, and adhere to medical care. It is therefore not surprising that some patients enter care quickly whereas others remain unconnected with the health care system for months or years after diagnosis.

The median delay of six months between diagnosis and primary care we report is slightly longer than other reports. Studies in New England, Arkansas, and Alabama each reported median delays of three months or less. This inconsistency may be due to efforts we took to enhance the validity of our data or because our clinic serves a different patient population. For example, we obtained dates of diagnosis from state surveillance records instead of self-reported estimates alone. We also excluded patients from the
analysis with both very short times to care and who were likely tested due to AIDS-related illness to prevent biasing our results by including a population that entered care due to symptoms and not due to testing results. Considering the proportion of people who had spent time in prison, been homeless, or ever had transactional sex, the delay in presentation for care we observe may reflect a patient population that is particularly disenfranchised from the health care system.

Levels of social support were very high in our study. Compared to both the ambulatory patient sample in which the scale was developed and a separate study at an urban hospital-based HIV clinic, patients in our study had higher median levels of tangible, affectionate, and emotional/informational support, despite having similar median network sizes. Levels of positive interaction were similar across studies, suggesting that health care systems may have little impact on creating a sense of social belonging. In our study, each subscale of functional support was available most to all of the time for the majority of patients (60.6%-81.5%). Tangible and emotional/informational support needs, the types of functional support most directly modifiable by HIV primary care and social services, were not being met for only 12% and 7% of the study sample, respectively. Consistent with previous reports, we found that those with a spouse or main partner reported higher median levels of affectionate support, emotional/informational support, and positive social interaction, highlighting that quality, not quantity, of support is most meaningful.

Tangible, affectionate, and emotional/informational support did not have an effect on delays between HIV diagnosis and primary care in this study. This observation is somewhat unexpected, given that the presence of some types of social support has been associated with shorter delays, such as having a living mother or having a spouse or partner. In addition, social support has been found to improve adherence in most studies. However, many of these studies did not use a validated scale – it is recommended that social support should be quantified with at least two of the three main aspects of social
support: 1) existence and quantity; 2) aspects of network structure; and 3) functional content and quality of relationships. Further, the high levels of support we observe may mask any true effect on the time to care. The one study that assessed social support using the MOS-SSS found no relationship between functional social support and the time from diagnosis to care.

In contrast to the null findings for tangible, affectionate, and emotional/informational support, we found a moderate association between positive social interaction and care initiation. Among those with a history of alcoholism, those with lower levels of positive social interaction were slightly less likely to enter care than persons with high levels of positive social interaction. However, persons who had never had a drinking problem, but had very little positive social interaction entered care about 40% more rapidly than those with the most positive social interaction. This small group (n=22) of persons was less likely to have ever been homeless (18 vs. 30%), spent time in prison (23 vs. 31%), had transactional sex (9 vs. 30%), or have a main partner or spouse (50 vs. 69%) than the rest of the study sample. This finding may suggest that some socially isolated individuals who do not abuse alcohol access care rapidly after diagnosis, perhaps to meet their support needs. They may have fewer outlets for distraction from their diagnosis than others, such as social interaction and substance abuse.

Our study, and other similar clinic based studies of delays between diagnosis and care, must be cautious against over interpretation of data with methodological limitations. As patients must be in care to participate in the study, we do not observe the person-time of patients who delay entering care past the study period. This truncation represents an important selection bias which is most apparent by examining the effect of year on delays after diagnosis. Later diagnoses (in calendar time) will always appear to be associated with shorter delays. Some investigators have accounted for this bias with carefully selected risk periods, and in our analysis we included year of diagnosis in the multivariable analysis.
addition, our analysis did not support the creation of linear social support terms, so we may have measurement error in our broad categories of perceived social support. Finally, as patients were interviewed once they were in care, we do not know if the levels of social support we observed were present at the time of diagnosis. An optimally designed study to answer questions about delayed presentation to care would follow a cohort of newly diagnosed individuals over time, but as Samet et al. points out, this study design may be biased by the Hawthorne effect and would require a lengthy follow-up period.\textsuperscript{19} However, as CDC recommendations for the adoption of routine HIV screening in all health care settings are implemented, effective linkage to HIV care will likely be a marker of program success, highlighting the need to understand and improve the process of care initiation.\textsuperscript{49}

We have found that ensuring timely access to HIV care remains a challenge in the southeastern U.S. Although much remains to be learned about care-seeking behavior after HIV diagnosis, our findings suggest that social belonging and social interaction are important elements of the decision to initiate care. It is unknown if tangible, affectionate, and emotional/informational support are important after the initiation of primary care, such as on the maintenance of care and adherence to therapy. Additional research on how to translate this information to practice could have beneficial outcomes for both the patient and the community.
TABLE 6.1. Sociodemographic, behavioral, and clinical characteristics of 216 patients with HIV infection in North Carolina, July 2000-June 2006. (Table continues on next page)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SOCIODEMOGRAPHIC CHARACTERISTICS</strong></td>
<td></td>
</tr>
<tr>
<td>Gender and risk behavior</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>87 (40.3)</td>
</tr>
<tr>
<td>Man who has sex with men / bisexual</td>
<td>72 (33.3)</td>
</tr>
<tr>
<td>Heterosexual man</td>
<td>57 (26.4)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>152 (70.4)</td>
</tr>
<tr>
<td>White</td>
<td>46 (21.3)</td>
</tr>
<tr>
<td>Other</td>
<td>18 (8.3)</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td></td>
</tr>
<tr>
<td>≤30</td>
<td>23 (10.9)</td>
</tr>
<tr>
<td>31-40</td>
<td>145 (68.7)</td>
</tr>
<tr>
<td>41 or greater</td>
<td>43 (20.4)</td>
</tr>
<tr>
<td>Year of Diagnosis</td>
<td></td>
</tr>
<tr>
<td>1981-1989</td>
<td>24 (11.1)</td>
</tr>
<tr>
<td>1990-1994</td>
<td>71 (32.9)</td>
</tr>
<tr>
<td>1995-1999</td>
<td>77 (35.6)</td>
</tr>
<tr>
<td>2000-2005</td>
<td>44 (20.4)</td>
</tr>
<tr>
<td>Education (highest completed)</td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>66 (30.6)</td>
</tr>
<tr>
<td>High school graduate or GED</td>
<td>74 (34.3)</td>
</tr>
<tr>
<td>Some college</td>
<td>47 (21.8)</td>
</tr>
<tr>
<td>College graduate or higher</td>
<td>23 (10.7)</td>
</tr>
<tr>
<td>Vocational/technical school</td>
<td>6 (2.8)</td>
</tr>
<tr>
<td>Annual income</td>
<td></td>
</tr>
<tr>
<td>&lt;$5,000</td>
<td>54 (25.4)</td>
</tr>
<tr>
<td>$5,000 to &lt;$10,000</td>
<td>88 (41.3)</td>
</tr>
<tr>
<td>$10,000 to &lt;$30,000</td>
<td>48 (22.5)</td>
</tr>
<tr>
<td>≥$30,000</td>
<td>23 (10.8)</td>
</tr>
<tr>
<td><strong>CLINICAL CHARACTERISTICS</strong></td>
<td></td>
</tr>
<tr>
<td>CD4 T-cell count at entry to care$^2$</td>
<td></td>
</tr>
<tr>
<td>≤200 cells/mm$^3$</td>
<td>71 (33.5)</td>
</tr>
<tr>
<td>201-350 cells/mm$^3$</td>
<td>36 (17.0)</td>
</tr>
<tr>
<td>&gt;350 cells/mm$^3$</td>
<td>105 (49.5)</td>
</tr>
<tr>
<td>AIDS defining illness at or before entry to care$^2$</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>28 (13.0)</td>
</tr>
<tr>
<td>No</td>
<td>188 (87.0)</td>
</tr>
<tr>
<td>Characteristic</td>
<td>N (%)</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Goes to other clinics or doctors for general health care</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>79 (36.9)</td>
</tr>
<tr>
<td>No</td>
<td>135 (63.1)</td>
</tr>
<tr>
<td><strong>SOCIAL SUPPORT</strong></td>
<td></td>
</tr>
<tr>
<td>Structural Social Support (network size)</td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>66 (30.8)</td>
</tr>
<tr>
<td>4-7</td>
<td>58 (27.1)</td>
</tr>
<tr>
<td>8-12</td>
<td>40 (18.7)</td>
</tr>
<tr>
<td>13 or more</td>
<td>50 (23.4)</td>
</tr>
<tr>
<td>Positive Social Interaction</td>
<td></td>
</tr>
<tr>
<td>Most to all of the time</td>
<td>131 (60.6)</td>
</tr>
<tr>
<td>Sometimes</td>
<td>49 (22.7)</td>
</tr>
<tr>
<td>None to little of the time</td>
<td>36 (16.7)</td>
</tr>
<tr>
<td>Tangible Support</td>
<td></td>
</tr>
<tr>
<td>Most to all of the time</td>
<td>167 (77.3)</td>
</tr>
<tr>
<td>Sometimes</td>
<td>23 (10.6)</td>
</tr>
<tr>
<td>None to little of the time</td>
<td>26 (12.0)</td>
</tr>
<tr>
<td>Emotional / Informational Support</td>
<td></td>
</tr>
<tr>
<td>Most to all of the time</td>
<td>163 (75.5)</td>
</tr>
<tr>
<td>Sometimes</td>
<td>37 (17.1)</td>
</tr>
<tr>
<td>None to little of the time</td>
<td>16 (7.4)</td>
</tr>
<tr>
<td>Affectionate Support</td>
<td></td>
</tr>
<tr>
<td>Most to all of the time</td>
<td>176 (81.5)</td>
</tr>
<tr>
<td>Sometimes</td>
<td>17 (7.9)</td>
</tr>
<tr>
<td>None to little of the time</td>
<td>23 (10.6)</td>
</tr>
</tbody>
</table>

1. Percentages may not add to 100 due to rounding. Numbers may not add to 216 due to missing data.

2. These factors were not included in Cox proportionate hazards models as they could not reasonably be assumed to be valid at the time of HIV diagnosis.
TABLE 6.2. Functional social support definition and scores from the modified MOS Social Support Survey among HIV clinic patients, North Carolina

<table>
<thead>
<tr>
<th>Functional Support Type</th>
<th>Definition</th>
<th>Scale Items</th>
<th>Mean Score (SD)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Social Interaction</td>
<td>Shared social activities, a sense of social belonging</td>
<td>Someone to have a good time or hang with  Someone to do things with and help you get your mind off things</td>
<td>71.5 (23.3)</td>
</tr>
<tr>
<td>Tangible Support</td>
<td>Provision of material aid</td>
<td>Someone to help you if you were confined to bed  Someone to take you to the doctor if you needed it  Someone to prepare your meals if you were unable to  Someone to help with daily chores if you were sick</td>
<td>79.8 (21.9)</td>
</tr>
<tr>
<td>Emotional / Information Support</td>
<td>Expressions of comfort and caring, provision of advice and guidance</td>
<td>Someone to give you good advice about a crisis  Someone’s whose advice you want  Someone you can count on to listen when you need to talk  Someone to share your most private worries and fear with</td>
<td>78.8 (19.4)</td>
</tr>
<tr>
<td>Affectionate Support</td>
<td>Expressions of love and affection</td>
<td>Someone who shows you love and affection  Someone who hugs you  Someone to love and make you feel wanted</td>
<td>83.7 (22.2)</td>
</tr>
</tbody>
</table>

**Overall Functional Support**

| 79.1 (18.5) |

1. See references ²⁷, ¹¹²

2. Functional social support scores range from 20 (low) to 100 (high).
FIGURE 6.1. Distribution of time from HIV diagnosis to the initiation of HIV care among 216 patients in North Carolina.
FIGURE 6.2. Kaplan-Meier curves of the percent of newly diagnosed patients in care over time by functional social support type. A) Affectionate support, log-rank p=.57; B) Positive social interaction, log-rank p=.84; C) Emotional / Informational support, log-rank p=.31; D) Tangible support, log-rank p=.83.
TABLE 6.3. Multivariable proportional hazards models of functional social support and time to presentation for medical care after HIV diagnosis.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median time from diagnosis to care, months (95% CI)</th>
<th>Unadjusted Hazard Ratio (95% CI)</th>
<th>Adjusted Hazard Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tangible Support</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most to all of the time</td>
<td>6.35 (4.28, 12.40)</td>
<td>Referent</td>
<td>Referent</td>
<td>0.80</td>
</tr>
<tr>
<td>None of the time or sometimes</td>
<td>4.01 (2.14, 20.23)</td>
<td>0.97 (0.69, 1.35)</td>
<td>0.93 (0.53, 1.63)</td>
<td></td>
</tr>
<tr>
<td><strong>Emotional / Informational Support</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most to all of the time</td>
<td>7.14 (4.90, 13.98)</td>
<td>Referent</td>
<td>Referent</td>
<td>0.44</td>
</tr>
<tr>
<td>None of the time or sometimes</td>
<td>3.55 (2.30, 9.84)</td>
<td>1.18 (0.86, 1.62)</td>
<td>1.23 (0.73, 2.09)</td>
<td></td>
</tr>
<tr>
<td><strong>Affectionate Support</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most to all of the time</td>
<td>6.20 (4.28, 11.55)</td>
<td>Referent</td>
<td>Referent</td>
<td>0.87</td>
</tr>
<tr>
<td>None of the time or sometimes</td>
<td>4.87 (2.30, 20.49)</td>
<td>0.90 (0.63, 1.29)</td>
<td>1.06 (0.56, 1.98)</td>
<td></td>
</tr>
<tr>
<td><strong>Positive Social Interaction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Had a drinking problem (ever)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most to all of the time</td>
<td>6.97 (4.15, 17.50)</td>
<td>Referent</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>None of the time or sometimes</td>
<td>21.27 (17.14, 60.76)</td>
<td>0.67 (0.42, 1.08)</td>
<td>0.71 (0.40, 1.28)</td>
<td>0.10</td>
</tr>
<tr>
<td>Never had a drinking problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most to all of the time</td>
<td>5.94 (3.03, 13.98)</td>
<td>Referent</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>None of the time or sometimes</td>
<td>3.22 (2.14, 5.20)</td>
<td>1.54 (1.08, 2.19)</td>
<td>1.43 (0.88, 2.34)</td>
<td></td>
</tr>
</tbody>
</table>

1. Confidence interval

2. Adjusted for gender and risk behavior, year of diagnosis, income, ever used drugs on a regular basis, ever had a drinking problem (main effect) and number of household members.

3. Represents the likelihood ratio test for the $\beta$ coefficient(s) equaling 0 in the adjusted model.
CHAPTER SEVEN: Barriers and Facilitators to HIV Testing and Primary Care: Narratives of People with Advanced HIV in the Southeast

ABSTRACT

Persons with unrecognized HIV infection forgo timely clinical intervention and may unknowingly transmit HIV to partners. However, in the United States, unrecognized infection and late diagnosis are common. To understand barriers and facilitators to HIV testing and care, we conducted a qualitative study of 24 HIV infected persons attending a Southeastern HIV clinic who presented with clinically advanced illness. The primary barrier to HIV testing prior to diagnosis was perception of risk; consequently, most participants were diagnosed after the onset of clinical symptoms. While most patients were anxious to initiate care rapidly after diagnosis, some felt frustrated by the passive process of connecting to specialty care. The first visit with an HIV care provider was identified as critical in the coping process for many patients. Implications for the implementation of recent CDC HIV routine screening guidelines are discussed.

INTRODUCTION

Unrecognized HIV infection has important public health consequences. In addition to limiting the benefits of early medical care including antiretroviral therapy and prophylaxis for opportunistic infections, persons with unrecognized infection may unknowingly transmit HIV to partners.\textsuperscript{41, 42} Despite these benefits, unrecognized infection and consequently, late diagnosis, are common among HIV infected adults. In the United States, 40% of those
tested in 2004 were diagnosed with AIDS less than one year after the initial HIV diagnosis.\textsuperscript{33, 62} Further, approximately 25\% of all adults living with HIV/AIDS in the U.S. do not know their status, and as many as one-third may not be receiving care.\textsuperscript{167} Even more concerning is that the severity of immune suppression at first presentation may be worsening among some groups.\textsuperscript{177} Promoting earlier detection of HIV was the focus of recent Centers for Disease Control (CDC) guidelines for the adoption of routine, voluntary HIV screening for patients in all health care settings.\textsuperscript{49}

Most of the research on late presentation to care has focused on descriptive characteristics of individuals who present late in the disease course, information often derived from medical records or clinical cohorts.\textsuperscript{12, 63, 177} While these data are informative about the population at risk, without context they limit causal inference and the subsequent design of public health interventions. Among people with late diagnosis, few have investigated the availability of voluntary counseling and testing services (VCT), the ease with which persons utilized the services, the barriers and facilitators to utilizing services, and the personal belief systems which influenced the decision-making process. Similar issues are relevant after diagnosis when the patient initiates HIV care. Although VCT services are widely available in most U.S. settings and safe and effective therapy has extended the life expectancy of those diagnosed with HIV to greater than 20 years, many obstacles to timely HIV diagnosis remain in the current U.S. system.\textsuperscript{75}

In the present study, our objective was to understand barriers and facilitators to HIV testing and care among HIV infected persons attending a Southeastern HIV clinic who presented with clinically advanced illness. HIV positive patients in this region of the U.S. may face different challenges than the rest of the country, given the rural nature of the region and the degree to which heterosexual involvement is evident in the epidemic.\textsuperscript{64} We developed a conceptual framework for VCT utilization based on constructs described in the Information-Motivation-Behavioral Skills (IMB) model and the Health Belief Model (HBM) to
inform the development of our interview guide (Figure 7.1). The IMB model postulates three determinants of risk reduction: 1) basic information about HIV transmission and prevention, 2) motivation to act on one’s knowledge about HIV transmission and prevention, and 3) behavioral skills for performing specific HIV preventative acts. The HBM consists of five dimensions which explain preventative health behavior: perceived susceptibility, perceived severity, perceived benefits and barriers, and cues to action. We felt that cues to action, factors that stimulate a person to action, were particularly relevant to understanding access and use of VCT services. Through detailed patient narratives, we describe the process of diagnosis and entering care among a unique group of HIV positive patients.

METHODS

Study Setting and Population
The source population for the study was a large, university-based medical center that follows approximately 1,300 HIV infected patients per year and provides comprehensive HIV primary care services. Patients of the clinic are typically followed every three months for therapeutic, virologic, and immunologic monitoring. Patients were eligible for the study if they (1) were at least 18 years of age, (2) entered care between April 2006 and April 2008 and had not received HIV care elsewhere, (3) had a CD4+ T-lymphocyte cell count <350 cells/mm³ at entry, and (4) were cognitively competent to participate in the study.

Recruitment
Eligible patients were approached by a clinic-based research assistant on their second or third clinic visits, after laboratory results were available and the patient was given the opportunity to discuss participation in various research projects. Patients interested in learning more about the study met with the study interviewer before or immediately after their regular clinic visit, at their next regularly scheduled clinic visit, or at a separate
appointment time selected by the patient. We employed a small purposeful study sample to collect in-depth narratives about barriers and facilitators to testing and care. The completion of data collection was guided by the achievement of theme saturation.\textsuperscript{151, 156}

\textbf{Data Collection}

A single female study interviewer explained the study and obtained written, informed consent at the start of the interview. In-depth, face-to-face, semi-structured qualitative one-on-one interviews were then conducted with study participants. All interviews were audio recorded and took place in a private and quiet interview room in the clinic. The average interview length was 43 minutes. Patients were compensated with a gift card to a local grocery retailer.

An interview guide approach was used to conduct the interviews. With this approach, the interviewer uses the guide to address specific pre-determined issues, but is free to change the sequence and the wording in the course of the interview.\textsuperscript{151} Interviews are conversational in style but the interview guide format ensures that data collection is systematic and consistent throughout the study. We identified in-person, qualitative interviews as the most appropriate method for our research question because we sought to understand the process, meaning, and context within which HIV positive persons make decisions about health care.\textsuperscript{152}

Interview questions were comprised of three main types of questions based on the HBM and IMB model.\textsuperscript{29, 30} \textit{Main questions} addressed the research themes and were broad in nature (e.g., “Tell me about your decision to get tested for HIV”). Follow-up questions and probes encouraged deeper, more detailed information (e.g., “Why did you decide to test?” “Did you think that you were at risk?” “Were there reasons you might have been reluctant?”).\textsuperscript{151} We assumed that most people would perceive HIV to be a severe disease so our interview instrument did not include questions about perceived severity. At the
completion of each interview, interview summaries were created by the interviewer to record the non-verbal attributes of the interview, first impressions of the data, and successes or suggested improvements for future interviews.

**Analysis**

All interviews were digitally recorded and transcribed verbatim. Analysis was ongoing and first involved single-case analysis, including the generation of memos and interview summaries, followed by cross-case analyses to identify emergent themes and patterns. A start list of deductive, descriptive codes were used to begin coding, however, coding was continuous and evolving. Interpretive, inductive codes were added to the code list as themes and patterns emerged from the data. Interviews were broadly coded for themes, examined for narrative structure, and compared to the conceptual framework. Segments of text were read for multiple dimensions, including the primary message content, attitudes, individual or group-level ideas, and the degree to which the ideas represent factual or hypothetical experience. Coding sorts were used to examine themes in more detail. Sub-themes of each code were evaluated with particular emphasis on differences in the variation and context of narratives within the same code. Atlas/ti qualitative analysis software was used for analysis.

**Human Subjects Protection**

All participants in the study provided written informed consent to participate in the interview and HIPAA authorization to provide access to medical information. This study was approved by the UNC Institutional Review Board.
RESULTS

The study was conducted from April 2007 through April 2008. During this time, 89 eligible patients had visits in the clinic, of which 41 of 46 (89%) approached about the study were interested in participation. Of these 41, 24 (59%) interviews were completed, one person refused, and the remaining 16 people could not be re-located or wanted to be interviewed at another time. Most (67%) patients presented to care with less than 200 CD4 T-lymphocyte cells/mm$^3$, and most initiated primary care quickly after diagnosis (Table 7.1).

HIV-related information and experience

Prior to diagnosis, HIV-related knowledge varied. Most participants reported understanding fundamental HIV concepts, including mode of transmission and clinical impact. The media was often cited as a source of information as well as experience with friends or family members living with HIV. However, there was a clear dichotomy of people who believed that an HIV diagnosis meant imminent illness and death and those who believed that HIV was a manageable illness. For example, one 43-year old female participant described her thoughts about HIV prior to diagnosis:

“I thought if you catch HIV it was death, you know. You were gonna just deteriorate, lose weight, and die because there was like no cure and I never knew about a lot of medications and stuff that are helping people like me now. I just thought, like I said, you gonna deteriorate and die.”

Similarly, a 41-year old male described his prior perceptions of HIV:

“I thought if you’re HIV positive you walk around and you’re really skinny, your bones are showing, you’ve got sores all over you, your hair is falling out.”

One participant stated that being infected with HIV meant that he was going to suffer. However, these views were not held by all participants. Several participants knew about advances in antiretroviral therapy, and knew that HIV was not generally a death sentence. Earvin “Magic” Johnson was cited several times as an example of how people living with HIV/AIDS could live long, productive lives.
More than half (71%) of participants knew someone with HIV prior to diagnosis. Despite having experience with people with HIV, many held stereotypes about the types of people affected by HIV. Often these stereotypes were supported by what they knew about their friends or relatives with HIV. For example, a 26-year old male explained why he did not perceive himself to be at risk for HIV:

“I had been in a monogamous relationship and I honestly felt that the people that got it, the people that I knew who got it were into drugs. And I was like they’re doing things that are extremely risky, the needles, I mean the anonymous sex, and things like that. And it was one of those things, OK, so maybe they should have had an idea that that sort of thing would have existed for them. I definitely perceived it as oh gosh, kind of scary, you know, and definitely dangerous. I mean their lifestyle that they were leading.”

Similarly, a 44-year old woman describes her perception of the people with HIV in her life:

“I had a cousin who lived in California and he was gay. But he was pretty much a drag queen, but he was doing drugs, he was on the streets, but I don’t know how long he had it. … One particular time he came home and he said he was going to stay. And he said that he had AIDS. … And he still carried on like normal, I mean, he was very attractive, very well spoken but his lifestyle was just wild. … And then I had another friend, two friends that passed from it. They were very sexually active, had numerous partners, you know. I don’t know, I just never thought I would because I wasn’t, I was totally opposite of that.”

Others held stereotypes about people with HIV that weren’t related to any personal experience with people living with the disease. These stereotypes tended to reflect perceptions of HIV being limited to the homosexual community.

**Perceived susceptibility**

The majority of participants did not perceive themselves as having been susceptible to HIV infection. The lack of perceived vulnerability could be broadly divided into three themes: people who did not recognize their behavior as risky, people who viewed their behavior as very low risk, and people who felt like exposure to HIV was unlikely, regardless of behavior. Among those who did not recognize any HIV risk, most felt as if HIV was not something that could happen to them. A 26-year old male described his shock at the diagnosis:
“It wasn’t something that had entered in my mind and I always knew that I could get in a car accident or things like that but I didn’t think that [HIV] was one of the possibilities, you know? That you could wind up with a disease. I just never really put any thought into that.”

Another man described why he was shocked at being offered an HIV test:

“I didn’t fit any of the, you know, I know I wasn’t using drugs, I didn’t sleep with men, and uh, I wasn’t sleeping around, you know.”

For some people, even those who had begun to experience clinical symptoms, the possibility of HIV infection was not considered. A 35-year old male described his rationale about the onset of symptoms: “It never occurred to me. Actually at one point when I was so sick I thought maybe I have cancer. Never occurred to me the HIV, I was that in denial.” However, he went on to describe that despite not feeling at risk prior to diagnosis, he now acknowledges his risk behavior and recognizes that he should have been tested earlier:

“I had tested once … and I was negative but soon there after I was having a lot of unsafe sex practices … It was one of those … Ignorance is bliss a little bit … In retrospect it was ridiculous that I didn’t go get tested. I could keep myself from a lot of, you know, illness there, the treatment. But, yeah, I think it was just easy to not think about it.”

This description highlights the simultaneous and often contradictory accounts of how participants thought about testing prior to diagnosis.

Several participants understood that they may have been engaging in risky behavior, but they felt as if their behavior wasn’t risky enough to expose them to HIV. When asked about how he’d thought about getting an HIV test before his diagnosis, one 33-year old male explained:

“I knew that maybe along my life maybe I did a few slip-ups here and there but nothing that would lead me to HIV. I never had any STDs or venereal diseases so I was like there’s no way I have HIV or AIDS or anything like that.”

Another 33-year old male felt his risk perception was clouded by substance abuse:

“I knew that I knew I was taking some chances when I went out. Um, I experimented with the same sex but I didn’t consider myself to be in that same category if that makes any sense. And, … in my addiction I got careless you know. You really don’t have any control over that drug. … Drugs’ll tell you anything and make you believe anything. Couple times it told me that I couldn’t get no STD.”

Others felt that regardless of their personal acknowledgement of risk, HIV acquisition was a very unlikely event. One participant noted, “If you look at the numbers, it’s still a small
percentage of all the people, so I just never thought about it.” Another man noted, “The likelihood is just pretty slim. And in most cases it would be. It’s just that I fell on the side of uh, the bad statistic. It’s like the girl that has sex once and gets pregnant.” Another man, despite knowledge of HIV epidemiology in the Southeast, was still able to deny his susceptibility.

“I pretty much knew to get tested and it affected African Americans a lot, especially in the male population. A lot of our women were suffering from it. Being in the homosexual community I knew that it was a big part. Get tested get tested. They promoted at clubs, they promoted at other venues. I knew that you needed to do it’s just I didn’t think it would come that close to home. I didn’t know anyone who had died from it within my circle.”

These narratives indicate that most participants felt that their behavior did not place them at enough risk to warrant seeking testing, either because of beliefs about risk behavior or denial of the risks of their behaviors.

**Perceived benefits and barriers**

Perceived benefits and barriers comprise the decisional balance of taking action against a health threat. Participants were probed about their beliefs prior to diagnosis about the value of seeking VCT services (perceived benefits) and about the material or psychological costs (perceived barriers). We separated benefits from cues to action, which are antecedent events that motivated participants to take action.

**Benefits.** Overall, few participants identified benefits of seeking an HIV test. Only three participants sought testing on their own, and all of them reported a cue to take action (the onset of symptoms or finding out a sexual partner was positive). In general, the facilitating factors to seek testing included being concerned about one’s health, wanting to take action in case one was positive, and being able to rule HIV out as a cause of illness.
**Barriers.** The lack of perceived susceptibility to HIV infection was the predominant barrier to testing. In addition to risk perception, participants listed numerous barriers to accessing VCT services. Fear and substance abuse were mentioned most frequently as reasons for not testing. One participant explained, “I think maybe I was scared. I think I was just scared to know or didn’t want to know or not that I thought I was but I just don’t know if I wanted to.” This sentiment was echoed by another who said, “In a way I felt like, you know, I ain’t got it so what’s the use of being tested? And then part of me was scared to find out, you know, if it was to come back positive.” Substance abuse was described as facilitating high-risk behavior as well as clouding one’s perception of risk. Both the presence and the absence of symptoms were described as barriers. Two participants reported feeling ill before their diagnosis, and not recognizing the symptoms as HIV-related. There were clearly missed opportunities for testing by both clients and their healthcare providers. While stigma was a predominant theme in the narratives about the trauma of discovering one’s HIV status, stigma was only mentioned explicitly by one person as a barrier to testing. However, patients expressed stigmatizing perceptions about the types of people affected by HIV, which was often related to an accurate personal perception of risk.

**Cues to take action**

All but one of the participants were eventually diagnosed because of an event that incited testing. The single participant that did not have a cue to action was diagnosed after donating blood in the mid-1980s. Overwhelmingly, participants were diagnosed after the onset of clinical symptoms, and the mechanism of diagnosis could be roughly grouped into three categories: contextual cues to action, cues to action that led to provider-initiated testing, and cues to action that led to client-initiated testing.

Several participants describe contextual situations where testing was directly offered. Their narratives do not suggest that testing was specifically recommended to the participant,
rather, they describe testing events or routine, structured testing. These situations included prison intake, a testing event at a residential substance abuse recovery program, and testing offered during clinical exams. Of the four patients with this mechanism of diagnosis, two were women. Participants reported being amenable to testing when it was readily available and free. One woman described being evaluated at the health department for a potential yeast infection:

“There was a young lady that came in that also said they were doing free HIV testing. And as the years before then I know I’ve had friends and I’ve had family members that have passed from that disease. I kept saying over the years that I was going to get an HIV test. So they were doing free testing and that was the only reason why I took it.”

This mechanism of diagnosis seemed particularly appropriate for individuals who did not perceive themselves to be at risk but wanted to be in control of their health. Although these participants indicated that they had thought about testing in the past, their narratives indicate that they did not have any immediate plans to seek testing before it was offered.

Most participants (58%) in the study were diagnosed because their provider initiated testing after the onset of symptoms. In some cases, HIV was a diagnosis of last resort, in others, HIV testing was recommended because of a clinically compatible presentation (e.g. Kaposi’s sarcoma) or the diagnosis of a sexually transmitted disease. Many patients relayed similar stories of constant illness or being hospitalized and undergoing an array of testing.

This experience was typified by one participant:

“I had been going through depression and things … I said well, I’m depressed. I’m going to the doctor and he ran test and ran test and said oh, there’s an issue, we need to look further. And then that’s where I got my HIV positive diagnosis was from one test led to another to another to another and it turned out that it was something that I personally never would have expected.”

In addition to those tested because of symptoms, some were offered testing by a health care provider for reasons unrelated to the onset of symptoms. In these cases, the narratives suggest that participants believe that they were offered testing because the health care provider evaluated them to be at risk. One 51-year old gay man describes being offered testing after requiring stitches for a fall:
“I was getting all sewed up and I guess they were able to tell, I must had some outward appearance of something that it signaled to them you need to get tested because if they hadn’t said it I wouldn’t have acknowledged it for sure. And so they said “do you want to get tested?””

In these cases, the combination of an available and free test was sufficient to motivate acceptance of VCT.

Few (n=3) participants sought testing on their own. Two participants suggested HIV testing to their provider after being admitted to the hospital for pneumonia-like symptoms. A 48-year old woman recalled that during her hospital stay "It just came to my mind to be tested." The third participant sought testing after finding out his ex-partner had recently died with HIV.

Connecting to medical care

Most patients were diagnosed due to symptomatic illness and consequently initiated medical care rapidly after diagnosis. However, some patients delayed medical care for 12 months or longer, and almost all participants reported having some fears or anxiety about initiating HIV care. Although the psychological impact of HIV was not the focus of this analysis, it was clear that the shock and devastation of diagnosis with advanced HIV had implications for connection to HIV specialty care with respect to deciding when and where to seek care.

Most patients were anxious to start care after diagnosis. The primary facilitator to enter care was avoidance of illness and death. In addition, many patients expressed wanting to take control of the situation and begin the journey toward health. When asked about any worries or fears about starting HIV care, a 26-year old man described his sense of urgency to schedule an appointment:

“I felt like I was kind of on autopilot. Like it wasn’t one of those things where I think I’ll do this, no. It was, I have to do this. I have to make this phone call. I have to get this underway, I have to. You know, because I didn’t want to wind up sick.”

Many patients learned at the time of diagnosis that they had an AIDS-defining condition, and this additional information added to their rush to take action. In addition to the avoidance of
illness, many participants experienced additional or continual symptoms after diagnosis which facilitated linkage to care. One patient entered care after a suicide attempt.

Patients listed several barriers to initiating medical care. While not a predominant barrier to VCT, stigma was often at the forefront of patient’s minds after diagnosis when considering attending an HIV clinic. Worries could be dichotomized into fears about being judged by healthcare professionals and fears about being recognized in the clinic. Patients reported not wanting to go through the ups and downs of care, and a handful expressed a willingness to die rather than deal with the medical system. One patient explained, “I wanted to die. I wanted to not go through this week you’re better, and next week you’re worse, and this week you’re better, and next week you’re worse. I didn’t want to go through that.” After diagnosis, five people reported feeling suicidal and of these, three made attempts. One man described the pain and depression of knowing that he may have infected someone else:

“I was going through a lot of depression and sometimes I felt like I just wanted to blow my head off or I wanted to hang myself, you know, it made me feel like I hurt somebody … And I haven’t been with a woman since and this is 4 years. But, I don’t feel that I want to have a relationship with anybody else because I feel that if I do I’m taking somebody else’s life. I try to be, you know, calm and relaxed and I go through a lot of depression still now. And still to this day sometimes I just, I can’t handle it, you know. I feel so bad that I just, I want to take my life, and I wish there was some way easier to do this.”

The desire to be remembered the way they were prior to getting sick was expressed by several patients. Transportation and financial concerns were rarely mentioned. Some patients reported challenges when being transferred from one doctor or institution to HIV specialty care. This phenomenon was described by one man as “passing the buck” and often patients felt isolated and frustrated about their healthcare provider’s lack of HIV knowledge. One patient described his experience being diagnosed by a rural doctor:

“At that point he completely said ‘well, I have no idea what to do. I’m going to try and get you an appointment at the hospital, but you are very sick and you need help immediately.’ And that was absolutely terrifying to me.”
Another woman described her primary care physician, “He’s always like, ‘well, there ain’t nothing I can do for you…but give you a referral.’” However, in most cases the desire to avoid illness and death outweighed the barriers.

Three patients delayed care for more than one year after diagnosis. The first delayed 13 months and his delay was related to being incarcerated at the time of diagnosis. He reported being assigned a case manager who would schedule his appointment but disappeared before the case management appointment happened. He subsequently did not enter care until he was hospitalized with pneumonia over a year later. Another patient delayed care 22 months after diagnosis. He reports being overwhelmed by his first visit and did not return for an additional eight months. He explains “They wanted to have more information about my body and how it works…and they were on top of me and it kind of made me scared. So when I went home I didn’t come back for a while.” The third patient was involved in a religious group after his diagnosis in the mid-1980s and did not enter care for over 20 years. Distrustful of western medicine, he reports avoiding any medical care that involved blood draws for fear of being “discovered” until he became ill in 2007. Together, these narratives suggest that the decision and process of engaging and maintaining care can be complex, and active referral may increase the chances of successful entry to care.

The first clinical visit for HIV care was identified as a turning point in the coping process for some participants. Up until their first visit in the HIV outpatient clinic, many who were diagnosed by non-HIV specialty physicians felt abandoned, confused, and terrified about the impending medical care to come. Some attempted to research HIV, often online, and felt overwhelmed by the findings. It was not until they met with an HIV specialist that their fears were reduced. One 34-year old described his first meeting with his physician, “I was really scared, and I said, am I dying? …She looked at me and said, ‘Look. HIV is not a death sentence anymore if you take care of yourself.’ And that, I live by that now.” The importance of the first visit was echoed by a 26-year old man:
“I went in thinking that it was like a death sentence and I came out thinking, oh wow, my doctor rocks, you know? … To talk to someone who knew what they were talking about for a change. Someone that I understood and someone that knew all the treatments and knew exactly where I was and things like that. I mean I walked out ten times the person that I was, you know. I think I probably walked in looking at the floor and walked out looking at eye level.”

For some, the first visit was the first time they felt in control since diagnosis. It was a time to allay some of the fears and haste they felt after learning how advanced their illness was. A 43-year old woman describes her first HIV care visit:

“When I first came up here, not knowing what a CD4 count or none of that is, when I come up here I find out my CD4 count, a normal person’s is supposed to be high. I found out mine is under 100, you know, and it’s like that’s a risk of AIDS right there already, and it was really scary. But then once I came in here and talked to her, [I] was a lot more relieved. It was a lot easier when I walked out the door.”

According to participants, the important things learned at the first visit were 1) basics about HIV pathogenesis and immunologic monitoring, 2) that death wasn’t imminent and that they had time to carefully consider decisions about therapy, and 3) although antiretroviral therapy may have side effects for some people, HIV can be a manageable disease. During the period from diagnosis until entry to care, patients without this basic information may be paralyzed, suicidal, and isolated as they come to terms with HIV.

DISCUSSION

In the U.S. Southeast, a substantial proportion of people living with HIV are diagnosed or enter care late in the course of illness. In the hospital outpatient clinic where our study was conducted, 75% of all patients have an indication for antiretroviral therapy at their first clinic visit, and 50% have a CD4+ T-cell count less than 200 cells/mm³. Likewise, in Birmingham, Alabama, 41% of patients presenting to an HIV/AIDS outpatient clinic had progressed to CDC-defined AIDS. These findings and the knowledge of the unique HIV epidemic in the South raise special concerns about access to testing and medical services in the region.
Our study examined barriers and facilitators to HIV testing and medical care among a group of HIV-positive patients in the southeastern U.S. who entered care with moderate to advanced immunosuppression. Our findings suggest that lack of perceived risk or lack of perceived susceptibility to HIV was the predominant barrier to early HIV testing. An accurate perception of HIV risk can act as a facilitator or barrier to HIV testing – either by increasing awareness and thus the likelihood of testing, or by increasing fear of testing positive.\textsuperscript{65-67} Although our study was comprised of a small purposeful sample that cannot be used to make generalizations, the participants’ narratives suggest that among this group, risk perception is influenced less by personal behavior than perceptions about who is affected by HIV. Participants reported knowledge of HIV transmission and etiology, but inaccurate and often outdated stereotypes about people living with HIV interfered with accurate risk perception. Consequently, utilization of VCT services was not identified as a necessary component of comprehensive health care. Our findings suggest a role for health education and the media to portray a new, more accurate, representation of who is affected by HIV infection.

The fact that public health messages to encourage HIV testing did not reach this group of individuals who were diagnosed recently, primarily in 2006 and 2007, is concerning. Southeastern residents live within a complex social and structural environment that may elevate their risk of HIV acquisition independent of personal behavior.\textsuperscript{39} Health and economic disparities are the underlying contextual framework for HIV transmission in the Southeast. High rates of sexually transmitted diseases increase the likelihood of HIV acquisition and transmission.\textsuperscript{37} The loss of African American men from their communities, either from excess mortality or incarceration, disrupts partnerships and promotes sexual concurrency.\textsuperscript{39, 178} Stigma, trust in providers, marriage rates, and injection and non-injection drug use are also associated with the epidemic.\textsuperscript{37, 38} These factors result in frequent heterosexual transmission and a non-urban epidemic.\textsuperscript{64} It is worrisome that public
awareness campaigns and routine contact with the healthcare system were ineffective in our study population, given the expanding HIV epidemic in the U.S. Southeast.

Predominantly, patients were tested and subsequently entered care due to the onset of clinical symptoms, consistent with other reports.\textsuperscript{7, 52, 62} This group of individuals missed the benefits of early medical care and some may have unknowingly transmitted to others. Our findings underscore the barrier that delayed diagnosis poses to HIV prevention efforts. Recent CDC testing guidelines for the adoption of routine testing in all healthcare settings may have an impact on reducing the numbers of individuals who first test positive late in the course of disease.\textsuperscript{49} From a public health perspective, even small changes in the proportion of persons living with HIV/AIDS who are aware of their serostatus can have large impacts in preventing new infections.\textsuperscript{179} In our study, most participants accepted testing when it was offered, suggesting that routine screening may increase the numbers of people tested and de-stigmatize the testing process. However, for the program to have impact, people living with unrecognized HIV infection must have contact with the healthcare system. Given that in the Southeast, HIV infection is often a disease of the rural and poor, new strategies to improve health care access will be a necessary precursor for any increased screening to reach the groups most at need.

Most patients felt an urgency to enter care after diagnosis, but also encountered multiple barriers and sources of frustration during this process. For some, the inability of their diagnosing health care provider to educate them about HIV or provide care for them left them feeling deserted. Participants were surprised that, after passive referral to an HIV care provider, no one contacted them to ensure that they successfully connected to care. As HIV screening becomes increasingly incorporated in non-traditional testing settings, specialized programs to rapidly and effectively link patients to care could bridge the gap between HIV diagnosis and primary care, and allay patient concerns during this unsettling time.\textsuperscript{128} For patients diagnosed late in illness, they must come to terms not only with the realization that
they are living with HIV, but also with the additional knowledge that they may have been infected for several years and are now facing an immediate health threat. At least 20% of participants in this study considered or attempted suicide after diagnosis. In this setting, active referral with follow-up should become the optimal standard of care. In addition, we have revealed an opportunity for physician education, as the approach to breaking bad news may have implications for coping with HIV after diagnosis.\textsuperscript{180, 181}

Fortunately, the issue of late diagnosis and delayed presentation to care is receiving increased attention among public health and medical professionals. As evidenced by this study, a rote or passive approach to increasing HIV testing and the subsequent linkage to care may miss segments of the population, some of whom are at high risk. A reliance on personal awareness of risk to initiate testing did not work for this group of people who entered care with moderate to advanced immunosuppression. Many felt disillusioned after diagnosis as they encountered difficulties when trying to navigate the health care system. Focusing research efforts toward these issues may help to avert late diagnosis and delayed entry to care in the future.

Contextual Factors
- Availability of testing services
- Insurance status
- Transportation
- Incarceration
- Substance abuse
- Healthcare utilization

Individual Factors
- Information about HIV transmission & prevention
- Information
- Behavioral Skills
- Motivation
- Cues to Action

Expectations
- Perceived benefits
- Perceived barriers

Threat
- Perceived severity
- Perceived susceptibility

Onset of symptoms
- STIs
- High-risk event
- Provider initiated testing
- Provider referral
- Partner notification

HIV Testing
TABLE 7.1. Descriptive characteristics of 24 HIV positive patients initiating HIV primary care between April 2006 and April 2008 at the University of North Carolina outpatient infectious disease clinic.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year of Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1985</td>
<td>1</td>
<td>(4.2)</td>
</tr>
<tr>
<td>2005</td>
<td>2</td>
<td>(8.3)</td>
</tr>
<tr>
<td>2006</td>
<td>15</td>
<td>(62.5)</td>
</tr>
<tr>
<td>2007</td>
<td>6</td>
<td>(25.0)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>19</td>
<td>(79.2)</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>(20.8)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>12</td>
<td>(50.0)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1</td>
<td>(4.2)</td>
</tr>
<tr>
<td>White</td>
<td>11</td>
<td>(45.8)</td>
</tr>
<tr>
<td>Age¹</td>
<td>42.5 years (26-62)</td>
<td></td>
</tr>
<tr>
<td>CD4+ T-cell count at entry to care (cells/mm³)¹</td>
<td>92</td>
<td>(17-332)</td>
</tr>
<tr>
<td>Time between diagnosis and entry to care (days)¹</td>
<td>40.5</td>
<td>(0- 22.7 years)</td>
</tr>
<tr>
<td>HIV testing method</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Provider-initiated</td>
<td>16</td>
<td>(66.7)</td>
</tr>
<tr>
<td>Client-initiated</td>
<td>3</td>
<td>(12.5)</td>
</tr>
<tr>
<td>Contextual (e.g., blood donation, prison)</td>
<td>5</td>
<td>(20.8)</td>
</tr>
</tbody>
</table>

1. Median (range)
CHAPTER 8: DISCUSSION

More than twenty-five years after the first reports of *Pneumocystis carinii* pneumonia among young men heralded the beginning of the HIV/AIDS pandemic, 33 million people live with HIV and two and a half million people were infected in 2007 alone. In North Carolina, home to two of the most prestigious HIV research institutions in the world, the story of HIV is one of poverty and disparity. Twenty-three percent of the state’s rural residents live in poverty, providing a backdrop of poor access to health care and competing health and economic priorities which facilitate HIV transmission. The rate of HIV infection for non-Hispanic blacks is more than eight times greater than for non-Hispanic whites, and North Carolina ranks second among states with the most AIDS cases from non-metropolitan areas. After a period of stability in the late 1990s and early 2000s, annual HIV disease reports have been rising since 2004. It is increasingly clear that routine HIV screening, in isolation, cannot slow HIV transmission. A comprehensive approach to VCT, risk-reduction, linkage to and retention in medical care, and adherence to antiretroviral therapy will be needed to have significant impact on the domestic epidemic.

Summary of Findings

In this dissertation, we described several findings which help to explain the HIV epidemic in the Southeast as well as highlight areas for additional public health intervention. In our first specific aim, we found that nearly one third of patients had another sexually transmitted infection at the time of the acute HIV diagnosis. This finding means that STIs are commonly
involved in HIV transmission in NC, either by increasing the risk of HIV acquisition or transmission, and also underscores the importance of routine screening for HIV among people with STIs. The variation we observed in HIV/STI co-infection by gender, risk category, and race helps to explain the epidemiology of the HIV epidemic in the southeastern U.S. where racial disparities are remarkable and heterosexual transmission is nearly as prominent as homosexual transmission.\textsuperscript{33, 162} The high prevalence of STIs in women with incident HIV is troubling, and partially explains the increasing HIV rate in Black women since 2004.\textsuperscript{185}

In our second specific aim, we found that structural and functional social support was not strongly associated with delayed presentation to care, leaving us with several important questions. First, it is unclear if the surprisingly high levels of social support we observed were associated with HIV care. It is probable that once in care, newly diagnosed patients have access to support services and resources which change their levels of perceived social support. Our cross-sectional data were limited in that we could not examine changes in social support over time. Second, it is interesting that patients reported high levels of affectionate, emotional/informational, and tangible support, while levels of positive social interaction were lower. It is unclear what, if any, role positive social interaction plays in HIV-related health services utilization. In addition, narratives from patients in the UNC ID clinic repeatedly cited social support as critical to the maintenance of care and adherence to medications (data not shown). While we found that there was little effect on the time to presentation to care, these data suggest that social support may be important for maintenance of care and adherence to therapy.

Our third specific aim focused on barriers and facilitators to care among people who presented to care with moderate to advanced immunosuppression. We found that the primary barrier to early detection of HIV was that most patients perceived themselves to be at low risk for HIV infection – a perception enforced by stereotypes about who is affected by
HIV. In addition, the patient narratives indicate that the referral to care process was often frustrating, particularly while trying to cope with coming to terms with HIV. The first visit to an HIV care provider was identified as a critical time point in the coping process for HIV. While the analyses presented in this dissertation have described barriers to testing and care, future analyses on these data will focus on the trauma of discovering one’s HIV positive status as well as on stigma and disclosure in the Southeast.

Together, these three studies have added to our understanding of the HIV epidemic in the Southeast. Our findings directly relate to the basic tenets of HIV transmission – biology and behavior. We found that STIs are an important biological factor in HIV transmission in the region. In contrast, inadequate health care access, utilization, and inaccurate perception of risk are important behavioral issues, shaped by underlying health and economic inequities. The biggest challenge for public health practitioners will be how to effectively influence biology and behavior within the complex social and economic context of the Southeast.

Public Health Significance

HIV testing is a critical point in the continuum of HIV care. It is the initial step toward accessing and maintaining HIV care, which has individual clinical benefit as well as public health benefit through risk-reduction counseling and the potential for reduced transmissibility via antiretroviral therapy. Persons who are aware of their serostatus tend to reduce their risk behavior and have lower onward transmission rates than persons unaware of their status. Increasing testing and encouraging earlier detection of HIV without stigmatizing high-risk groups is one objective of the routine HIV screening recommendations issued by the CDC in 2006.

Our findings suggest that the adoption of routine HIV screening recommendations in healthcare settings may have an effect on earlier detection of HIV. The streamlined, opt-out
approach to testing without the requirements of a separate consent or prevention counseling may eliminate an important barrier to HIV testing – an accurate perception of HIV risk. Our qualitative data suggest that provider initiated testing was the predominant mechanism of diagnosis among patients who presented with moderate to advanced immunosuppression. When suggested by their healthcare provider, most of the patients in our study were amenable to testing, even those who perceived themselves to be at little to no HIV risk. The removal of risk-based testing criteria may de-stigmatize the risk perception and HIV testing process, resulting in fewer missed opportunities, increased screening, and more client acceptance.

However, three important issues remain unaddressed by the CDC HIV testing guidelines. The first is access to medical care. The value of increased screening in all healthcare settings is based on the premise of contact with the health system, which will be limited for the uninsured and those living in medically underserved communities. The U.S. South has the highest proportion of people living in poverty (13.8%) and the highest proportion of people uninsured (19%). As a result, emergency departments (ED) serve as the healthcare safety net and provide care to many uninsured patients. EDs are a setting where time constraints may significantly oppose HIV screening efforts, although demonstration projects have indicated that ED-based screening is feasible, even using a voluntary opt-in approach. Further data are needed to describe successful routine testing programs at EDs and other non-traditional testing sites to reach those without regular health care providers. Similarly, the financial concerns of newly diagnosed patients need to be addressed as early as possible after diagnosis to allay economic concerns and encourage entry and retention in care.

The second issue is prompt linkage to care after diagnosis. While the screening guidelines note that newly diagnosed patients “should receive or be referred for clinical care promptly,” recommendations on how best to execute this recommendation are scant.
Currently, in North Carolina, most newly-diagnosed patients are passively referred to HIV primary care by their diagnosing physician, post-test counselor, or DIS officer in the field. Is this system working? Our data suggest a need for improvement – 31% of patients participating in the CSDS survey in the UNC outpatient clinic were not in care two years after diagnosis and in 2005, approximately 7,000 North Carolina residents living with HIV who were aware of their status were not in care. Our qualitative data, with the significant limitation that all of the participants were in care at the time of the interview, provides evidence that passive referral to care can be ineffective and add to patient anxiety about wanting to take action. The patients we interviewed were motivated to enter care quickly and most did so, but one could speculate that the barriers they experienced may be significantly worse for other unobserved patients who remain unconnected with the healthcare system for years after diagnosis.

With respect to onward transmission, a recent analysis of patients with AHI in North Carolina found that 28% of named partners with established HIV did not have a current care provider. Further, only three acute-acute transmission partnerships were identified, suggesting that HIV transmission in the southeastern U.S. may be driven by chronically-infected persons, as opposed to the importance of acute to acute HIV transmission postulated in urban areas. Ensuring that people with established HIV infection receive HIV care, periodic prevention counseling, and antiretroviral therapy, when indicated, needs further attention from policymakers.

Finally, how much will routine screening cost? With the opt-out testing strategy without pretest counseling and an initial rapid test followed by a confirmatory Western blot, the cost per seropositive patient is US$97 and US$13 for seronegative patients. The cost for testing the approximate 166 million people not already being tested for HIV would be roughly 2.2 billion US dollars. In addition, once identified and in care, HIV positive patients on antiretroviral therapy incur approximately US$14,000 annually in prescription drug costs.
alone. In 2007, although AIDS Drug Assistance Program state waiting lists have been nearly eliminated and client enrollment increased, state budget shortfalls and declining federal funding threaten future funding needs – for some of the most vulnerable individuals with HIV/AIDS. While HIV screening is cost-effective even in low prevalence settings, the financial impact of testing, diagnosis, and care of the nearly 250,000 people unaware of their HIV positive status is unknown.

**Future Directions**

An ideal study design to evaluate questions about HIV testing and care utilization would follow a defined population prospectively to identify causal factors associated with HIV testing. Newly diagnosed individuals would be followed to determine how and when they access HIV care. Of course, this idealized study design is infeasible because of the intensive resources required to follow a population over time and the rarity of the outcome. Further, it may produce biased results due to the Hawthorne effect. In the absence of this “optimal” design, we must make inferences to improve public health practice based on information at the point of care (e.g. VCT sites, HIV outpatient care).

An important surveillance project is already in the planning stages in North Carolina that will elucidate questions about when people test for HIV. Beginning in late 2008, people with a new HIV diagnosis in NC will be offered a free CD4 count on their initial testing specimen. These data will help to answer some important questions about the epidemiology of HIV in NC, such as the degree of immunosuppression at diagnosis overall and within strata of race, gender, and age. These data will also help to identify geographic areas and testing locations where people are diagnosed, on average, earlier or later than a specified referent group. A secondary goal of the study is to determine what proportion of newly diagnosed people have entered care within specified time intervals, using minimally
invasive, brief telephone questionnaires that will hopefully minimize any Hawthorne Effect biases.

In this dissertation, an important finding was the challenges many newly diagnosed HIV positive persons face when initiating HIV primary care. As discussed in Chapter Seven, patients often felt isolated and deserted by their diagnosing healthcare provider when they received a passive referral to HIV specialty care. To further investigate this problem in a quantitative design, one could conduct a case-control study of patients initiating HIV primary care to compare people who rapidly initiated care to those who delayed care. It would be important to investigate factors such as where and how the diagnosis was made and how the patient eventually established care. Most research to date indicates that financial considerations and transportation only partially explain delays between diagnosis and care.

On a national level, the Medical Monitoring Project is an ongoing CDC-sponsored patient survey designed to answer questions about health service utilization among people living with HIV. Including data from 19 states and Puerto Rico, the survey is designed to describe how many people with HIV are receiving care, barriers to care and prevention services, and what needs of people living with HIV are not being met. North Carolina is one of the study sites, so we look forward to learning more about the findings of the Medical Monitoring Project to inform HIV care and policy in NC.

Conclusions

As routine HIV screening is adopted in all healthcare settings, accurate surveillance and monitoring of programmatic results will be paramount to evaluation of the program's success. We envision several key outcomes. First, who is tested – and who is not tested – will quantify areas where additional implementation guidance, funds, or training are needed as well as groups who may be more inclined to opt-out of screening. Second, the numbers of newly diagnosed persons with HIV who are successfully linked to care will provide an
idea of how well routine screening can improve patient outcomes. Patients aware of their serostatus who do not enter HIV care may reduce onward transmission without individual clinical benefit. In addition, newly diagnosed patients identified as part of routine health screening may be particularly vulnerable to prolonged periods without care, especially if they did not perceive HIV risk at the time of testing. Finally, the implementation of routine screening requires a parallel effort of operations research to determine the combination of test type, staffing, and process which optimizes the logistical and financial feasibility of the program. Monitoring these outcomes will be essential to evaluating the long-term ability of routine screening to have impact on HIV transmission.
APPENDIX A. Results for Specific Aim 1B

INTRODUCTION

In specific aim 1b, we sought to evaluate variation in the time from HIV acquisition to testing among individuals with acute HIV infection by the presence of a STI at the time of HIV testing and the testing site type. We hypothesized that persons diagnosed with acute HIV and a concurrent STI would be diagnosed earlier than those without a concurrent STI because of the short incubation periods of many bacterial STIs. We also hypothesized that persons diagnosed with acute HIV at STD testing sites are diagnosed earlier than those diagnosed at non-STD testing site types because of the routine HIV testing that is conducted among STD clinic clients.

METHODS

The study population, coding of covariates, and a detailed description of the methods for this specific aim is described in detail in Chapter Four. In brief, the outcome for this analysis was the time from HIV infection to HIV testing. The date of HIV acquisition was estimated using the dates of symptom onset and seroconversion reported by DIS. For individuals with symptoms consistent with acute retroviral syndrome, the date of HIV infection was calculated as 14 days prior to the date of symptom onset.\(^{134-136}\) For individuals without symptoms, we utilized an average plausible seroconversion interval of 35.5 days with a two week window on either side (21.5 to 49.5 days, see Table 4.1).

The main exposures for the analysis were testing site type and the presence of an STI co-infection at the time of acute HIV detection. A proportional hazards model was used to examine variation in the time from HIV acquisition to HIV testing by STI co-infection and testing site type. We evaluated all exposures and covariates for the assumption of proportional hazards and then evaluated all covariates for effect measure modification.
and/or confounding of testing site type or co-infection in bivariable models. We then constructed a single, fully adjusted model with both main exposures and all relevant interaction terms and confounders. We did not evaluate the presence of acute retroviral symptoms in the model as this variable is in the causal pathway. Patients not tested after 35 days were censored in all proportional hazards models.

RESULTS

Of the 75 patients with acute HIV infection from November 2002 through October 2006, dates of seroconversion were available on 72 (96%). Fifty-four (75%) patients reported symptoms consistent with acute retroviral syndrome with a median time from infection to testing of 20.5 days. Of the 18 (25%) patients without symptoms, the median time to testing was 28.5 days (range: 14.5 to 42.5).

The effect of testing site type on the time to testing differed by age, so all unadjusted testing site type results are presented stratified by age (Table A.1). People ≤30 years who were tested at CTS sites were tested the earliest after infection at 16.5 days. The longest times to testing were observed for individuals over 30 at CTS sites and individuals ≤30 at other types of clinics (30 days). The median time from infection to testing did not differ by the presence of an STI co-infection (22.5 days vs. 23.0 days, p=.33).

The final multivariable model included testing site type, STI co-infection, gender, risk behavior (heterosexual man, MSM, female), and age. In the adjusted model, there was variation in the effect of testing site type on the time to testing by age. The hazard of being tested among patients ≤30 years at CTS sites was more than six times the hazard of those >30 at CTS sites (HR: 6.81, 95% CI: 2.10, 22.07). Similarly, patients of all ages tested at STD sites were more likely to be tested earlier than those >30 years who attended CTS sites. Patients >30 at other types of testing sites were more likely to be tested earlier than
those who attended CTS sites (HR: 1.70, 95% CI: 0.55, 5.24). The presence of an STI co-infection did not have an effect on the time to HIV testing.

DISCUSSION

Counter to our hypothesis, the presence of a concurrent STI infection at the time of HIV infection was not associated with shorter times between infection and testing. Due to the short incubation periods of many STIs, we expected that people with HIV and STI co-infections would seek care earlier than those without co-infections, as they have a biological “cue” to seek testing. The lack of difference that we describe could be due to asymptomatic, unobserved STIs, or because the incubation periods of some STIs may be longer than average in an HIV infected host. Another feasible explanation is that our estimate of the date of infection is inaccurate, either by under- or over-estimating the time between HIV acquisition and seroconversion. Finally, our results could indicate that there is no effect of concurrent STIs on HIV testing behavior, although this is unlikely given the HIV testing recommendation for all people seeking care for STIs.49

The time from infection to testing varied by the type of HIV testing facility and age. Clients ≤30 at CTS sites had the shortest time from infection to testing. This finding could be explained by the risk perception of the clients at CTS sites. CTS sites may attract a more risk-aware clientele, which is a key factor associated with testing. 66, 67 In this case, anxiety over the risk of exposure may be a key factor that drives HIV testing shortly after infection. Similary, STD clinic clientele are routinely tested for HIV, which may account for the elevated hazards of testing we observe for this group.

The data presented in this analysis suggest that there is variation in the testing site where people who were recently infected with HIV seek VCT. Further research, including a study to elucidate reasons for testing during acute HIV, will help to explain testing behavior during this highly infectious time.
TABLE A.1. Unadjusted and adjusted hazard ratios (HR) comparing the estimated time from HIV acquisition to HIV testing by testing location and the presence of an STI co-infection at diagnosis among patients with acute HIV infection in North Carolina.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median time to testing (days) $^1$</th>
<th>p-value $^2$</th>
<th>Unadjusted HR (95% CI)</th>
<th>Adjusted HR $^3$ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testing Location and age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV Counseling and Testing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30</td>
<td>16.5</td>
<td></td>
<td>5.70 (1.87, 17.35)</td>
<td>6.81 (2.10, 22.07)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>30.0</td>
<td>&lt;0.01</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>STI Clinic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30</td>
<td>23.8</td>
<td>&lt;0.01</td>
<td>1.98 (0.74, 5.31)</td>
<td>2.55 (0.89, 7.29)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>21.5</td>
<td></td>
<td>3.00 (1.05, 8.63)</td>
<td>3.12 (1.05, 9.33)</td>
</tr>
<tr>
<td>Other type of clinic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30</td>
<td>30.0</td>
<td></td>
<td>1.04 (0.33, 3.29)</td>
<td>1.00 (0.31, 3.18)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>23.0</td>
<td></td>
<td>1.63 (0.53, 4.98)</td>
<td>1.70 (0.55, 5.24)</td>
</tr>
<tr>
<td>STI co-infection at diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>22.5</td>
<td>0.33</td>
<td>1.32 (0.76, 2.27)</td>
<td>0.91 (0.49, 1.70)</td>
</tr>
<tr>
<td>No</td>
<td>23.0</td>
<td></td>
<td>Referent</td>
<td>Referent</td>
</tr>
</tbody>
</table>

1. The date of infection was assumed to be 14 days prior to ARS symptom onset (symptomatic patients) or 35.5 days prior to the date of seroconversion (asymptomatic patients).

2. Log-rank test for equality of the survival curves.

3. Adjusted for gender, risk behavior and age. An interaction was found between testing location and age in the multivariable model, so the unadjusted results are presented stratified by age to facilitate comparison.
**APPENDIX B. Results of Linear Regression Model of log_{10}(HIV RNA) Change**

**TABLE B.1** Univariate linear regression models of serum HIV RNA (log_{10}copies/ml) slope and selected demographic factors among 44 patients with acute HIV in NC.¹

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Parameter Estimate</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender and risk behavior</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Man who has sex with men</td>
<td>0.01 (-1.18, 1.20)</td>
<td>0.94</td>
</tr>
<tr>
<td>Heterosexual man</td>
<td>0.23 (-1.19, 1.64)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 25</td>
<td>0.66 (-1.89, 0.48)</td>
<td>0.46</td>
</tr>
<tr>
<td>26-35</td>
<td>0.03 (-1.41, 1.47)</td>
<td></td>
</tr>
<tr>
<td>≥ 36</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td><strong>Race or ethnic background</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>White, Hispanic or Black</td>
<td>0.66 (-1.93, 0.18)</td>
<td>0.27</td>
</tr>
<tr>
<td><strong>Testing Location</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV Counseling and Testing site</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>STD Clinic</td>
<td>-1.33 (-2.53, -0.13)</td>
<td>0.06</td>
</tr>
<tr>
<td>Other type of clinic</td>
<td>-1.42 (-2.73, -0.11)</td>
<td></td>
</tr>
<tr>
<td><strong>STI co-infection at diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.13 (-0.97, 1.22)</td>
<td>0.15</td>
</tr>
<tr>
<td>No</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td><strong>Symptoms of acute retroviral syndrome at or before testing</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.60 (-0.43, 1.63)</td>
<td>0.24</td>
</tr>
<tr>
<td>No</td>
<td>Referent</td>
<td></td>
</tr>
</tbody>
</table>

1. Forty-four clients with AHI had both initial and confirmatory values available for analysis. Seventeen (38.6%) had increasing viral loads between the initial and confirmatory samples.

2. Positive parameter estimates indicate increasing HIV RNA slopes.
INTRODUCTION

The date of HIV diagnosis is a critical measurement for many epidemiologic studies of health care access, quality of care, and clinical outcomes. However, measurement of the date of diagnosis can vary substantially. Some investigators rely on self-report, whereas other investigators use a confirmed laboratory testing date. Little is known about how different measures of HIV diagnosis date differ. The goal of this analysis was to compare the self-reported date of diagnosis to the date recorded in the UNC medical record and the date reported to the NC HIV/AIDS Reporting System (HARS) through routine name-based morbidity surveillance.

METHODS

Measurement of Self-Reported Date of HIV Diagnosis

The study population was comprised of HIV positive patients who provided written informed consent to participate in the CSDS Survey. Consent to participate in the CSDS includes authorization to acquire medical information from the UNC medical record as well as other providers and facilities, including state health department records. The self-reported date of diagnosis was the answer to the question “When were you first told that you were HIV-positive?” In the first version of the CSDS, patients were asked to identify the year of diagnosis. In subsequent versions of the questionnaire, patients were asked to identify the full date (month, day, year) of diagnosis. Due to this inconsistency, we will present the analysis by year of diagnosis only.

Measurement HIV Diagnosis Date in the UNC Medical Record

The date of diagnosis in the medical record was obtained by medical record abstraction by
trained personnel and was defined as the date of Western Blot confirmation or the first provider report of HIV. In cases where only the year was known, the date was considered to be the midpoint of the year (June 15th). Likewise, missing days were coded as 15 and missing months were coded as June.

**Measurement HIV Diagnosis Date in the NC HIV/AIDS Reporting System**

To obtain the earliest date of diagnosis in the HARS reporting system, patients who completed the CSDS were matched to HARS using a 4-step algorithm. First, patients were matched deterministically using the first four letters of the last name, first three letters of the first name, month and year of birth, and sex. In the second stage, single matches are removed and the remaining non-matched subjects were matched deterministically by social security number, if available. The remaining non-matched subjects were then manually matched by record lookup using an inexact matching algorithm and rotating the first name, last name, date of birth, and sex though the lookup system to identify changed names, gender errors, etc. Finally, multiple matches for a single patient were investigated and resolved and all matches were manually reviewed for error.

**Statistical Analysis**

We compared the self-reported year of diagnosis with earliest date reported in the UNC medical record or the HARS system. Data management and analysis was conducted with SAS software (version 9.1.2, Cary, North Carolina).

**RESULTS**

Since July 2000, 332 patients completed the CSDS interview and were eligible for the study. All but four reported a year of diagnosis (98.8%). Of the 328 with a self-reported date of diagnosis, 273 (83.2%) had been reported to the HARS system and 316 (96.3%) had a
diagnosis date in the UNC medical record. Overall, 322 (98.2%) matched to at least one system.

**Comparison of Medical Record and HARS Dates of Diagnosis**

In most cases (75.2%), the UNC medical record date of diagnosis was earlier than the date reported to the HARS system. For the 268 participants that had both the UNC medical record date and the HARS date available, the absolute difference between the two dates was on average 23.6 months, standard deviation 42.1 months (median difference 2.5 months). Comparing year only, 166 (61.9%) had the same year of diagnosis. An additional 32 (11.9%) were only discrepant by one year, and 70 cases (26.1%) were discrepant by two or more years (range: 2-16).

**Comparison of Self-Reported Date to HARS or UNC Medical Record**

We compared the earliest of the UNC medical record or HARS date to the self-reported date of diagnosis. Overall, 200 of the 322 participants (62.1%) with a self-reported date and either a UNC or HARS date reported concordant years of diagnosis. An additional 61 (18.9%) were only discrepant by one year. The mean difference was 1.1 years. Sixty-one (18.9%) participants reported years of diagnosis two or more years different than that in the HARS or UNC system (range: 2-14). Of the 122 patients with non-matching years, 63 (51.6%) reported years of diagnosis that were earlier than either the UNC or HARS system and 59 (48.4%) reported years that were later than the UNC or HARS system. Of the 265 participants that had a self reported, HARS, and UNC medical record year of diagnosis, only 45% of the time did all three years match.

**DISCUSSION**

In this study, we found variation in the year of diagnosis reported by patients, abstracted
from their medical record, and reported to the NC Department of Health and Human Services. While we did not have access to the true diagnosis date, our study should encourage other investigators to identify and describe the sources of bias that influence the date of diagnosis source used in their research endeavors.

While name-based reporting of HIV has been mandated in North Carolina since 1990 and AIDS reporting has been required since 1984, only 83% of cases had been reported to the state. As the source for the most comprehensive data on patterns of new diagnoses, morbidity reporting is essential for effective targeting of health resources. In addition to epidemiologic monitoring of the epidemic, HIV/AIDS reporting is used for Ryan White funding distribution to pay for medical care and treatment of un- and underinsured people living with HIV/AIDS. It is concerning that nearly 20% of patients were not located in the HARS system, despite all having received HIV primary care and all of them reporting that they were diagnosed in 2004 or earlier. In three-quarters of the cases that were reported to the HARS system, the year of diagnosis in the medical record was earlier than the year reported to the HIV/AIDS Reporting System, highlighting a disconnect between patient records and morbidity reporting. With the data available to us at the time of the analysis, it was impossible to know what the true date of diagnosis was for direct comparison.

The self-reported year of diagnosis matched the earliest documented year of diagnosis in 62% of cases, and matched within a year in 81% of cases. This concordance is better than expected. Roughly 20% of participants reported a year of diagnosis that was earlier than either the UNC or HARS system. This is less than the 30% of people who reported earlier dates of diagnosis compared to a national analysis of 16 states in the HARS system. While this indicates that NC may be doing better than the national average, there is still room for improvement.

Many epidemiologic studies of linkage to primary HIV care after diagnosis and health care outcomes after care and treatment initiation use the date of diagnosis as “time zero” for
HIV-related events. Our analysis has demonstrated that there is variation in each of these measurements. As a result, investigators should make efforts to identify the sources of bias for each measurement and when applicable, conduct sensitivity analyses to determine the impact of these biases on their results.
REFERENCES


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<thead>
<tr>
<th></th>
<th>Author(s)</th>
<th>Title</th>
<th>Source</th>
</tr>
</thead>
</table>


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