Screening for Syphilis and HIV in North Carolina Jails

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ABSTRACT

LYNNE A. SAMPSON: Screening for syphilis and HIV in North Carolina jails
(Under the direction of William C. Miller)

Sexually transmitted diseases are prevalent among incarcerated populations. Screening for STDs in county jails serves as a form of community screening, often reaching individuals with poor access to other health care services. The goal of this dissertation was to develop and test screening algorithms to improve the effectiveness of jail screening for syphilis and human immunodeficiency virus (HIV) infection and to examine the costs of adding syphilis screening to existing HIV programs. The studies included men and women screened for syphilis (and some also for HIV) in seven North Carolina jails in 2002-2005.

A screening algorithm derived from predictive modeling of new syphilis cases can improve screening efficiency for male inmates. Age, race/ethnicity, and reporting an STD diagnosis in the last six months were all associated with new syphilis infections. When resulting risk scores were applied to hypothetically testing ~50% of the inmate population, the algorithm was able to detect 83% of the cases. Women were more likely than men to have syphilis (OR 2.5, 95% CI 1.8 – 3.4) but the data did not yield a useful predictive model. The prevailing strategy of screening as many women as possible is recommended.

Programmatic and funding changes have resulted in a shift to HIV screening in NC jails and new protocols must be designed with HIV as the primary goal. Screening for

syphilis under this new paradigm is effective and low cost and should continue. A predictive model of HIV infection among jail inmates included age, race/ethnicity, gender, history of HIV testing and, for men, men who have sex with men status. Risk scores derived from the model yielded screening algorithm with 83% sensitivity for detection of HIV when applied to testing ~50% of the population. This same algorithm was able to detect 73% of syphilis cases. Using the algorithm for targeted screening decreased the cost per HIV case detected from ~$2,200 to ~$1,300. The cost of adding syphilis to the existing HIV jail screening program was low (less than $300 per case detected) and is recommended in areas with incident syphilis.

DEDICATION

For my dearest Robby. I could never have done this without your support, patience, and love. For the sleepless nights, the foregone vacations, and the solo childcare duties, words can not express my gratitude.

And for Gretchen and Desmond. You are my world and every minute that I spent on this dissertation rather than with you was a difficult one. I did it for my commitment to public health and so that you could grow up knowing that your Mama does eventually finish what she starts. I look forward to moving on to a new phase where we can spend more time learning and growing together.

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The completion of this dissertation has been an exercise in extremes. On one hand, it is the largest solo project I have ever undertaken and at times it has left me feeling very alone. At the same time, I have never had more help and support than I have had over these many years.

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Jay Kaufman took me on as a student early on, even though the research topic was a bit outside his usual area of work. He never let me drop off his radar. For years, he regularly sent me articles, and even job postings, related to syphilis, incarceration, and STDs. I received each email as a reassuring note that he still believed in me and wanted me to carry on.

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Throughout the years, we picked up a few more members (Sue Hall and Eric Miller). One by one, the group did what it set out to do – defend dissertations and graduate. By the summer of 2004, I was the last one left and everyone vowed to stick with me until the end. Then our collective world came crashing in with the sudden death of our dear Rebecca James (Baker) and her unborn daughter Alexandra Jane. We were all

devastated and though I didn't realize it at the time, I wasn't able to regroup and face the dissertation again for over a year.

When I did hit the books again, the members of the dissertation group were right there with me, though few of us remained in Chapel Hill. Through email and phone calls, they, and another good friend Annie McNeill, gave advice, reviewed drafts, celebrated each step as a small victory, and always maintained that I would finish. Despite being a strong candidate for ABD status (full time job, young children), no one ever suggested that I drop out. The only questions were "WHEN are you going to finish and HOW can I help?" To these remarkable women (and Eric!) I owe a depth of gratitude that can not be repaid. It will be a true honor to join you as an alumna of the UNC School of Public Health.

Even though my colleagues in the dissertation group finished long before I did, they were at least in a position to understand the issues I was facing. Family and friends without PhDs did not have this perspective. I can only assume that it was pure love that kept your support and reassurances coming despite my many delays. Believe me, I needed that love and I thank you. I especially want to thank Aunt Inez who did a great deal of babysitting in the name of the dissertation completion 'cause'.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

Abbreviation	Definition
AIDS	Acquired Immune Deficiency Syndrome
AOC	NC Administrative Office of the Courts
ART	Automated Reagin Test (syphilis screening test)
Assoc	Associated with
CDC	US Centers for Disease Control and Prevention
CLIA	Clinical Laboratory Improvement Amendments
CSF	Cerebrospinal fluid
CSW	Commercial Sex Work
Ct	Chlamydia trachomatis
DHHS	Department of Health and Human Services
DIS	Disease Intervention Specialists
Dx	Diagnosis
EL	Early Latent Syphilis
F	Female
FTA-ABS	Fluorescent Treponema Antibody Absorption test (syphilis confirmatory test)
Gc	Gonorrhea
GEE	Generalized Estimating Equations
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
Hetero	Heterosexual
HIV	Human Immunodeficiency Virus
HMA	High Morbidity Area
HPV	Human Papillomavirus
HSV	Herpes Simplex Virus (genital herpes)
Hx	History of
IDU	Injection Drug Use(r)
LET	Leukocyte Esterase Test (marker for Ct, Gc infection)
M	Male
MHATP	Microhemagglutination-*Treponema pallidum* test (syphilis confirmatory test)
MSM	Men who have Sex with Men
MSM/IDU	Men who have Sex with Men and Inject Drugs
OCR	Optical Character Recognition
OR	Odds Ratio
Prev	Previous
PS	Primary & Secondary Syphilis
PSEL	Primary, Secondary and Early Latent Syphilis (early syphilis)
RPR	Rapid Plasma Reagin test (syphilis screening test)
Rx	Medication
SEP	Syphilis Elimination Project

Abbreviation	Definition
Sex PN	Sex Partner(s)
SEXDM	Trade Sex for Drugs or Money
SLPH	NC State Laboratory of Public Health
STD	Sexually Transmitted Disease
Syph	Syphilis
TB	Tuberculosis
TP-PA	*Treponema pallidum* Particle Agglutination test (syphilis confirmatory test)
Trich	Trichmoniasis infection
TRUST	Toludine Red Unheated Serum Test (syphilis screening test)
Tx	Treatment
VDRL	Venereal Disease Research Laboratory test (syphilis screening test)
w	With

I. REVIEW OF THE LITERATURE

1.1 INTRODUCTION

Incarcerated populations are at high risk for sexually transmitted diseases (STD)[1] and screening in correctional settings is highly recommended by the Centers for Disease Control and Prevention (CDC)[2, 3]. Jails offer an opportunity for broad impact due to high turnover and short durations of stay[4, 5]. Screening jail inmates at booking serves as a form of community screening, often reaching individuals that do not otherwise have contact with the health care system. A study of syphilis diagnosis and partner notification found that compared to other venues, jail screening identified more 'high value' syphilis cases with high likelihood of transmission to others[6].

Jail screening for syphilis was implemented in 7 county jails (located in 6 North Carolina counties) as part of the CDC Syphilis Elimination Effort (SEE). The program was launched in 1999 after CDC found that that over 50% of reported primary and secondary syphilis cases in the United States came from just 28 counties[7]. North Carolina has six counties in the project, more than any other state. Since 1999, new case rates in North Carolina have declined dramatically, in part due to the success of SEE efforts to improve clinical services, surveillance, outbreak response, and community awareness. However, an ongoing reservoir of transmission remains and jail screening may play a key role in accessing this important group for case detection and treatment.

Epidemiologic linkages between syphilis and human immunodeficiency virus (HIV) have been extensively documented[8-16]. Syphilis is also posited to increase susceptibility to subsequent HIV infection[17]. Both the CDC and the North Carolina Department of Health and Human Services (NC DHHS) recommended that all persons

screened for syphilis under SEE programs also be tested for HIV though only two of the seven jails chose to do so.

As of 2007, the CDC still recommended screening jail inmates for syphilis[3] though much of the funding for Syphilis Elimination had been reduced[18]. At around this same time, another division of CDC made sweeping changes to its policies, including recommendations for widespread HIV testing in health care settings, including jails and prisons[19]. Many of the jail screening programs formerly funded under SEE are now funded as HIV testing projects and new protocols must be designed with HIV as the primary objective.

Personnel and other constraints limit the number of inmates that can be screened on any given shift in the jails. It is therefore desirable to focus efforts on those inmates at highest risk for testing positive. Any protocols used to determine which inmates to screen require not only effectiveness but also ease of use in the jail setting.

The goal of this dissertation was to use SEE jail surveillance data (2002-2005) to describe the prevalence of syphilis, HIV, and associated risk factors in North Carolina jail populations and to develop and test screening algorithms to target screening efforts. The descriptive information provided can assist prevention programs both within the jail and out in the community in identifying and understanding their clients. The algorithms were designed to enhance the effectiveness of screening in currently participating jails. An assessment of HIV and syphilis screening costs was also done to address the issue of adding syphilis to HIV jail screening programs.

1.2 SPECIFIC AIMS

The specific aims of this dissertation are as follows:

1.2.1 Aim 1

To (a) examine the prevalence of syphilis and associated risk factors in male and female North Carolina jail inmates, (b) develop predictive models for syphilis infection based on demographics and self-reported risk factors, and (c) to use the models to develop and test a risk score to be used to improve the effectiveness of the jail screening program.

1.2.2 Aim 2

To (a) examine the prevalence of syphilis, HIV, syphilis-HIV coinfection, and associated risk factors in male and female inmates in two NC jails, (b) develop predictive models for infection with HIV and either syphilis or HIV, (c) to use the models to develop and test a risk score to be used to improve the effectiveness of the jail screening program, and (d) to conduct a cost assessment of the HIV program alone and the incremental cost of adding syphilis to an existing HIV screening program.

1.3. BACKGROUND AND SIGNIFICANCE

1.3.1 The natural history of syphilis

Cases of syphilis can be diagnosed at one of several different stages of infection, with differing implications for ongoing disease transmission. Correct diagnosis and staging of a syphilis case is an involved process that goes beyond simple laboratory

results. It is necessary to understand the complexity of this disease in order to fully appreciate the methods of data collection and outcome measures proposed in this study.

Stages of Infection

Syphilis is caused by infection with the bacteria *Treponema pallidum*. Transmission is primarily through sexual contact. It is also remotely possible for syphilis to be spread parenterally and all US blood supplies are screened. Transmission via needle sharing is thought to be rare[20]. Pregnant women can also pass the infection to their infants in utero resulting in congenital syphilis.

Untreated syphilis in adults will evolve through a series of stages defined by symptoms and duration of time since original infection. Correct diagnosis of these stages is critical for understanding the epidemiology of the disease and the potential for ongoing transmission.

The first stage (primary syphilis) is characterized by the presence of one or more chancres at the site of infection (usually genital, sometimes oral or anal). This lesion first appears 10 – 90 days after initial infection. The lesion is most often painless and heals in a few weeks. Untreated, the disease will then move to the next phase (secondary syphilis). The classic symptoms of this stage are a rash on the palms of the hands and soles of the feet and enlarged lymph nodes. Other symptoms can include a flu-like syndrome (fever, sore throat, malaise), and hair loss (alopecia). Left untreated, these symptoms will also resolve within a few weeks. At this point, the patient will become asymptomatic. Approximately 25% of untreated patients will relapse into a recurrence of secondary symptoms and then return to an asymptomatic state[21, 22]. Up until the first full

year after the initial infection, this asymptomatic (and relapse) period is called early latent syphilis. The first three stages combined (primary, secondary, and early latent) are together called early syphilis.

After the first full year of infection, the patient will move into the stage called late syphilis. Most patients with late latent syphilis will have no further complications (late latent syphilis) but approximately a third will go on to develop tertiary syphilis[20, 22]. Such patients can be in late syphilis for many years without noticeable symptoms. Meanwhile, the spirochetes of *T. pallidum* can invade many different organ systems causing tumor-like growths called gummas. These may eventually become physically apparent if affecting bone, skin, or mucosal tissues. Tertiary syphilis can also be fatal, particularly when cardiovascular or nervous tissue has been affected[20, 22-26].

Syphilis treatment

Fortunately, syphilis remains relatively simple to treat. Penicillin has remained the first line of therapy since the 1940s and no known antibiotic resistance to it has developed[20, 22, 27]. Early syphilis can be effectively treated with a single subcutaneous shot of long-acting benzathine penicillin. Late stage patients may require up to three shots over a period of three weeks. Patients allergic to penicillin are either sensitized to penicillin and then treated or treated with an alternate regimen of doxycycline or azithromycin[20, 28]. Macrolide resistance (to azithromycin) has been detected in at least one study[20]. Penicillin remains the treatment of choice generally and is the only recommended treatment for pregnant women[20, 28].

Sexual transmission of syphilis

During the (approximately) 3-4 week period between initial infection and the development of a primary lesion, infected individuals can not transmit syphilis[21]. Upon development of the lesion, patients become infectious to their sexual partners and remain so for the entire period of early syphilis (the first year of infection). Transmissibility is especially high for the primary and secondary stages and drops off during the early latent stage. Identifying and treating early syphilis cases is critical to halt ongoing transmission and control outbreaks. When late stage syphilis cases are identified, the primary benefit is to the patient who needs treatment to prevent the serious sequelae of late stage syphilis.

Congenital syphilis

Congenital syphilis is an even more serious outcome of adult syphilis infection. Many infected infants will die in utero resulting in spontaneous abortion or stillbirth. Those born alive can have very serious sequelae including bone and dental abnormalities, deafness, and nervous system damage. Women can pass the infection to their infants in utero as early as the 9th week of pregnancy. The likelihood of transmission is highest when the mother has early syphilis but it is important to note that the infectious period for congenital syphilis can last up to 8 years past the date of her initial infection. For this reason, finding female syphilis cases at any stage of infection is critical to prevent continuing cases of congenital syphilis[20, 29].

Laboratory testing

At this time, most syphilis testing is done with intravenous blood samples. New tests that use saliva samples are currently under evaluation but have not entered general use[30]. When neurosyphilis is suspected, cerebrospinal fluid (CSF) samples may also be taken.

Syphilis testing is done in two steps. The first test is done with a highly sensitive non-treponemal assay RPR (Rapid Plasma Reagin) test or a TRUST (Toludine Red Unheated Serum Test) and results in a titer (level of dilution at which the assay still reacts positively). Titers are from low to high 1:1, 1:2, 1:4, 1:8 … 1:1024, a higher titer indicating a greater concentration of antibody in the blood. Initial testing can also be done with a more simple test known as a STAT RPR which essentially gives a yes/no reaction but no titer. There are a number of factors that can cause these tests to give false-positive results including advanced age, other infections, cancer, autoimmune diseases, pregnancy, and drug use[20, 22]. Whether quantitative (titered) or qualitative, initial positive tests should be followed by a highly specific confirmatory test.

Confirmatory testing is done using a treponemal-specific assay, most commonly the TP-PA (*Treponema pallidum* Particle Agglutination) test or MHATP (microhemagglutination-*Treponema pallidum*) test. Under certain conditions, the more complicated FTA-ABS (Fluorescent Treponema Antibody Absorption test) may also be done and CSF samples are tested using the VDRL (Venereal Disease Research Laboratory) test. Any of these tests can eliminate false-positive non-treponemal tests but once a person has ever been infected with syphilis, these tests will be positive for life in

most cases[28]. So, if the patient has a documented past history of syphilis, there is little point in doing a confirmatory test.

Patients may exhibit extremely low titers in the first weeks of infection before the body has built up an immune response. After that, patients in the early stages will often have quite high titers. Successful treatment should cause the titer to drop but for many patients, it will never disappear entirely. There are a lot of other factors that can affect the titer level so, an individual titer may not be very informative but a titer history on an individual patient often is. Importantly, if a patient with a known history of syphilis infection and successful treatment is seen to experience a four-fold titer increase (for example, 1:4 increasing to 1:16), reinfection should be suspected[28].

Stage diagnosis

Syphilis testing and diagnosis are complex. A diagnostic test alone does not supply adequate information to accurately diagnose and stage a syphilis case[27, 31, 32]. Lab test results should be followed with a patient interview to determine if and when symptoms were present. If the patient is currently experiencing symptoms of primary or secondary syphilis, the stage diagnosis is relatively straightforward. However, if the patient has progressed to one of the asymptomatic stages, more information is needed. Sometimes this approach will not yield results. For example, women often can not recall the painless chancre because it was inside the vagina and not visible to them. Recall of the classic palmar/plantar rash of secondary syphilis can also be missed when patients have particularly dark skin. In such cases, correct staging of a known, infected sexual partner may assist in estimating the date of original infection.

Thorough patient interviews and partner notification procedures are necessary to correctly distinguish early latent syphilis cases (asymptomatic, less than one year from infection) from late latent cases (asymptomatic, greater than one year from infection). Such policies are not applied equally in all states, making primary and secondary syphilis diagnoses the only truly reliable ones for comparative purposes. For this reason, and because primary and secondary cases have the highest sexual transmission potential, CDC reports that aggregate data to describe national trends or compare states to one another focus on primary and secondary syphilis. The extent of these diagnosis errors was documented in a CDC chart review of syphilis reports in six jurisdictions which found that half of the reported early latent cases were misclassified. In contrast, over 94% of primary and secondary syphilis reports were classified correctly[31].

North Carolina has an excellent system of Disease Intervention Specialists (DIS) who provide contact tracing and partner notification for all syphilis and HIV cases in the state. The program has exhibited success rates of approximately 98% in locating and interviewing suspected cases[33]. For this reason, confidence in the validity of early latent syphilis diagnoses is high and it is appropriate to describe the North Carolina trends in terms of 'early syphilis' (primary, secondary, and early latent).

1.3.2 Context and history of syphilis

Syphilis is unique among sexually transmitted diseases. It has been well known since the late Renaissance period in Western Europe and is the first STD for which effective testing and treatment were developed, in the early 20th Century. This long history permits archaic perceptions of disease to pervade modern ones. For this reason, present-day syphilis carries a stigma and emotional impact not commonly associated with

other STDs such as gonorrhea and chlamyidal infection. This unique context affects syphilis prevention, detection, and treatment programs including those proposed in this study.

Europe

Syphilis as we know it first appeared in Europe around 1495. There remains to this day considerable disagreement as to whether or not Columbus brought the disease back with him from the New World[34, 35] or if the disease was European in origin and evolved from a milder form[36], or from yaws, which is caused by a similar spirochete[35]. Others have posited that the disease existed far longer and that some Biblical references to 'leprosy' could be attributed to syphilis[34]. In either case, the massive troop movements associated with a French attack on Naples during 1494 propagated the disease rapidly across Europe. By 1498 the disease had spread to India and by 1505 to China[35].

Much of what we know about it today is from the 1530 'Poeme de Contagione' which described how the early epidemic took hold and most interestingly, how the symptoms seemed to have changed over time from one more characterized by ulcers to one predominantly characterized by gummas[34, 36]. During this early period, there was no stigma associated with the disease and special hospitals were created to treat the infected with mercury[37], despite the fact that venereal spread was well understood[34].

For the next 350 years, syphilis remained in Europe but was often misconceived. Doctors mistook gonorrhea for another stage of syphilis[20, 22, 34, 38] until the primary, secondary and early latent stages were formally described by Ricard in 1837[20, 22, 38]. It wasn't until the end of the 19th century that the complexities of late syphilis and

congenital syphilis were finally understood. The spirochete itself was identified by German researchers in 1905 and a test to identify infected individuals (the Wasserman test) was developed in 1906[20], though few physicians had access to it in the first years of its existence.

United States

Soon after its development, the Wasserman test was put to use for widespread testing of soldiers and those about to be married. A survey of US army recruits in 1917 revealed that 6% were positive for syphilis infection[39]. The Venereal Disease Division of the US Public Health Service was created in 1918 and states began to collect surveillance data on cases in the 1930s[40]. By 1938 twenty-six states had laws that forbade marriage of infected persons. That same year, congress passed a bill to provide funding for local venereal disease control programs and by the end of 1941 there were over 3000 clinics functioning in the US[39]. During World Wars I and II, the Army conducted massive "venereal disease" prevention campaigns that included syphilis testing[39].

In the early 1900s, lengthy, toxic treatments involving mercury, bismuth, and arsenic were used with some success[39, 41]. In 1943 the new drug penicillin was found to be effective against both syphilis and gonorrhea[20, 38]. This development had an enormous impact within just a few years; by the end of 1944 the US Army had treated over 100,000 patients and reported cure rates from 90-97%[38].

The availability of testing and treatment most certainly led to improvements in health status of the US population through the treatment of infected individuals and the prevention of new cases. However, the military and marriage campaigns of the 1940s

may have caused other damage. During the War, syphilis was often portrayed as a weapon of the Axis powers: it debilitated soldiers and made them unable to fight and when brought home to "pure" American wives and children it destroyed the country's future. This association of syphilis with both moral failure and, indirectly, treason, may have contributed to the unique stigma associated with the disease today.

The Tuskegee Syphilis Study

The Tuskegee Syphilis Study began at the crossroads of this time of discovery and ended forty years later in scandal. The study began in 1932, prior to the existence of an effective cure. The desire of the US Public Health Service researchers was to observe the medical outcomes of late stage syphilis. They enrolled 600 African-American sharecroppers in Macon, Alabama in their 'study'. The men were observed without treatment, even after it became medically available in 1943. Much was learned about the progress of late stage syphilis but at a terrible price. It is estimated that 28-100 men died of syphilis throughout the course of the study which finally ended in 1972 when a reporter from the Associated Press exposed the study to the media[42]. A formal apology to the men and their families was made by President Clinton in 1997.

The legacy of the Tuskegee Syphilis Study has been to exacerbate black mistrust of public health and other medical personnel. Many wrongly believe that the men in the Tuskegee study were purposely infected with syphilis by the government doctors. This view is so prevalent that the CDC website addresses the issue directly in the 'Tuskeegee frequently asked questions' page[43]. Mistrust of the health care system may prevent some infected people from seeking care and may ultimately contribute to ongoing transmission.

1.3.3 Context and history of HIV

In stark contrast to syphilis, HIV has a very recent history of high emotions and rapid change. As a result, HIV infection is treated differently than any other infectious disease in the eyes of politicians, public health officials, and the general public. Understanding this context is useful for framing questions posed in this dissertation.

It is generally accepted that the epidemic "began" in July of 1981 when CDC noticed increases in two rare disorders (Kaposi's sarcoma and pneumocystis carinii pneumonia) among gay men in New York and California[44]. It is now known that there were cases of HIV infection dating back to the 1950s but at the time it was brand new. It was known as a cluster of symptoms and opportunistic infections and it wasn't at all clear that it was an infectious disease. Many names were used, including GRID (gay-related immune deficiency).

By December of 1981, the acronym 'GRID' was already out of date as the first cases were reported among injection drug users[45]. Over the next year, the CDC reported cases of the syndrome in Haitians[46], hemophiliacs[47], transfusion recipients[48], and newborns[49]. Reports of a similar disease came in from Europe and Africa as well. In September of 1982 the CDC began to refer to the disease as acquired immune deficiency syndrome (AIDS)[50]. Based on the groups affected, an understanding of sexual and bloodborne transmission evolved. The discovery of the etiologic agent was several years away.

Working simultaneously, the Pastuer Institute in France[51] and the National Institutes of Health in the United States[52] both reported discovery of the virus that caused AIDS. It later became clear that they had both isolated the same virus (LAV to the

French, HTLV-3 to the Americans). Human immunodeficiency virus (HIV) was a name proposed in 1986 to resolve the dispute between the two laboratories[53].

The first breakthrough for AIDS patients came in 1987 with the announcement that an old cancer drug azidothymidine (AZT) was effective in warding off some of the opportunistic infections in AIDS patients[54]. For many, the victory was short-lived as the virus developed resistance to the drug. A 1994 study showing that AZT might be effective in reducing mother to child transmission was welcome news[55]. A series of other more effective drugs were introduced in the coming years and US AIDS deaths declined in 1996, the first decline since reporting began[56].

Throughout this early period, there was a great deal of fear surrounding the new disease. New risk groups were constantly being identified and the precise modes of transmission were not clear. Gay men and Haitians of all sexual persuasions were banned from donating blood. Infected health care workers faced discrimination in the workplace. In 1985, thirteen year-old Ryan White was banned from attending school in Indiana[57]. AIDS was also added to the list of diseases for which immigrants could be barred entry to the United States. In protest, the International AIDS Society (IAS) moved its 1990 conference from Boston to Amsterdam and has not held a conference on US soil since[58]. The AIDS community, largely gay men, responded to this environment with strength and organization. Groups such as ACT UP (AIDS Coalition to Unleash Power) brought recognition to issues as diverse as drug company price gouging and federal policy regarding funding for needle exchange programs.

The tone of these early years has had lasting effects on HIV policies in the United States. Fear of discrimination has meant that today HIV information is afforded levels of

security well beyond those for other infectious diseases. This fact is well illustrated by the surveillance data. At first, the disease was classified as a syndrome (AIDS). Later, when antibody testing became available, activists were concerned about the possibility of health departments having a list of everyone with HIV and fought for anonymous testing. States with this policy might know how many positive tests were done in a given year but could not calculate any true prevalence rates because there was no way of knowing how many of the tests were duplicates.

CDC issued recommendations in 1999[56] and 2005[59] urging states to move toward name-based reporting. As of the July 2005 letter, all states had moved to some form of HIV reporting but 14 were of limited value nationally because they were not name-based. The list included states with some of the largest cities, and presumably, the most organized activists: California, Illinois, Massachusetts, New York, Oregon, Washington. As of April, 2008, all 50 states had finally adopted the same name-based reporting scheme[60]. The fact that it took over 20 years to get all states reporting a brand new, invariably fatal disease is quite extraordinary and illustrates the social complexity of HIV.

1.3.4 Current epidemiology of syphilis

Syphilis in the United States

With widespread use of penicillin, US primary and secondary syphilis rates declined dramatically from over 500 cases per 100,000 population in 1945 to less than 150 cases per 100,000 in 1955[61]. Rates continued to decline through the mid 1970s (to around 10/100,000). In the mid 1980s rates began to climb again in an outbreak associated with the twin epidemics of HIV and crack cocaine[62]. This epidemic peaked in

1990 with 20.3 cases of primary and secondary syphilis per 100,000 population[7]. By 2000, national P&S syphilis rates had declined to the lowest ever recorded since 1941 (2.2/100,000 population)[61]. Since that year, overall rates have increased slightly each year from 2001 to 2004[63]. These increases have been associated with documented outbreaks of syphilis among men who have sex with men in a number of US cities[64, 65].

Congenital syphilis rates generally follow the pattern of early syphilis rates among adult females. In recent years, US congenital syphilis rates peaked in 1991 (107.3 cases/100,000 live births), one year after the highest adult rates, and have been declining steadily since to 8.8 in 2004[63].

Syphilis epidemiology is marked by inequalities of age, race, gender, and geography. Within the US, syphilis rates in the South (AL, AR, DC, DE, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA, WV) have long exceeded those in other areas of the country[63, 66]. The region reported 48% of all US primary and secondary syphilis cases in 2004[63]. In the last 20 years, the Southern P&S syphilis rate peaked in 1990 at around 33 cases/100,000 population. Since that year, gaps between the regions have narrowed and rates in all regions declined until 2001 when rates began to rise again.

The highest P&S rates are currently reported among males in the 35-39 year-old age group (12.4/100,000 in 2004) and among younger females age 20-24 (3.0/100,000 in 2004)[63]. This gender disparity is indicative of long-term trends of higher male rates. Throughout the 1980s the gap between them was fairly wide (around 2-3 times higher). As rates for both genders declined after 1990, the gap narrowed to a low of 1.2 times higher in 1996[67]. Since then, the gender disparity has increased, driven by outbreaks among MSM in several cities (Figure 1). In some of the most affected cities, the 2004

male to female rate ratios are dramatic (181.4 in San Francisco, 40.5 in St. Petersburg, FL) while in other areas, the epidemic appears to be largely heterosexual (1.3 in Albuquerque, Newark, and Jacksonville, FL)[67].

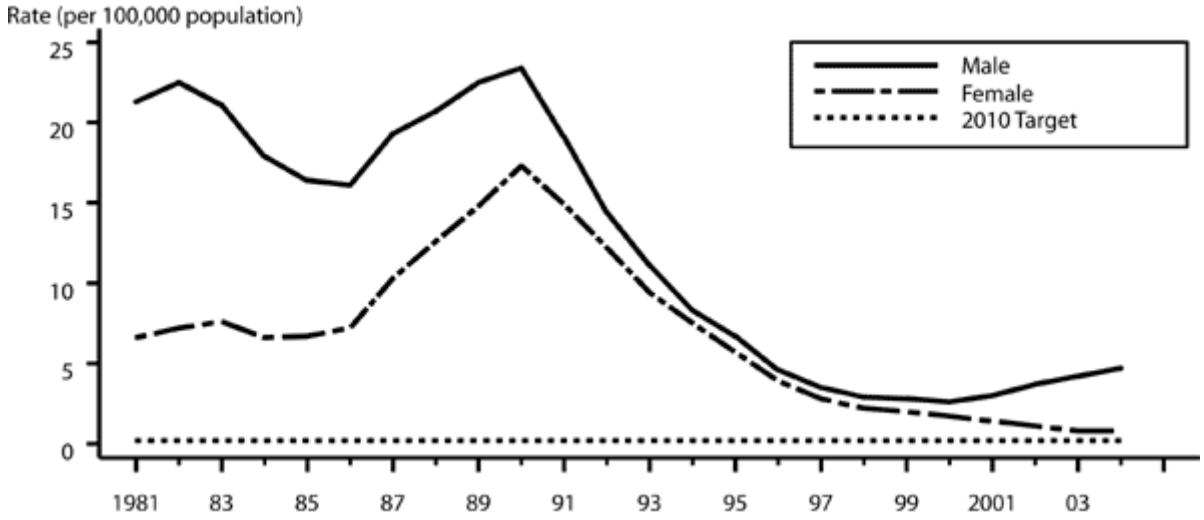
Severe racial disparities mark the most dramatic and disturbing trend in US syphilis epidemiology (Figure 2). When national P&S syphilis rates peaked in 1990, rates among non-Hispanic blacks were approximately 50 times higher than the rates among non-Hispanic whites[67]. Rates for other racial minorities were also higher than those for non-Hispanic whites but to a far lesser degree. In the following years, rates among all racial and ethnic groups followed overall trends of decline through 2000 and then slight increases. In 2004 the black P&S syphilis rate was 5.6 times higher than that for non-Hispanic whites, a great improvement but a still unacceptable ratio[67].

Grassly and colleagues have developed a model based on host immunity responses to explain the periodic rise and fall of US primary and secondary syphilis rates[68]. However, this model assumes that the same populations are at risk over time. A more stratified analysis reveals that syphilis peaks in 1982, 1990, and 2000 involved very different subpopulations[64]. Concurrent HIV epidemics have also been an important factor both in facilitating transmission and in decreasing the number of susceptibles[15].

Syphilis in North Carolina

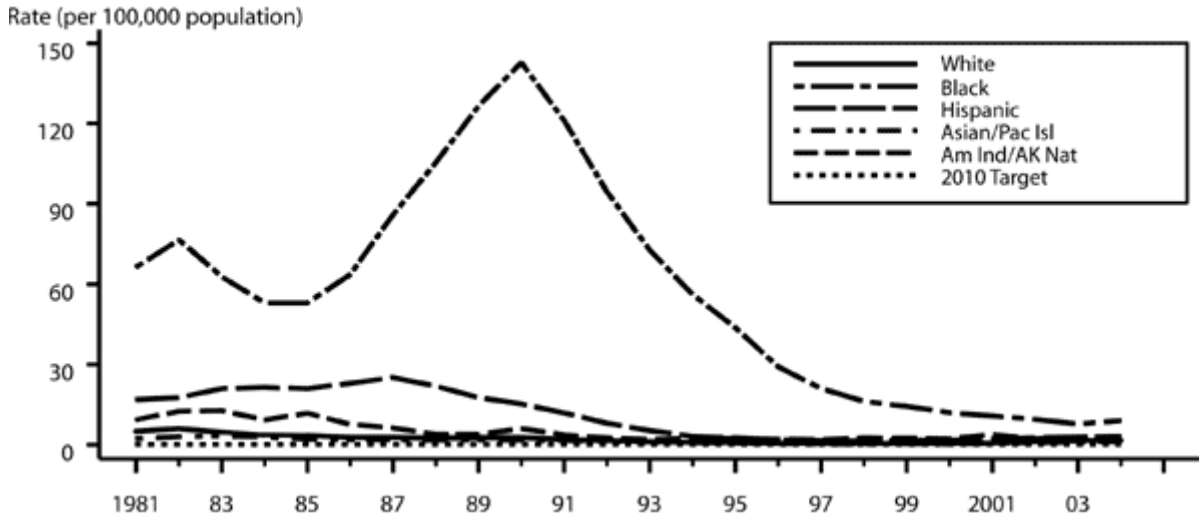
North Carolina is a state disproportionately affected by syphilis. When the primary & secondary syphilis rate peaked in North Carolina in 1992, it was nearly three times higher than the national rate that year (36.2 vs. 13.3/100,000)[69]. From 1993-2003, North Carolina ranked in the top 10 states in primary and secondary syphilis rates and in

Figure 1.1: Primary and secondary syphilis – Rates by sex: United States, 1981-2004 and the Healthy People 2010 target



Note: The Healthy People 2010 target for P&S syphilis is 0.2 case per 100,000 population.
Source: CDC STD Surveillance Report, 2004[63]

Figure 1.2: Primary and secondary syphilis – Rates by race and ethnicity: United States, 1981-2004 and the Healthy People 2010 target



Note: The Healthy People 2010 target for P&S syphilis is 0.2 case per 100,000 population.
Source: CDC STD Surveillance Report, 2004[63]

the top 20 for congenital syphilis rates. In 2003 North Carolina dropped to a rank of 19th among states with a primary and secondary syphilis rate of 1.8/100,000 with n=152 cases reported[70]. That rate has since increased to 3.6 for 2006 and a slightly higher rank of 12th with n=309 cases reported[71].

Within the state, the demography of early syphilis cases (primary, secondary, and early latent) was often distinct from the national trends. From 2002-2006, early syphilis cases were most frequently reported among 20-39 year-old males and females[72]. Since 1990, the male to female ratio of early syphilis cases remained close to one for more than a decade, evidence of a largely heterosexual epidemic[72]. While the number of cases among both men and women declined each year from 2000-2003, the ratio of males to females rose steadily from 1.0 in 2000 to 1.5 in 2003. The number of early syphilis cases reported among men began to increase in 2004 and MSM outbreaks in several cities were identified[72]. Cases among women rose in 2006.

Syphilis also disproportionately affects minority populations in North Carolina. The vast majority of early syphilis cases were among non-Hispanic blacks (approximately 70% per year, 2000-2006) though they make up only 22% of the State's population. Racial disparity among men has generally declined in recent years. An outbreak in 2001 caused a spike in Native American cases that year but otherwise, the general trend for all racial and ethnic groups has been declining early syphilis rates from 2000-2004. Rates for black non-Hispanic and Hispanic males began to increase again in 2004. Black males suffer the greatest disparity with a 2000 early syphilis rate of 50.5/100,000, 21 times higher than the non-Hispanic white rate for that year. This

disparity narrowed to 7 times higher in 2006. Hispanic disparity dropped from 9 to 2 times higher than white rates[72].

For women, early syphilis rates for all racial and ethnic groups are falling but the disparity between the races is increasing because the white rates are dropping the fastest. During the 2001 outbreak, the Native American women actually experienced rates more than 30 times higher than the white rates but the current disparity is just 2 times higher. Black disparity increased from 9 to 17 and for Hispanics the increase was from 4 to 9 times higher[72].

1.3.5 Current epidemiology of HIV

HIV in the United States

National trends in HIV infection have been difficult to assess. In the early years of the epidemic, the only data available were for AIDS cases. At that time, no treatments were available so progression to AIDS was much more rapid and certain. Still, AIDS data was not really ideal for estimating the incidence of new HIV infections because there was a delay between infection and AIDS. In the late 1990s, new treatments dramatically slowed progression of disease, making the use of AIDS data to estimate HIV incidence even more problematic. Through 2007, AIDS cases were the only measure that had been consistently reported for all 50 states[60]. The Ryan White Care Act used AIDS cases to allocate funding until a 2006 reauthorization incorportated HIV infection data for the first time[73].

By the end of 1988, over 82,000 cases of AIDS had been reported to CDC, 91% of them among men[74]. The majority of these were white MSM[75]. About 70% of cases among heterosexual men, women, and children were of black or Hispanic race/ethnicity.

For women, injection drug use (either the patient or a sex partner) was associated with half of white AIDS cases and three quarters of black and Hispanic cases[75]. At this time in 1988, nearly all patients died within five years of their AIDS diagnosis. AIDS was responsible for 10% of all deaths among US men age 25-44 and 2% of all deaths for women age 25-44[74].

Ten years later, the epidemic had grown in both size and scope. By this time, there were effective treatments available for HIV infection, prolonging progression to AIDS and death. AIDS reports began to represent failures of public health; HIV infections that should have been identified and patients that should have been treated before developing AIDS. Over 44,000 cases of AIDS were reported in 1998 alone and nearly a quarter of them were among women[76]. For men, MSM remained the highest risk factor (53%), followed by IDU (27%). The majority of female cases (61%) were attributed to heterosexual transmission while only 12% of male cases had that risk. Racial disparities grew; only 36% of male and 17% of female cases were among whites[76].

More recent data indicate that the distribution of AIDS cases seen in 1998 is largely repeated in 2006. There were over 36,000 cases reported that year and about a quarter of them were female[77]. Heterosexual transmission was the highest risk factor for women (73%) followed by injection drug use (24%). Among men, slightly more cases were attributed to MSM (59%) and heterosexual transmission (17%) and less to IDU (16%)[77].

HIV in North Carolina

Name-based reporting of HIV infection has been required by law in North Carolina since 1990[72]. Anonymous HIV testing was discontinued in 1997 which means that the reporting data from 1998 forward theoretically includes all persons diagnosed with HIV. This discussion of HIV infection in North Carolina will use the measure 'HIV disease' which is the first report of HIV infection for an individual, regardless of stage of infection (HIV infection only or HIV infection and meeting AIDS case diagnosis criteria).

New HIV disease reports in North Carolina were at their peak from 1992-1995, averaging over 2000 reports per year. This same period also had the highest number of syphilis case reports and the highest HIV prevalence found in the Survey of Childbearing Women[72]. HIV disease reports dropped below 1500 per year in the late 1990s, rising again in 2001. Currently about 1700 new cases are reported each year. Of these new HIV reports, about 30% are new AIDS cases which indicates lost opportunities for screening.

HIV disease reports in NC have consistently been the highest among persons age 30-49[72]. A recently identified outbreak among college students in the state has brought new attention to the disease in younger age groups[78]. The North Carolina epidemic is also marked by substantial racial disparities. In 2006, 66% of HIV disease cases were reported among non-Hispanic blacks though they make up only 22% of the state population[72]. Hispanics represented 8% of HIV cases and just 6% of the population.

Among men, the largest number of HIV disease cases reported in 2006 were attributed to MSM activity (69%) and most of the rest to heterosexual sex (24%). North Carolina differs from the national AIDS data in that the proportion of cases associated

with injection drug use is very low. Among men only 4% were IDU and 2% MSM/IDU[72], compared to 18% and 5% in the CDC AIDS data[77]. For women only 11% of NC cases were associated with IDU compared to 24% of national AIDS cases. The HIV epidemic in North Carolina women is almost exclusively connected to heterosexual sex (86%).

1.3.6 Twin epidemics of syphilis and HIV

Epidemiology

It would seem obvious that individuals at risk for one sexually transmitted disease would be at risk for another STD because the same risk behavior (unprotected sex) is associated with both infections. These joint risks, however, are not equally distributed among populations and it has been long understood that certain STDs tend to 'travel' more often together. Since the earliest days of the HIV epidemic in the US, syphilis has been associated with HIV. Studies of HIV-infected populations have documented high rates of incident syphilis infection[16, 79] and syphilis studies have established HIV infection as a consistent risk factor[9, 10, 12, 13]. Likewise, other studies have shown syphilis to be a predictor of HIV infection[8, 11, 14].

To a certain extent, the association of these two epidemics is a function of the similar sexual networks in which the diseases happen to travel. Biologic explanations have also been documented. Fleming and Wasserheit's comprehensive review formally established the association between sexually transmitted infections and ongoing HIV transmission. Their case was strongest for the ulcerative STDs (syphilis, chancroid) in which the STD both increases infectiousness (viral shedding) and susceptibility[17]. Studies

of syphilis biology reveal that the same immune cells that are most sucsceptible to infection by HIV were found in high concentrations at the site of syphilis lesions[22].

Risk Behaviors

Syphilis and HIV cases come from a similar group of susceptible individuals. Despite the reports of recent outbreaks among men who have sex with men[64, 65], sexual networks that include drug users, incarcerated populations, and those who trade sex remain an important reservoir of syphilis infection. Case-control studies in US STD clinics (using non-syphilis patients as controls) have found syphilis to be associated with trading sex for drugs or money[80, 81], reporting a greater number of sex partners[12, 80, 81], use of crack or cocaine[80, 81], and reporting a history of incarceration[12]. Other US case-control studies that used reported cases of adult syphilis[82] or congenital syphilis[83, 84] and community-based controls found associations with trading sex for drugs or money[82], reporting more partners[82], and use of cocaine[83, 84]. A cohort study of street-recruited injection drug users in Los Angeles also found incident syphilis infection to be associated with trading sex for drugs or money, reporting a greater number of partners, crack smoking, and cocaine injection (as opposed to injection of other drugs in this IDU population)[85]. A behavioral survey of female detainees in Chicago found that 32.5% report trading sex for drugs or money and 18.8% reported injection drug use[86]. These risks are themselves linked as prostitution and drug possession/sale are among the most common reasons for arrest[87].

Surveillance data for HIV infection are painstakingly collected and already include a behavioral risk component. Injection drug use, heterosexual sex with high risk

partners, and for men, MSM sex have all been identified as high risk activities. Other behavioral studies have found that like syphilis, HIV has also consistently been associated with trading sex for drugs or money[88], illicit drug use[11, 14, 88], and history of incarceration[11, 14].

1.3.7 Syphilis and HIV in incarcerated populations

Jails and prisons

Because both syphilis and HIV are highly prevalent in incarcerated populations, numerous screening programs to detect new infections have been proposed and/or implemented in jails and prisons across the US. It is very important to distinguish the difference between these two types of institutions and the purpose of screening in each. It is also important to note that some states and localities operate correctional systems that combine jail and prison into one facility. North Carolina is one of 44 states that maintains separate jail and prison systems[89].

Jails are locally operated (city or county) and serve to house persons arrested and awaiting trial and those sentenced to short terms of generally less than one year. The average inmate stays in jail for less than two days[4], most posting bond and awaiting trial outside jail. Others remain in custody longer because they are unable to post bond or a judge has required that the individual await trial under custody. A much smaller proportion of inmates are sentenced to short terms (less than one year) and serve their time in the local jail. Those sentenced to longer terms would be transferred to a prison under state or federal jurisdiction. In North Carolina, only about 23% of the jail population at any given time are serving sentences; the remainder are pretrial detainees[90].

Because most inmates are housed for only a matter of days, conditions are crowded and opportunities for inmate recreation are limited, decreasing the opportunities for sexual contact (and ongoing transmission) within the institution. In many cases, the screened inmate will have been released long before screening test results have returned from the lab. In such settings, STD screening programs serve as community-level screenings, reaching a population that often has limited contact with other health care services and screening opportunities.

Prisons are generally under state or federal control and are designed to house inmates sentenced to terms of one year or longer. Essentially all prison inmates will have spent some time in jail before trial, sentencing, and finally entering prison. Screening for STDs in this setting has very different functions: to maintain the health of the inmate population while they are in custody and prevent ongoing transmission within the facility.

Screening incarcerated populations for syphilis

Syphilis screening programs have been implemented in prisons and jails and have consistently found syphilis rates many times higher than the general population. Studies of female inmates have found syphilis prevalences ranging from 1.4-22.2%[8, 13, 14, 82, 91-99] while male screening finds prevalences from 0.6%-5.7%[8, 11, 92-95, 98, 100, 101]. Several studies that did not stratify results by gender found 0.1-2.0% syphilis prevalence[102-104]. The number of cases detected through screening will be affected by the level of disease in the communities from which the inmates arise and screening and control practices there. However, studies that include both male and female inmates have consistently found higher syphilis prevalence among women[8, 92-95, 98].

Another reason for the width of these ranges is the wide variety of syphilis case definitions used. As previously described, syphilis case diagnosis is complex and requires titer history, treatment history, and patient interview in order to be complete. Table 1.1 describes some of the case definitions used in increasing order of completeness. For a detailed summary of syphilis screening studies in US incarcerated adults, please see Appendix A.

As stated above, female inmates consistently show higher prevalence of syphilis than their male counterparts. Syphilis is also more likely to be detected in inmates in older age groups (≥ age 30)[91-94, 101] and among those of Black[91, 93, 94, 98, 101, 104] or Hispanic[94, 101] race-ethnicity. One study also reported an association with low education[101] and another with unmarried status[98].

Only a small number of studies directly assess the relationship between arrest charges and syphilis outcome. Cohen and colleagues found no association in their study of male arrestees in Los Angeles while Beltrami et al found a weak association with misdemeanor (vs. felony) status in New Orleans[98]. Felony theft charges were found to predict syphilis case status for male inmates in one study[93]. Among females, charges related to drugs[13] and prostitution[13, 93] were significant. Less directly, Farley and colleagues found high numbers of syphilis cases among women incarcerated for prostitution (10%) and drug charges (7%)[82] and Blank et al documented a high rate (8.1%) of incident syphilis among recidivist female inmates in New York City[96].

Even fewer studies collected data related to behavioral risk and made direct comparisons to syphilis status. Past history of STD was predictive of syphilis for both males[101] and females[13]. History of injection drug use was associated with female

Table 1.1: Case Definitions used in Syphilis Screening Studies

Case Definition	Studies used
Screen test +, Confirmatory test +	(Altice 2005)[14], (Solomon 2004)[102], (Altice 1998)[11], (Beltrami 1997)[98], (Bickell 1991)[99], (Weisfuse 1991)[8]
Screen test with high titer (≥1:8)	(Finelli 2002)[92], (Mertz 2002)[94]
Screen test with high titer (≥1:8), Confirmatory test +	(De Ravello 2005)[91]
Screen test +, Confirmatory test + if negative at baseline, Screen test + with 4-fold titer increase if positive at baseline	(Blank 1999)[96]
Screen test +, Confirmatory test +, Treatment history if available	(Kahn 2002)[93], (Rich 2001)[13], (Silberstein 2000)[95], (Blank 1997)[97], (Farley 1990)[82]
Full case diagnosis and staging: Screen test +, Confirmatory test +, Treatment history, Patient interview, Staging	(Chen 2002)[100], (Heimberger 1993)[104], (Cohen 1992)[101]

syphilis[13] while history of cocaine use and reporting ≥3 sex partners in the last 90 days were associated with male cases[101].

Screening incarcerated populations for HIV

Like syphilis, HIV is highly concentrated in incarcerated populations and screening programs have been implemented to improve case detection in correctional settings. HIV prevalences for male inmates range from 0.8-16.1%[8, 11, 100, 105-108] and for females from 1.0-25.8% [8, 14, 91, 106-108]. Studies that did not stratify by gender found prevalences from 2.3% to 16.8%[102, 103, 109]. Studies that included data for both males and females found consistently higher prevalence of HIV infection among females[8, 106-108].

The factors associated with HIV infection in incarcerated populations are similar to those for syphilis. Higher prevalences have been found among those in older age groups[11, 14, 91, 105, 107] and among those of Black[11, 14, 91, 103, 105, 107] or Hispanic[8, 11, 14, 105]

race-ethnicity. None of the reviewed studies directly assessed the relationship between arrest charges and HIV status.

A limited number of studies examined the associations between risk behaviors and HIV infection. Men who reported sex with other men, either with or without IDU were at increased risk for HIV infection[108]. Injection drug use was identified as a risk factor among males[11, 105, 106, 108], females[14, 106], and mixed gender populations[107]. Heroin use was also associated with both male and female HIV infection[8]. Altice and colleagues found use of crack cocaine and history of any STD associated with infection in males[11]. The same group also found non-injection drug use, commercial sex work, and recidivism associated with HIV in females[14].

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II. METHODS

2.1. PRELIMINARY STUDIES

2.1.1 The Syphilis Elimination Effort

In 1995, the CDC convened a meeting of experts and researchers to discuss the issue of persistent high rates of syphilis in the southeastern United States in an era when US rates were declining to all time lows[1]. Over the next several years, much work was done and numerous articles published describing the ways in which syphilis had become highly concentrated in the US[1-5] and discussing issues in syphilis control[6-12]. The CDC examined 1998 data and determined that over 50% of all U.S. primary and secondary (P&S) syphilis cases were reported from just 28 counties. This concentration of disease and the fact that rates were at all-time lows provided an opportunity for the possible elimination of U.S. syphilis transmission. The disease has no animal reservoirs and identification and treatment of all early cases can effectively halt ongoing transmission. In October of 1999, CDC announced the beginning of The Syphilis Elimination Effort (SEE) which provided funding to the 28 high-morbidity areas (HMAs) for enhancements in surveillance, outbreak response, clinical and laboratory services, health promotion and community involvement[13].

2.1.2 Syphilis Elimination in North Carolina

North Carolina was a unique and important player in the Syphilis Elimination Effort. It had more SEE counties than any other state (five) and unlike the majority of SEE counties in other states, several in NC were rural or had only small cities. The State of North Carolina received extra funding to prevent syphilis in these counties. The HIV/STD Prevention and Care Branch in the North Carolina Division of Public Health

coordinated many of the SEE activities and had several CDC assignees designated to the project. The team determined that a 6th county (Durham) should be included in the SEE work because syphilis was a significant problem there, even though it did not make the CDC list of 28. Table 2.1 shows the P&S syphilis rates in these counties and places them in context with the state and US as a whole.

The CDC also provided extra funding (above and beyond the regular SEE funding) to 3 counties as demonstration sites for Syphilis Elimination. These included Marion County, IN (Indianapolis), Davidson County, TN (Nashville) and Wake County, NC (Raleigh).

As part of the enhanced surveillance component of Syphilis Elimination, screening for syphilis in jail populations was recommended by CDC. Four of the six SEE counties began screening early on in their Syphilis Elimination activities. However, little information was collected to further the objective of enhanced surveillance. Modifications were made to the existing testing protocols in 2002 and new jails were added to the project. As of the fall of 2002, seven jails in the cities listed in Table 2.2 were participating in the project. Screening personnel in the jails provided counseling and education on syphilis and other STDs, collected risk factor information from the inmates, and drew blood for screening.

Table 2.1: Primary and Secondary Syphilis Cases and Rates, North Carolina, US, 2000-4

Location	2000		2004	
	Cases	Rate/100,000 pop	Cases	Rate/100,000 pop
DURHAM	18	8.0	12	5.1
FORSYTH	24	7.8	3	0.9
GUILFORD	69	16.3	38	8.8
MECKLENBURG	45	6.4	40	5.3
ROBESON	58	47.0	16	12.7
WAKE	32	5.1	20	2.9
All NC	483	6.0 state rank = 2	193	2.3 state rank = 15
All US	5,979	2.1	7,980	2.7

Sources: NC HIV/STD Surveillance Report 2004, CDC STD Surveillance Report 2004

Table 2.2: North Carolina Syphilis Elimination Effort Counties and Major Cities

County	Primary City	City Population (Census 2000)	County Population (Census 2000)
DURHAM	Durham	187,035	223,314
FORSYTH	Winston-Salem	185,776	306,067
GUILFORD	Greensboro	223,891	421,048
	High Point	85,839	
MECKLENBURG	Charlotte	540,828	695,454
ROBESON	Lumberton	20,795	123,339
WAKE	Raleigh	276,093	627,846

Source: North Carolina State Center for Health Statistics

2.2. Research Design and Methods

2.2. RESEARCH DESIGN AND METHODS

2.2.1 Project Description

Goals and Rationale for Jail Screening Evaluation

Both the North Carolina HIV/STD Prevention and Care Branch leadership and Syphilis Elimination partners at CDC were very interested in evaluating all aspects of SEE activities, including jail screening. One of the primary objectives of the jail screening program was to monitor the prevalence of syphilis in the jails as part of enhanced surveillance. In this sense, jail detainees serve as a sentinel population which may provide early warning regarding new outbreaks of syphilis in the community. Another goal of the evaluation was to directly assess the role of jail screening in syphilis case detection. Assuming that jail screening is deemed valuable with respect to both surveillance and case detection, a final objective of the project was to use the collected data to inform and guide future screening efforts as syphilis rates decline and the need for more targeted screening is warranted. To this end, the first aim of this dissertation was to develop screening algorithms for targeted syphilis screening.

In the years since Syphilis Elimination began, the funding climate has changed with important consequences for the jail screening program. In the past two years, the funding for SEE has been cut dramatically[14] but the recommendation to screen jail inmates for syphilis remains intact[15]. Meanwhile, the HIV Division of CDC announced a series of new recommendations, including screening for HIV in jails and prisons[16]. The end result has been that NC has been able to keep most of the former SEE jail screening programs in operation by converting them to HIV testing programs. The second aim of this dissertation was changed from a syphilis-centered study to the development of HIV

testing algorithms and examination of the addition of syphilis screening to HIV testing programs in the jails.

2.2.2 Study Population

All inmates entering NC jails (n=102)[17] are assessed upon entry (within the first hours of arrival) for wounds or other medical conditions requiring immediate attention. This inquiry includes major chronic illnesses that require treatment (such as diabetes) and infectious diseases such as tuberculosis that might pose a danger to other inmates or jail staff. Since most jail inmates have a very short duration of stay in the facility, medical screening of inmates at this stage is generally minimal and confined to immediate concerns. Approximately half will bond out in the first 48 hours and many others will do so in the first two weeks. Once an inmate has been in the facility for a full two weeks, the focus of the jail medical staff shifts. At this point it is likely that the inmate will be in the jail for a longer stay and the focus of medical attention shifts from short term to long-term concerns. Inmates undergo a thorough medical evaluation called "14-day physical" which includes screening tests for a number of diseases. These differ by jail but most of the time this includes syphilis screening.

The Syphilis Elimination jail screening project (n=7 jails) was intended as a form of community screening and aimed to reach the large number of inmates that would not be accessed through the 14-day screening process. Ideally, the goal was to reach inmates in the first 24-48 hours before they posted bond. Whenever possible, the screening took place at or near the intake area of the jail which provided access to inmates very shortly after their arrival and often before they had been assigned to a cell. The physical layout of the jail and the availability of correctional staff to provide security determined whether or

not this was feasible. If not, the screening sometimes took place in the housing areas of the jail. In these situations, the program was generally screening inmates who had been in the facility longer than a day but shorter than two weeks.

The screening program included both male and female inmates. At this point there were no guidelines used to determine who would be screened. However, due to the importance of screening women to prevent congenital syphilis, SEE staff were advised to screen as many female inmates as possible.

2.2.3 Data Collection

Syphilis data collection form

North Carolina began receiving Syphilis Elimination funding in 1999 and by the spring of 2001 four jails had begun syphilis screening programs (Durham, Forsyth, Robeson, and Wake). The SEE staff working at each jail developed their own data collection forms. Two sites collected only demographic information while the other two opted to collect risk factor information. Examination found that the risk information was inadequately designed, not systematically collected, and differed between the two sites. It became clear that an adequate evaluation of jail screening would require that standardized data collection procedures and tools be developed and implemented in all sites.

In 2001 a standardized data collection instrument was developed for the project. The current jail screening staff were very involved with the design to ensure that it would meet their needs. To reduce redundant effort, the new form was designed to serve as both the data collection form and the lab slip to go with the blood sample to the lab for testing. The form also had to meet a Clinical Laboratory Improvement Amendments (CLIA) requirement that the name of the receiving laboratory be printed on the form. For ease of

use, the form was designed to scan into the computer using Optical Character Recognition (OCR) technology which allows the use of regular handwriting rather than filling in bubbles. A variable was added to the form to allow for the evaluation of screening activities in settings other than the jail.

For a copy of the syphilis data instrument, please see Appendix C. Please note that although there are six different versions of the form (one for each county), only one is shown.

HIV data collection form

The two jails in Guilford county (Greensboro and High Point) offered HIV testing to inmates screened for syphilis under this SEE project. These tests were funded with CDC HIV counseling and testing (CTS) monies and processed at the State Lab in Raleigh. A standard form, used for all CTS testing in the state, was used to collect the information related to the HIV test. There was also a place on the syphilis form to indicate whether or not an HIV test was done and to record the form ID number for the HIV test. The HIV forms were sent with the samples to the State Lab. Syphilis screening form data were later matched to SLPH data to obtain the HIV test results. For a copy of the HIV data instrument, please see Appendix C.

Data Collection Procedures

The new form was put to use in all seven SEE jails in 2002. Prior to implementation, screening personnel were trained in the use of the new form. By September 2002, all 7 jails were both screening inmates for syphilis and collecting data.

Additional site visits were conducted after implementation to address any issues and ensure compliance with established procedures.

In all jails, the screening process began with the screener providing syphilis information and education to the inmates followed by administration of the questionnaire and drawing blood for testing. When screening took place at booking, this was often an entirely 'one on one' process. In other situations, the education component was delivered to a group and then individuals were taken aside for the risk interview and blood draw. The trained screener asked all the questions of the inmate and filled out the form (forms were *not* to be filled out by the inmate). In some cases the person asking the questions was the same as the person drawing the blood sample, in others the screening was done with a team of two.

The jail screener then tore off the back portion of the data collection form (which served as the lab slip) and sent the sample to the appropriate laboratory. If the sample was positive and no confirmatory test was on file for that patient, the sample was sent to the State Lab (SLPH) in Raleigh for confirmatory testing. In Robeson county, a STAT RPR (non-titered) test was performed locally and then all samples were forwarded to the State Lab for titered screening and confirmatory tests as needed.

The rest of the form was either held by the screener or forwarded to a designated person who waited for the first titered results to come back and marked them on the form. The forms were then sent the HIV/STD Prevention & Care Branch.

In the two jails also offering HIV testing, a separate HIV form was filled out in addition to the syphilis form and sent with the sample to the SLPH in Raleigh for testing.

The HIV form number was recorded on the syphilis form so that the data could later be matched to obtain the test results.

Case Followup

All positive samples detected through this project were reported to the appropriate health department and investigated according to standard procedures, described below.

By North Carolina law, all positive syphilis and HIV tests must be reported to the local health departments and ultimately to the state. In some cases (as with HIV tests performed by private labs) the state is notified first and then the county. This notification is often done by phone and case investigation begins immediately. The HIV/STD Prevention and Care Branch has a system of eight Regional Offices that manage contact tracing and partner notification activities for syphilis and HIV. Positive test information is forwarded from the county or state to the appropriate office (based on the patient's county of residence) for followup. These offices maintain databases of patients with positive syphilis tests for their region because titer history is needed to determine if a positive test represents a past case who is serofast, a past case who may be reinfected, or a possible new case of syphilis. Likewise, it is necessary to determine whether or not an incoming positive HIV test represents a previously reported infection.

Patients who may represent new cases of syphilis or HIV will be contacted and interviewed by Disease Intervention Specialists (DIS). This interview has many purposes: behavioral counseling to prevent ongoing transmission, identification of partners who may have been exposed and who require testing themselves, diagnostic staging and assuring treatment of syphilis cases, and gathering of data regarding individual and

community risks associated with infection. When these interviews are complete, the resulting data is gathered and entered into the patient management database for that region. New cases are formally reported to the State Health Department in Raleigh for inclusion in official statistics and reporting to CDC.

Inmates positive for syphilis and/or HIV under this SEE project were reported to the state health department and case investigations were conducted as needed. This took place independently from the marking of syphilis test results on the SEE jail screening forms and their submission for data entry.

2.2.4 Outcome Measures

Jails forwarded syphilis screening forms to the State Health Department in Raleigh via FedEx about once a month. FedEx was used for security of the data, not to expedite delivery. Incoming syphilis screening forms should include patient demographics, the date of the blood draw, risk factors, screening location, and the preliminary titered result. Upon receipt, all forms were reviewed for completeness and attempts were made to locate missing information whenever possible.

Completed forms were separated by syphilis test result. Negative screens were ready for data entry at any time. Forms for positive inmates were matched to surveillance data at both the regional and state levels determine final case status. After this thorough assessment, each positive was assigned a code as seen in Table 2.3. This complete case diagnosis approach is rarely used in syphilis screening studies and is a distinct strength of this study.

2.2.5 Data Management

The SEE jail screening forms were scanned using optical character recognition (OCR) software to 'read' the letters, numbers, and checkmarks in the boxes. For this project, the system had been configured to require human verification of all fields. The software (Cardiff Teleform v7.0) provided its best 'guess' as to what the data field contains and the human verifier confirmed or corrected the information. For checkboxes, the software was nearly always correct in its assessment of whether or not there is or is not a mark in the box. Fields that contain letters or numbers required much closer attention. Numeric fields were best because there are only 10 possible responses. Alphanumeric fields were the most difficult due to the high number of possibilities (n=36) and problematic similarities between 0 and O, 1 and I, 8 and B, etc. Errors were highest when the data collector failed to write within the lines. Despite these issues, the scanning system worked very well. Most of the verification time was spent on the handful of fields with letters and numbers. Clicking through the checkboxes, which were almost always correct, was quite fast. It took less than one minute to "verify" a scanned form. This was much faster than manual data entry and approximates a double entry system.

Verified form data was output to a Microsoft Access database which was later imported into SAS for data management and analysis. SAS programs were run to check the data for inconsistencies (males who are pregnant, illegal dates, etc.) and create composite variables.

Table 2.3: Outcome Measures for Syphilis Screening Data

Code	Outcome	Notes
000	False Positive	Applied when titered result is positive but confirmatory test is negative
710	Primary Syphilis	Requires confirmation of specific physical symptoms on the patient.
720	Secondary Syphilis	Requires confirmation of specific physical symptoms on the patient.
730	Early Latent Syphilis	Applied to asymptomatic cases in which it can be confirmed that the infection was acquired *less* than one year ago. Requires confirmation of specific physical symptoms on the patient or a partner.
740	Late Latent Syphilis of Unknown Duration	Applied to asymptomatic cases in which meet very specific criteria: unable to document that infection was acquired less than one year ago, age 13-35, and titer ≥ 32
745	Late Latent Syphilis	Applied to asymptomatic cases in which it can not be documented that the infection occurred less than one year ago and that do *not* meet the criteria above.
765	Neurosyphilis	Requires confirmation of specific physical symptoms on the patient.
777	Past Syphilis Case	Applied when the patient record confirms a past case of syphilis but the current titer does not indicate a new infection. These patients are not interviewed. Also called 'record search closure'.
888	Administrative Closure	Some cases are closed without interview because they fall into a demographic not likely to be a new case (generally older persons with very low titers). This is done to prioritize field interview assignments.
999	Lost to Follow Up	Applied when DIS attempt but are unable to locate and interview a person with a positive screening test.

HIV Data Entry

SEE jail screening forms from Guilford County included a check box to indicate whether or not the patient had a test for HIV. This was the only HIV variable on the

syphilis screening form (see Appendix C). The rest of the information associated with the HIV test was completed on the HIV form (Appendix C) and sent to the SLPH along with the sample for analysis. This CDC form was first adopted for use when North Carolina offered anonymous HIV testing (prior to 1997) and identified patients using numbers preprinted on the form.

When the jail screening staff in Guilford county screened an inmate for syphilis and HIV, they marked the box for "HIV test" on the syphilis form and indicated the form number associated with that test. These numbers were later matched against an HIV testing database from the SLPH to obtain HIV risk information and test results for those inmates.

Multiple Observations for Individuals

Some inmates appeared in the dataset multiple times because they were arrested more than once during the four-year study period. SEE jail screening staff were instructed to re-test individuals that had previously been screened if they had been out of jail and at risk for syphilis in the interim. These observations were legitimately 'eligible' to be in the numerator of new syphilis infections and it was therefore reasonable to retain them in the dataset. Their inclusion, however, could bias the demographic and risk profile towards recidivist inmates because their characteristics were 'counted' multiple times.

Other inmates were re-tested multiple times in order to confirm that treatment of their syphilis case had been effective. The data collection instrument has a box to indicate when testing is being performed for this reason and these 'test of cure' observations were dropped from the dataset.

Missing Data

Information was missing for some variables due to failure of the jail screener to ask for the information, failure of the jail screener to record the information, or inmate refusal to answer questions. Demographic data on each inmate was already been recorded by jail staff as part of the arrest record by the time the syphilis screener had access to the individual. At that point the individual had no reason to refuse disclosure of date of birth or other information since the jail already had this information. If demographic data was missing, it was assumed that it was missing at random. If an inmate had multiple observations in the dataset, demographic data from another observation was used to fill in missing data in another.

Missing data for risk questions were addressed using sensitivity analyses, described in detail in section 2.6.6.

Sample size considerations

One goal of this dissertation project was to develop simple, yet effective, screening algorithms using the fewest possible variables. The limits that the study size placed on the number of possible variables in the models is described here. Table 2.4 illustrates the number of inmates screened in the study and the number found to be cases. These numbers are used to calculate the maximum number of possible variables in the (meaningful) logistic regression model, using the formula below by Harrell[18] where n is the total population screened, n_1 represents cases, and n_0 noncases.

$$MaxVariables = \frac{3 * n_1 * n_0}{n * 10}$$

Table 2.4: Inmates screened for syphilis and HIV in NC Jails 2002-2005 and calculations for maximum number of variables in logistic regression models

	Male	Female
SYPHILIS		
Screened (n)	19,403	4,607
New cases (n_1)	98	57
Noncases ($n_0 = n - n_1$)	19,305	4,550
Max # variables in model	29	17
HIV		
Screened (n)	2,985	641
Prevalent cases (n_1)	34	12
Noncases ($n_0 = n - n_1$)	2,951	629
Max # variables in model	10	4

2.2.6 Study Design – Aim 1

Aim 1 sought to: (a) examine the prevalence of syphilis and associated risk factors in male and female North Carolina jail inmates, (b) develop predictive models for syphilis infection based on demographics and self-reported risk factors, and (c) to use the models to develop and test a risk score to be used to improve the effectiveness of the jail screening program.

Study population and outcome measures

The data for these analyses included all male and female inmates screened for syphilis through the SEE jail screening project in 7 jails in 6 counties, 2002-2005. Data for repeat screening of individuals was used and appropriate statistical techniques were used to account for within-person variation. Separate models were developed for men and women using new syphilis cases as the outcome measure.

Data analysis and statistical methods

Frequencies, distributions, and missing values of the demographic, risk behavior, and syphilis test result data were examined. Variables with excessive missing values were removed from the analysis. Unadjusted odds ratios and 95% confidence intervals were calculated to describe the associations between each covariate and new syphilis infection. Logistic regression for clustered data was used to account for lack of independence between multiple observations for individuals.

Sensitivity analyses were performed to address two key questions. First, data were analyzed using generalized estimating equations and using logistic regression for clustered data. There were no meaningful differences in which variables would have been chosen for inclusion in full models

Predictive models

Candidate variables for the reference or "full" model included those with bivariate $p \leq 0.25$ and others identified from the literature, regardless of p-value. The predictors in the reference model were examined for collinearity using eigenvalues and tolerances. Final models for men and women were developed using manual backward elimination from the reference models. At each step, the variable with the highest p-values was removed until all variables remaining in the model had $p \leq 0.05$. Each successive model was assessed for performance using the Liklihood ratio test and goodness of fit using the Hosmer-Lemeshow test. The area under the receiver operating characteristic (ROC) curves for the reference and final models was also compared.

Risk score development and testing

In order to preserve the multiplicative nature of the logistic models, risk scores were based on the beta coefficients from the models[19-21]. For purposes of comparison, we created three sets of risk scores. The first was a simple summation of the beta coefficients for each risk factor present. These fractional coefficients would not be practical to use in a screening algorithm so they were simplified. Unweighted scores were created by assigning a value of 1 to each factor present, 0 for each absent and summing across all variables. For weighted risk scores, beta coefficients were transformed by multiplying by two and rounding to the nearest whole integer.

Cutoff points for sensitivity and specificity of the models were determined under the assumption that a limited number of tests could be performed in the screening program. We compared cutpoints for screening ≤30%, ≤50%, and ≤70% of the target population. Internal validity of the resulting models and risk score sensitivity and specificity was examined using bootstrap analysis in which the study population was resampled 1000 times with replacement[18].

Sensitivity Analyses

Sensitivity analyses were performed to address two key questions. First, data were analyzed using both generalized estimating equations and using logistic regression for clustered data. There were no meaningful differences in ORs or 95% CI and the same set of variables would have been chosen for inclusion in full models. Logistic regression for clustered data was ultimately used because it allowed the use of likelihood ratio tests and GEE would not.

Second, the data collection instrument did not record yes and no responses to the risk behavior questions. Rather, the box was marked if the answer was yes and left blank if the answer was no. If all questions were asked and the inmate responded no to all of them, the screener was supposed to mark the box 'none' (please see screening form, Appendix C). With this design, there was no way to really know if (a) the screener asked some of the risk questions but not all of them or (b) the inmate refused to answer some of the risk questions but not all of them.

To assess the impact of these coding issues, the data were analyzed two different ways. First, it was analyzed assuming that the form was used correctly. Each time a box was left blank, it was coded as "no". This is the methodology reported in the results for this dissertation. A more conservative coding scheme was also created in which it was assumed that if any one of the risk questions or the "none" box was marked, then all the questions were asked and blanks were set to "no". If none of the risk boxes nor the 'none' box was marked, it was assumed that none of the questions were asked and those responses were all set to "missing" rather than "no". We found that there were no meaningful differences between these two schemes and that using the criteria of bivariate $p<0.25$, the same variables would have been included in the reference model under either one.

2.2.7 Study Design – Aim 2

Aim 2 sought to: (a) examine the prevalence of syphilis, HIV, syphilis-HIV coinfection, and associated risk factors in male and female inmates in two NC jails, (b) develop predictive models for infection with HIV and either syphilis or HIV, (c) to use the models to develop and test a risk score to be used to improve the effectiveness of the

jail screening program and (d) to conduct a cost assessment of the HIV program alone and the incremental cost of adding syphilis to an existing syphilis screening program.

Study population and outcome measures

The data for these analyses included male and female inmates screened for HIV and syphilis through the SEE jail screening project in 2 jails in 1 county, 2002-2005. Some inmates were screened multiple times during the study period. However, because the focus of this study was HIV, not syphilis, the study population was restricted to the first observation (i.e. first arrest) for each individual. Separate models were developed using two outcomes: (1) HIV infection and (2) HIV infection or new syphilis case (hereafter HIV/syphilis). Gender was included as a predictor in both models.

Data analysis and statistical methods

Frequencies, distributions, and missing values of the demographic, risk behavior, and HIV and syphilis test result data were examined. Variables with excessive missing values were removed from the analysis. Unadjusted odds ratios and 95% confidence intervals were calculated to describe the associations between each covariate and the two outcomes (HIV and HIV/syphilis).

Models and risk scores

Separate models for HIV and HIV/syphilis were developed using the same techniques described for Aim 1. The development of the risk scores was also similar. Predicted probabilities and unweighted scores were the same. Several possible methods

for creating the weighted scores were tested. It was determined that simply rounding the beta coefficients from the models to the nearest integer produced the optimal result.

Testing of the risk scores was different for this study. All risk scores were set to cutpoints for hypothetically testing 50% of the jail population. Then the performance of the risk scores (sensitivity and specificity) was assessed for each of three outcomes: HIV only, Syphilis only, and HIV/syphilis. So, even though one of the models was designed to predict HIV infection, the ability of those same criteria to predict syphilis and HIV/syphilis was also examined. Again, internal validity was assessed using bootstrap analysis as described in Aim 1.

Cost Assessment Analysis

To address the issue of whether or not syphilis screening should be included in jail screening programs for HIV, program costs were examined. Four hypothetical cost scenarios based on screening strategy were prepared (standard testing for HIV only, standard testing for both syphilis and HIV, targeted testing for HIV only, and targeted testing for both syphilis and HIV). Fixed costs included salaries for screening personnel and the cost of initial screening tests for all samples. Variable costs included quantitative and confirmatory testing performed on positive screening samples and were dependent upon the number of positive screening tests expected. Prevalence estimates for the standard scenarios were taken directly from the study population and those for the targeted scenarios were taken from the new populations that would be screened using the weighted risk scores from the HIV only model.

Estimates of personnel costs and the number of inmates that could be screened per shift were obtained from the budgets for the North Carolina SEE jail screening project.

Estimated costs for laboratory tests were based on Medicaid reimbursement rates and were taken from an impact analysis performed by the North Carolina Division of Public Health in association with a change in HIV testing laws[22]. Costs per HIV case detected included the cost of HIV screening and confirmatory tests and all personnel costs because the HIV screening program was the funded entity. Since the addition of syphilis screening to the existing HIV program was in question, costs per case detected included only the cost of additional testing.

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III. MANUSCRIPT 1

Screening inmates for syphilis in North Carolina jails: development of a screening algorithm

3.1 ABSTRACT

Background

As recommended by the Centers for Disease Control and Prevention, North Carolina instituted syphilis screening in county jails as part of its Syphilis Elimination program. Resource constraints limit the number of inmates that can be screened on any given shift in the jails. This paper aimed to develop and test algorithms to select inmates for screening at NC county jails.

Methods

This study included inmates screened for syphilis in seven North Carolina jails under Syphilis Elimination in 2002-2005. Study data were matched to surveillance records to obtain true syphilis case status. We created separate models for male and female inmates and used the β coefficients to develop weighted risk scores to predict new syphilis cases. The scores were applied to screening hypothetical proportions of the population and the sensitivity of the resulting cupoints in detecting syphilis was assessed.

Results

For men, the model yielded weighted risk scores with good sensitivity for the detection of new syphilis cases (82.7, 95% CI 75.0 – 90.3) when applied to testing 50% of the available inmates. The model included age, race/ethnicity and history of STD diagnosis. A sensitivity analysis found that background syphilis rate is not a good substitute for race/ethnicity and results in much weaker sensitivity (73.4%). For women,

no model could be developed because only one predictor, cocaine use, was associated with infection.

Conclusions

We recommend targeting syphilis screening for men based on the algorithm developed using race/ethnicity. Due to heightened concerns about congenital syphilis, screening all women is recommended.

3.2 INTRODUCTION

North Carolina is a state disproportionately affected by syphilis. When primary & secondary syphilis rates peaked in North Carolina in 1992, its rate was nearly three times higher than the national rate that year (36.2 vs. 13.3/100,000)[1]. Within the state, the vast majority of reported early syphilis cases are among non-Hispanic blacks (approximately 70% per year, 2000-2004) though they make up only 22% of the State's population[2]. Though much smaller in numbers, non-Hispanic Native Americans make up about 6% of reported early syphilis cases 2000-2004 but just over 1% of the state population[2].

In 1998, the Centers for Disease Control and Prevention (CDC) recognized that over 50% of reported primary and secondary syphilis cases in the United States came from just 28 counties. In response, the CDC launched the Syphilis Elimination Effort (SEE) in 1999[3]. North Carolina has six counties in the project, more than any other state. Since 1999, new case rates in North Carolina have declined dramatically, in part due to the success of SEE efforts to improve clinical services, surveillance, outbreak response, and community awareness[2]. However, an ongoing reservoir of transmission remains. Jail

screening may play a key role in accessing this difficult to reach group for case detection and treatment.

Jails are locally operated and house persons arrested and awaiting trial and those sentenced to short terms of generally less than one year. In North Carolina, about 23% of the jail population at any given time are serving sentences; the remainder are pretrial detainees[4]. Because the average inmate stays in jail for less than two days[5], screening in the jail setting functions as a form of community screening, often reaching individuals that do not otherwise have contact with the health care system.

Personnel and other constraints limit the number of inmates that can be screened on any given shift in the jails. It is therefore desirable to focus efforts on those inmates at highest risk for testing positive. Any protocols used to determine which inmates to screen will require not only accuracy and effectiveness but also ease of use in the jail setting. The purpose of this analysis is to develop and test the performance of syphilis screening algorithms for use in North Carolina Jails.

3.3 METHODS

3.3.1 Study Population

This study included men and women age 18 years and older screened for syphilis in seven North Carolina jails as part of Syphilis Elimination, 2002-2005. No exclusion or inclusion criteria were used to determine who would be screened. However, due to the importance of screening women to prevent congenital syphilis, SEE staff were advised to screen as many female inmates as possible. Refusal rates were not formally tracked but

interviews with jail screening staff have indicated that most inmates who received education also accepted the offer of screening.

3.3.2 Data Collection

Screening procedures varied slightly depending on jail resources. In order to reach the largest number of inmates before they were able to post bond, screening typically took place at or near the intake area of the jail whenever possible. When intake screening was not feasible because of the physical layout of the jail or the availability of correctional staff, screening was conducted in the housing areas of the jail. In these situations, the program was generally screening inmates who had been in the facility longer than a day but shorter than two weeks.

Health department or jail medical staff provided education on syphilis and other sexually transmitted diseases (STD) to inmates alone or in groups and then offered screening. Two of the seven jails also offered HIV testing. Inmates who agreed to screening were then taken aside for the administration of a risk questionnaire and to have their blood drawn for testing. Samples were then forwarded to the appropriate laboratory for processing and the data collection forms went to the NC Division of Public Health for analysis.

As required by North Carolina law, all positive syphilis tests were reported to the local county health department. Reports were then forwarded to the NC Division of Public Health for investigation. For many patients, a past history of treated syphilis and titer readings indicated that the person did not have a new syphilis infection and the case was closed. Individuals with positive tests who were possible new cases of syphilis were contacted and interviewed by Disease Intervention Specialists (DIS). New cases were

staged (primary, secondary, early latent, latent, latent of unknown duration, late with symptoms, neurosyphilis)and then reported to the State Health Department in Raleigh. Positive screening results for this study were matched to surveillance records to determine the outcome of these investigations and final case status.

Inmates screened from 2002 to 2005 were included in this study. The study was approved by the University of North Carolina Public Health and Nursing Institutional Review Board (IRB).

3.3.3 Measures

The outcome for this study is the diagnosis of a new syphilis case of any stage (primary, secondary, early latent, latent, latent of unknown duration, late with symptoms, neurosyphilis). This complete case diagnosis approach is rarely used in syphilis screening research and was possible because the study data were linked to surveillance records that established case status and staging.

The likelihood of acquiring an STD is related not only to individual risk behaviors but also to the likelihood of infection among the chosen pool of sex partners. To account for this concept, we included in our models a measure of background syphilis rate. We chose county rates to approximate communities; North Carolina has 100 counties which generally contain only one major city or town. Due to reporting delays, state surveillance data are typically not available until six months after the close of the year. To ensure that information would be available for implementation of the screening algorithm, we used the early syphilis (primary, secondary, and early latent) rate for two years prior for any given year. For example, the county X rate for 2000 would be applied to an inmate screened in county X in 2002. The SEE counties by definition have a history of high rates

of syphilis so the rates were classified as being in the top 10% or bottom 90% among all 100 NC counties.

Other possible predictor variables from the interview questionnaire include demographic information (gender, age, race/ethnicity, marital status, pregnancy status) and risk behaviors and conditions in the last six months (homelessness, victim of domestic violence, men having sex with men, multiple sexual partners, diagnosis of any STD, trading sex for drugs or money, use of: marijuana, alcohol, injection drugs, or cocaine).

For bivariate and multivariate analyses, the race/ethnicity variable was collapsed to four categories based on prevalence of syphilis in the sample: black/African American non-Hispanic, Native American non-Hispanic, and Hispanic are compared to all other races (white, Asian/Pacific Islander, mixed race, and all others).

3.3.4 Statistical Analyses

Over the four year period of the study, 3,765 of the 18,506 inmates were re-arrested and screened again. Therefore we present frequencies and distributions for all observations and for the first observation only to describe the dataset and population, respectively. We stratified all analyses by gender because (a) important predictors of new syphilis infection vary greatly by gender and (b) the benefits of screening also differ by gender which may necessitate divergent screening plans.

Inmates repeatedly screened were at risk for syphilis each time they re-entered the community, leading us to use all observations in regression analyses. To develop syphilis prediction models, we used unconditional logistic regression for clustered data and obtained robust standard error estimates that adjust for within-subject correlation[6, 7].

A "full" or reference model was developed using candidate variables from the literature, regardless of bivariate p-value, and covariates with bivariate $p \leq 0.25$. Candidate variables were assessed for collinearity by examining eigenvalues and tolerances.

We used a manual backward elimination procedure to reduce the model until all variables remaining in the model had $p \leq 0.05$. The reference and final models were assessed for goodness of fit using the Hosmer-Lemeshow test. The area under the receiver operating characteristic (ROC) curve for the reference and final models were compared to ensure that variables removed did not greatly change model performance.

The final models were used to create risk scores to be used in NC jails for screening. We created three sets of risk scores using the β coefficients from the models[8-10]. First, we summed the β coefficients for each risk factor that was present. This was done for comparison purposes only as it would not be practical to use this system in the field. Next we calculated unweighted risk scores by assigning 1 to each risk factor present and 0 if not present. Finally, we computed weighted scores by transforming the fractional β coefficients to integer values by multiplying by a constant and rounding. We calculated risk scores using several constants and chose to use the ones with the best sensitivity (2 for males, 1 for females).

We applied the risk scores to hypothetically screening different proportions of the total available study population ($\leq 70.0\%$, $\leq 50.0\%$, $\leq 30.0\%$) and obtained cutpoints for screening. Individuals with risk scores at or above the cutpoint would be chosen for screening, those below the cutpoint would not be screened. We then calculated the sensitivity and specificity of these different risk score cutpoints. We performed an examination of internal validity of risk score performance using bootstrap analyses in

which the cohort was resampled 1000 times with replacement[11]. We conducted statistical analyses using Stata SE version 8.0 (Stata Corporation, College Station, TX).

3.4 RESULTS

3.4.1 Study Population

From 2002 to 2005, the North Carolina Syphilis Elimination Project performed 24,171 syphilis screens on jail inmates age 18 years and older. We removed 125 observations with missing screening results and another 36 with positive screening results but no documented outcome (new syphilis case, not a case, etc.). This study sample comprised 24,010 observations from 18,506 different people.

Among the 18,506 individuals represented in the dataset, 14,746 (80%) had only one observation; 2,674 (14%) had two observations and 711 (4%) had three. The remaining 375 (2%) had 4-12 observations. No study participants experienced more than one syphilis event.

Women represented 18% of the total individuals in the study population and 19% of the total observations. The average age at first observation was 32 years old for males and 33 for females. The screened inmates were primarily of black non-Hispanic race/ethnicity (59% of men and 51% of women)(Table 3.1). The study also included many Native Americans (11% of men and 14% of women screened) because one of the six SEE counties has a large Native American population.

Women were far more likely to have a reactive syphilis screening test (8.1% vs. 2.7% for men, OR 3.3, 95% CI 2.7 – 3.9) or to be diagnosed with a new, confirmed

syphilis case (1.2% vs. 0.5% for men, OR 2.5, 95% CI 1.8 – 3.4). Overall only about one in 5 reactive tests represented a new case.

3.4.2 Results for Men

Men who were black non-Hispanic (OR 3.5, 95% CI 1.5 – 8.2) or Hispanic (OR 7.6, 95% CI 3.1 – 18.9) were more likely to be diagnosed with a new syphilis infection compared to whites and others (Table 3.2). Syphilis was also associated with age and STD diagnosis (OR 2.5, 95% CI 1.5 – 4.2). Marijuana use had an inverse relationship (OR 0.6, 95% CI 0.4 – 1.0). In addition, background syphilis rate, reporting multiple sex partners, alcohol use, and cocaine use were all associated enough for inclusion in the multivariate models ($p \leq 0.25$).

The full or "reference" model included all variables significant in the bivariate analysis at $p<0.25$. After variable reduction, the final model included age, race/ethnicity, and history of STD diagnosis (Table 3.3). The ROC areas of the two models were similar (ROC_{ref} =0.761, ROC_{final} =0.755, χ^2 p=0.539) indicating that model performance was retained after variable reduction.

To minimize potential concerns about using race/ethnicity as a screening criterion, we examined background syphilis rate as a possible surrogate in a sensitivity analysis. When background syphilis rate was substituted for race/ethnicity in the final model, the area under the ROC curve decreased substantially compared to the reference model (ROC_{ref} =0.761, ROC_{comp} =0.691, χ^2 p=0.002) indicating that this substitution dramatically reduced the performance of the model.

The weighted risk scores ranged from zero for a white/non-Hispanic man, age 18-24 years with no self-reported STD diagnoses in the past six months to a score of 11 for a Hispanic man, age 45 years or older, with previous STDs (Table 3.3). The use of this model to screen less than 50% of the inmate population had a screening "cutoff" of 4 and sensitivity of 82.7, specificity of 55.0 (Table 3.5). This scoring scheme would detect far more cases than either the unweighted score (sensitivity 15.3) or the weighted score for the comparison model with background syphilis rate substituted for race/ethnicity (sensitivity 73.4). The weighted score model performed consistently when validated using 1000 bootstrap samples.

3.4.3 Results for Women

In contrast to the analysis for males, new syphilis diagnosis was not strongly associated with race/ethnicity or age (Table 3.2). However, several risk behaviors were associated with the outcome: cocaine use (OR 3.1, 95% CI 1.8 – 5.3), trading sex for drugs or money (OR 2.3, 95% CI 1.6 – 4.5), reporting multiple sex partners (OR 2.4, 95% CI 1.4 – 4.0), homelessness (OR 2.1, 95% CI 1.1 – 3.8), and STD diagnosis (OR 2.0, 95% CI 1.2 – 3.5). Background syphilis rate was also associated with new syphilis diagnosis.

As with men, we included all variables significant at $p<0.25$ in the bivariate analyses, and also included age based on a priori expectations ($p<0.26$). After model reduction, only one variable remained: reported cocaine use in the past six months (OR 3.1, 95% CI 1.8 – 5.3) (Table 3.4). The area under the ROC curves for the two models was different and both were substantially smaller than the models for men (ROC_{ref}

=0.701, ROC_{final} =0.636, χ^2 p=0.119) indicating inferior model fit and that predictive value was lost in the model reduction.

With only a single variable in the model, cocaine use, we were unable to produce meaningful risk scores. Screening less than 50% of the population based on this predictor alone yielded a very poor sensitivity of 64.9 (95% CI 52.1 - 77.7).

3.5 DISCUSSION

We developed useful risk scores with good sensitivity to predict syphilis infection in male jail inmates (Table 3.4). Using the weighted risk scores and a cutoff of "4 or higher" for screening, we created a simple algorithm that could be used in the jail setting to select inmates for screening (Figure 3.1). The person conducting the screening would proceed through a series of three questions (age, race, and STD diagnosis in the past 6 months) until the patient reaches a score of "4" and is selected for screening or reaches the end and is not recommended for screening. The results of this study provide a way to screen for syphilis more effectively. Targeted screening is especially important for male inmates because there are more of them in the jails (over 80% in 2006[12]) and their rates of syphilis are lower than rates for female inmates (Table 3.1).

The models were less useful in developing a model to select women for screening. Only one predictor, cocaine use, was strongly associated with syphilis and its sensitivity was poor. Given the higher prevalence of syphilis among female inmates and the potential risk of transmission of syphilis from mother to child, we recommend a policy of screening all women in SEE jails.

The use of race/ethnicity as a criterion for screening for any disease, particularly a sexually transmitted disease, is likely to provoke controversy. Jail inmates are a

marginalized group. Screening for STDs in this setting may perpetuate negative stereotypes. Inclusion of race/ethnicity as a criterion may exacerbate this problem. For this reason, we evaluated the possibility of substituting another variable that was highly correlated with race/ethnicity and would have a high likelihood of association with the outcome. Background early syphilis rate represents the likelihood of exposure to a person with syphilis in a person's home community. We used this parameter as a substitute for race/ethnicity to develop an alternative risk score. Unfortunately, the results of this evaluation were disappointing. Compared to the model with race/ethnicity, the weighted risk score based on background syphilis rate had substantially lower sensitivity (73.4% vs. 82.7%), which corresponds to missing over a quarter of the cases. Inclusion of race/ethnicity would yield nearly 10% more cases with the same number of tests.

Despite the possible problems associated with race/ethnicity as screening criteria, we recommend the use of the screening algorithm we developed (Figure 3.1). Because resources will not allow the SEE to screen all male inmates, the risk score will facilitate targeting the screening program to those men who are most likely to have a new case of syphilis. It is possible that the impact of the sensitive issue may be mitigated somewhat by the realities of the administration of the algorithm. Age and race/ethnicity are routinely recorded in the course of the criminal booking process in the jails. The person performing the syphilis screening assessment would not need to ask these questions again. In practice, most inmates offered screening based on age or race/ethnicity information would not be aware of the criteria. Those who did not meet age or race/ethnicity criteria would be asked a single question: "Have you been diagnosed with a

sexually transmitted disease in the last 6 months?" Those responding "yes" to this question may not be surprised or offended by an offer for syphilis screening.

Personnel using the screening tool would, however, be familiar with the criteria and it is possible that the larger community may also become aware of it. It would be important to incorporate frank discussion of the issue into the training protocol for screening staff. They should be informed that the recommendations are being made after a great deal of research and consideration led to the conclusion that too many cases of syphilis would be missed if the race/ethnicity information were left out. The same would apply to the general public, should the issue arise.

It is tempting to view the truthfulness of self-reported risk behaviors as a validity concern. In our study, high proportions of inmates were willing to disclose behaviors such as cocaine use (14.6% of men, 34.0% of women), and having multiple sexual partners (26.2% of men, 30.8% of women) (Table 3.1), indicating a certain level of trust in the screening staff. However, the aim of this study was not to explain or quantify risk behaviors in this population. Our goal was to develop screening algorithms. When applied in the field, these algorithms will rely on self-reported data therefore the use of such data to develop them is appropriate.

The validity of our results does depend on the classification of the outcome and the representativeness of the study population. As previously described, there was no mechanism in place to document those who refused testing. This would be a problem if the models were meant to be explanatory. Since the implementation of the screening tool in the future would also be under a voluntary testing scenario, our study population should be a reasonable representation of this target population.

We were able to use surveillance records to follow up each of the positive test results in our study population. This true case approach is a distinct strength of this study because it provides a profile of newly diagnosed syphilis cases, the outcome of interest for jail screening programs. A diagnostic test alone does not supply adequate information to accurately diagnose and stage a syphilis case[13-15]. A large proportion of positive screening tests actually represent persons who have had syphilis in the past but are currently disease-free. To correctly diagnose current infection, test results should be compared to the patient's titer history and if necessary, followed with a patient interview to determine if and when symptoms were present. Most research studies are unable to follow up positive screening results in this way and must rely on surrogates that do not actually measure new infections.

The identification of previously undiagnosed syphilis cases through jail screening has benefits at several levels. Transmissibility of syphilis is especially high for the primary and secondary stages and drops off during the early latent stage[16]. Identifying and treating early syphilis cases is critical to halt ongoing transmission and control outbreaks. When late stage syphilis cases are identified, the primary benefit is to the patient who needs treatment to prevent serious sequelae of late stage syphilis. Because women can transmit syphilis to their infants in utero up to eight years past the initial date of their own infection, finding female syphilis cases at any stage is critical to the prevention of congenital syphilis cases[17, 18].

We believe that the models developed would perform well in the SEE screening counties from which the study population was drawn. These counties were the counties with the highest incidence and prevalence of new syphilis cases when they were chosen

for SEE in 1999. Generalization to other counties with much lower rates of syphilis may be more problematic. However, this screening approach may translate well to jail screening programs in other high prevalence counties in the Southern United States where inmate demographics may be similar. The selective screening guidelines developed here can improve the efficiency of jail screening programs for men and reinforce the importance of screening women.

Table 3.1: Characteristics of Inmates screened for syphilis in NC Jails 2002-2005

	MALES				FEMALES			
	All Observations		Individuals (1st obs only)		All Observations		Individuals (1st obs only)	
Characteristic	n	%	n	%	n	%	n	%
SYPHILIS								
Screened	19403	100.0	15098	100.0	4607	100.0	3408	100.0
Reactive Syphilis Test	515	2.7	382	2.5	375	8.1	250	7.3
New Syphilis Case (any stage)	98	0.5	85	0.6	57	1.2	42	1.2
Age								
18-24	5306	27.4	4262	28.2	844	18.3	663	19.5
25-34	6499	33.5	5078	33.6	1776	38.6	1263	37.1
35-44	5226	26.9	3904	25.8	1577	34.2	1148	33.7
45+	2372	12.2	1854	12.3	410	8.9	334	9.8
Race/Ethnicity								
White	3585	18.5	2925	19.4	1386	30.1	1052	30.9
Black NH	11453	59.0	8837	58.5	2261	49.1	1726	50.7
Native Am NH	2468	12.7	1598	10.6	771	16.7	467	13.7
Hispanic	1654	8.5	1507	9.9	139	3.0	117	3.4
Asian/PI	57	0.3	57	0.3	11	0.2	8	0.2
Other/Unknown	88	0.5	84	0.6	22	0.5	21	0.6
Missing	98	0.5	98	0.7	17	0.4	17	0.5
Any Pregnancy Last 12 mo (incl current)								
Yes	--	--	--	--	324	7.0	241	7.1
No	--	--	--	--	2595	56.3	1882	55.2
Missing	--	--	--	--	1688	36.6	1285	37.7

	MALES				FEMALES			
	All Observations		Individuals (1st obs only)		All Observations		Individuals (1st obs only)	
Characteristic	n	%	n	%	n	%	n	%
PSEL Rate in top 10% NC Counties	9189	47.4	6482	42.9	2306	50.1	1546	45.4
RISKS								
Homeless	1220	6.3	952	6.3	634	13.8	456	13.4
Domestic Violence Victim	--	--	--	--	861	18.7	644	18.9
Men Sex w. Men	119	0.6	100	0.7	--	--	--	--
Multiple Sex Partner	5024	25.9	3960	26.2	1488	32.3	1048	30.8
STD Diagnosis	1721	8.9	1341	8.9	863	18.7	604	17.7
Trade Sex for Drugs or Money	927	4.8	724	4.8	943	20.5	620	18.2
Alcohol Use	10637	54.8	8325	55.1	2114	45.9	1560	45.8
Marijuana Use	6461	33.3	4854	32.2	1716	25.5	798	23.4
Injection Drug Use	223	1.2	183	1.2	156	3.4	111	3.3
Cocaine Use	3127	16.1	2210	14.6	1756	38.1	1160	34.0

NH = non-Hispanic, PSEL = Primary, secondary and early latent syphilis

Table 3.2: Bivariate Associations of Demographics and Risk Factors with New Syphilis Case Diagnosis among Inmates screened for syphilis in North Carolina Jails, 2002-2005

	MALES				FEMALES			
Characteristic	Cases	OR	CI	p	Cases	OR	CI	p
Age								
18-24	10	Ref	Ref	<0.01	5	Ref	Ref	0.26
25-34	22	1.8	0.85 – 3.8	--	27	2.6	1.0 – 6.7	--
35-44	39	3.9	2.0 – 8.0	--	19	2.1	0.7 – 5.5	--
45+	27	6.1	2.3 – 12.0	--	6	2.5	0.7 – 8.2	--
Race/Ethnicity								
White/Other	6	Ref	Ref	<0.01	13	Ref	Ref	0.42
Black NH	65	3.5	1.3 – 8.2	--	34	1.7	0.87 – 3.1	--
Native Am NH	7	1.8	0.59 – 5.3	--	9	1.3	0.55 – 3.0	--
Hispanic	20	7.6	3.1 – 18.9	--	1	0.8	0.10 – 5.9	--
Any Pregnancy Last 12 mo (incl current)	--	--	--	--	2	0.5	0.12 – 2.2	0.36
PSEL Rate in top 10% NC Counties	54	1.4	0.91 – 2.0	0.13	34	1.5	0.87 – 2.5	0.15
RISKS								
Homeless	8	1.3	0.64 – 2.7	0.45	14	2.1	1.1 – 3.8	0.02
Domestic Violence Vict	--	--	--	--	10	0.9	0.47 – 1.8	0.82
Men Sex w. Men	1	1.7	0.23 – 12.1	0.61	--	--	--	--
Multiple Sex Partners	19	0.7	0.42 – 1.1	0.14	30	2.4	1.4 – 4.0	<0.01
STD Diagnosis	19	2.5	1.5 – 4.2	<0.01	18	2.0	1.2 – 3.5	0.01
Trade Sex for Drugs or Money	4	0.9	0.31 – 2.3	0.75	23	2.7	1.6 – 4.5	<0.01
Alcohol Use	48	0.8	0.53 – 1.2	0.25	26	1.0	0.6 – 1.7	0.97
Marijuana Use	23	0.6	0.38 – 1.0	0.04	14	1.0	0.51 – 1.7	0.87
Injection Drug Use	1	0.9	0.12 – 6.4	0.91	3	1.6	0.49 – 5.2	0.44
Cocaine Use	20	1.3	0.82 – 2.2	0.24	37	3.1	1.8 – 5.3	<0.01

NH = non-Hispanic, PSEL = Primary, secondary and early latent syphilis

Table 3.3: Males -- Adjusted Odds Ratios and Risk Scores for New Syphilis Diagnosis among Inmates screened for syphilis in North Carolina Jails, 2002-2005

	Reference Model Obs = 19,305 ROC Area = 0.7614		Final Model With Race/Ethnicity Information Obs = 19,305 ROC Area = 0.7555				Comparison Model With Background Syphilis Rate Obs = 19,305 ROC Area = 0.6909			
Characteristic	OR (95% CI)	β	OR (95% CI)	β	W	U	OR (95% CI)	β	W	U
AGE										
18-24	ref	ref	ref	ref	0	0	ref	ref	0	0
25-34	1.7 (0.81 – 3.7)	0.54	1.8 (0.84 – 3.8)	0.58	1	1	1.8 (0.84 – 3.8)	0.58	1	1
35-44	4.3 (2.1 – 8.1)	1.46	4.6 (2.3 – 9.3)	1.53	3	1	3.9 (2.0 – 7.9)	1.37	3	1
45+	6.7 (3.2 – 14.0)	1.89	7.3 (3.5 – 15.0)	1.98	4	1	6.0 (2.9 – 12.4)	1.78	4	1
RACE/ETHNICITY										
White/Other	ref	ref	ref	ref	0	0	--	--	--	--
Black NH	3.2 (1.4 – 7.5)	1.16	3.1 (1.3 – 7.3)	1.14	2	1	--	--	--	--
Native Am. NH	1.9 (0.64 – 5.5)	0.63	1.9 (0.64 – 5.6)	0.64	1	1	--	--	--	--
Hispanic	11.1 (4.3 – 28.4)	2.41	10.8 (4.3 – 27.1)	2.38	5	1	--	--	--	--
PSEL Rate top 10%	--	--	--	--	--	--	1.5 (0.97 – 2.3)	0.39	1	1
RISKS										
Multiple Sex Partners	0.73 (0.41 – 1.3)	-0.32	--	--	--	--	--	--	--	--
STD Diagnosis	2.6 (1.5 – 4.4)	0.94	2.4 (1.4 – 4.1)	0.87	2	1	2.6 (1.5 – 4.6)	0.97	2	1
Alcohol Use	0.77 (0.49 – 1.2)	-0.26	--	--	--	--	--	--	--	--
Marijuana Use	1.1 (0.65 – 1.8)	0.09	--	--	--	--	--	--	--	--
Cocaine Use	1.3 (0.77 – 2.3)	0.29	--	--	--	--	--	--	--	--
Constant	--	-7.44	--	-7.60	--	--	--	-6.59	--	--

ROC = Receiver Operator Characteristic curve, NH = non-Hispanic, OR = odds ratio, CI = 95% confidence interval, β = model beta, W = weighted risk score, U = unweighted risk score

Table 3.4: Females -- Adjusted Odds Ratios and Risk Scores for New Syphilis Diagnosis among Inmates screened for syphilis in North Carolina Jails, 2002-2005

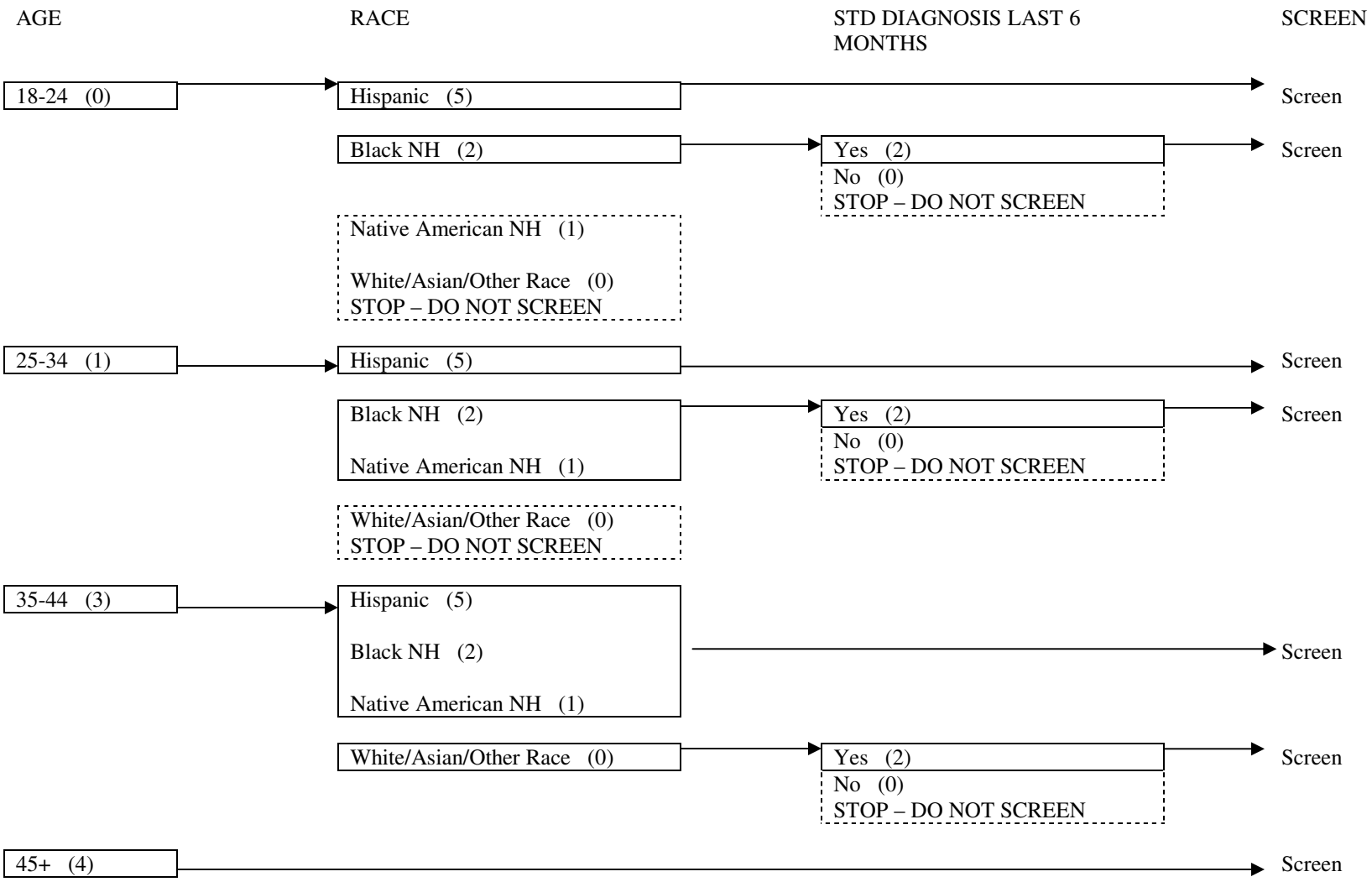
	Reference Model Obs = 4,607 ROC Area = 0.7005			Final Model Obs = 4,607 ROC Area = 0.6357				
Characteristic	OR	CI	β	OR	CI	β	W	U
AGE								
18-24	ref	ref	ref	ref	ref	ref	--	--
25-34	2.1	0.81 – 5.6	0.76	--	--	--	--	--
35-44	1.7	0.63 – 4.6	0.54	--	--	--	--	--
45+	2.3	0.70 – 7.7	0.84	--	--	--	--	--
County PSEL Rate in Top 10%	1.7	0.95 – 2.9	0.50	--	--	--	--	--
RISKS								
Homeless	1.2	0.62 – 2.3	0.18	--	--	--	--	--
Multiple Sex Partners	1.3	0.62 – 2.9	0.29	--	--	--	--	--
STD Diagnosis	1.4	0.74 – 2.5	0.30	--	--	--	--	--
Trade Sex for Drugs or Money	1.3	0.55 – 3.2	0.28	--	--	--	--	--
Cocaine Use	2.0	0.98 – 4.2	0.71	3.1	1.8 – 5.3	1.11	1	1
Constant	--	--	-5.92	--	--	-4.95	--	--

ROC = Receiver Operator Characteristic curve, OR = odds ratio, CI = 95% confidence interval, β = model beta, W = weighted risk score, U = unweighted risk score

Table 3.5: Performance of Selective Screening Criteria among Inmates screened for syphilis in North Carolina Jails, 2002-2005

Scoring Method	MALES Final Model With Race Information (n=19,305)			MALES Comparison Model With Background Syphilis Rate (n=19,305)			FEMALES Final Model (n=4,607)		
% Tested	Cutoff	Sensitivity 95% CI	Specificity 95% CI	Cutoff	Sensitivity 95% CI	Specificity 95% CI	Cutoff	Sensitivity 95% CI	Specificity 95% CI
Predicted Probability									
≤70	0.002	91.8 86.3-97.4	33.3 32.7-34.0	0.004	81.6 73.8-89.4	40.3 39.7-41.0	--	--	--
≤50	0.003	82.6 75.0-90.3	55.0 54.3-55.7	0.004	73.4 64.6-82.4	55.9 55.2-56.6	0.021	64.9 52.1-77.7	62.2 60.8-63.6
≤30	0.008	49.0 38.9-59.1	84.0 83.5-84.6	0.006	56.1 46.1-66.1	70.3 69.7-71.0	0.021	64.9 52.1-77.7	62.2 60.8-63.6
Weighted Risk Score									
≤70	3	91.8 86.3-97.4	33.4 32.7-34.0	2	81.6 73.8-89.4	40.3 39.7-41.0	--	--	--
≤50	4	82.7 75.0-90.3	55.0 54.3-55.7	3	71.4 62.3-80.5	57.5 56.8-58.2	--	--	--
≤30	6	49.0 38.9-59.1	84.0 83.5-84.6	4	53.1 43.0-63.1	72.5 71.9-73.2	--	--	--
Unweighted Risk Score									
≤70	2	87.8 81.1-94.4	39.0 38.3-39.7	2	57.1 47.2-67.1	59.6 58.9-60.3	--	--	--
≤50	3	15.3 8.1-22.6	94.1 93.8-94.4	2	57.1 47.2-67.1	59.6 58.9-60.3	--	--	--
≤30	3	15.3 8.1-22.6	94.1 93.8-94.4	3	9.2 3.4-15.0	98.2 98.1-98.4	--	--	--

Figure 3.1: Syphilis Screening Algorithm – Males



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IV. MANUSCRIPT 2

Should jail-based HIV screening programs include syphilis testing: screening algorithms and program costs

4.1 ABSTRACT:

Background

The Centers for Disease Control and Prevention has recently shifted focus from syphilis to expanded HIV screening in county jails. We address (a) whether or not jail HIV screening should be targeted and (b) whether or not syphilis screening should be added to the HIV screening programs.

Methods

This study includes inmates screened for both syphilis and HIV in two North Carolina jails under Syphilis Elimination in 2002-2005. We created models to predict two different outcomes: HIV only and HIV or syphilis. We created risk scores from the models and assessed sensitivity and specificity of the models to detect HIV only, syphilis only, and either infection. We applied the prevalence estimates from the original study data and from the most optimal models to program cost models in order to assess the additional costs of targeted screening and of adding syphilis to the protocol.

Results

The weighted risk scores from the HIV only model had the best sensitivity for the detection of HIV (82.6, 95% CI 71.2 – 94.0). If inmates are selected for screening based on this model, the sensitivity for detection of new syphilis cases is also good (73.3, 95% CI 56.5 – 90.1). Under this scenario, the overall cost of the screening program increases slightly with targeted vs. not targeted screening (<5.0%). However, the cost per HIV case detected declines dramatically (from $2,189 to $1,262).

Conclusions

We recommend targeting HIV jail screening based on HIV data. In communities with incident syphilis infections, we recommend adding syphilis screening to the HIV protocol.

4.2 INTRODUCTION

Incarcerated populations have high rates of both human immunodeficiency virus (HIV) and syphilis. The HIV prevalence has been found to range from 3.8-25.8% for women[1-5] and 1.8-16.1% for men[1-3, 6-8]. In correctional settings, the highest rates are among women[1-3], older age groups[3-6, 8], and those of Black[3-6, 8, 9] or Hispanic[1, 4, 6, 8] race-ethnicity.

Syphilis rates are also high in correctional settings, from 1.4-22.2% for women[1, 4, 5, 10-19] and 0.6%-5.7% for men[1, 6, 7, 12, 15, 17-20]. Female inmates consistently have higher prevalence of syphilis than their male counterparts[1, 12, 15, 17-19]. Syphilis is also more likely to be detected in inmates in older age groups (≥ age 30)[5, 17-20] and among those of Black[5, 12, 18-21] or Hispanic[19, 20] race-ethnicity.

HIV and syphilis screening programs have been implemented in correctional settings throughout the United States to detect cases and link patients to treatment and care. Jail screening in particular has the capacity for broad impact. Most jail inmates are released in less than two days[22]. Consequently, screening in the jail setting functions as a form of community screening, often reaching individuals who might not otherwise get an HIV or syphilis test. For each case diagnosed, additional cases may be detected through partner notification and contact tracing.

Jail administrators are charged with housing inmates who are awaiting trial or have received a short sentence (generally less than one year). Their primary mission is to maintain the safety of the inmates and the jail employees. Public health programs like STD screening must operate subordinate to that mission. Screening personnel must be escorted by guards to maintain their safety and to ensure that testing supplies such as needles do not end up in the hands of inmates. Even with unlimited health department staff, the availability of guard support would limit the amount of screening that can actually be accomplished. Therefore, screening programs must be designed to screen the right inmates with limited time available.

The Centers for Disease Control and Prevention (CDC) specifically recommended screening for syphilis in jails in the 1999 publication "National Plan to Eliminate Syphilis from the United States"[23]. More recently, CDC funding for the Syphilis Elimination Effort (SEE) has decreased dramatically[24]. At the same time, the agency has provided new funding for the expansion of HIV testing programs, including a large jail screening inititative[25]. An important question is whether continued syphilis screening will fit into this new paradigm. In this analysis, we use data from the Syphilis Elimination jail screening program in North Carolina (2002-2005) to develop screening algorithms for HIV screening with and without the addition of syphilis screening.

4.3 METHODS

4.3.1 Study Population

As part of the enhanced surveillance objective of Syphilis Elimination, the North Carolina Division of Public Health (DPH) conducted syphilis screening in seven county jails in six counties. This study used data collected in the two jails (in one county) that

opted to add HIV testing to their syphilis screening programs. Male and female inmates age 18 and older, screened for both syphilis and HIV from January 1, 2002 to June 30, 2005 were included in the analysis.

4.3.2 Data Collection

Staff from the local health department, jail medical unit, and a local community-based organization (CBO) provided education on syphilis and HIV to inmates alone or in groups and then offered screening. Inmates who agreed to screening were then taken aside for the administration of a risk questionnaire and to have their blood drawn for testing. Staff were encouraged to screen as many women as possible as a means to prevent perinatal HIV transmission and congenital syphilis.

Samples for HIV testing were forwarded to the State Laboratory of Public Health (SLPH) in Raleigh and underwent antibody testing using standard HIV type 1 (HIV-1) enzyme immunoassay (EIA) and Western blot (WB) analysis. Samples negative or indeterminate on EIA were placed in pools of 90 specimens (containing 9 pools of 10) and screened by nucleic acid amplification (NAAT) for HIV-1 RNA as described previously[26]. Samples for syphilis testing were forwarded to the lab at the Guilford County Department of Public Health for screening using Rapid Plasma Reagin (RPR) tests. Positive samples were then forwarded to the SLPH for confirmatory testing using *Treponema pallidum* particle agglutination test (TP-PA) or MHATP microhemagglutination-*Treponema pallidum* test (MHATP). Questionnaires were sent to the NC Division of Public Health for entry and were later linked to test results.

Refusal rates were not formally tracked, but interviews with jail screening staff have indicated that most inmates who received education also accepted the offer of

testing. About 98% of male and female inmates who accepted syphilis testing also agreed to be tested for HIV. The study was approved by the University of North Carolina Public Health and Nursing Institutional Review Board (IRB).

4.3.3 Measures

We conducted two sets of analyses. In the first, we used HIV infection alone as the outcome to reflect the current environment with respect to CDC funding. Samples testing positive for HIV-1 antigen (Western Blot) or HIV-1 RNA (NAAT) were considered to be positive[26]. In the second set of analyses, we used a composite variable of HIV infection or new syphilis case (hereafter HIV/syphilis) to reflect the possibility of adding syphilis screening to HIV screening regimens. The syphilis outcome incorporated initial screening with rapid plasma reagin (RPR), linked to NC syphilis surveillance data to establish the current case status and stage of infection (primary, secondary, early latent, latent, latent of unknown duration, late with symptoms, neurosyphilis).

Potential predictor variables were taken from the interview questionnaire and included demographic information (gender, age, race/ethnicity) and risk behaviors and conditions in the last six months (homelessness, men having sex with other men, multiple sexual partners, diagnosis of any STD, trading sex for drugs or money, use of: marijuana, alcohol, injection drugs, or cocaine). Participants were also asked to report whether they had ever been tested for HIV.

For bivariate and multivariable analyses, the race/ethnicity variable was collapsed into two categories to address the issue of small cell sizes and with the aim of creating a high risk and a low risk group. The high risk category included black/African American non-Hispanic and Hispanic of any race and the low risk group included all other race

ethnicity combinations: white non-Hispanic, Native American non-Hispanic, Asian/Pacific Islander non-Hispanic, mixed race, and all others. Both HIV and syphilis literature support the inclusion of black non-Hispanic and Hispanic in the high risk group[1, 3-6, 8, 9, 12, 18-21].

To describe gender and male sexual risk groups, we created a composite variable with three categories: men who reported having sex with men (MSM), men who did not report MSM (i.e. heterosexual men), and women. The referent category was set to "men who did not report MSM" because this group had the lowest risk for both HIV and syphilis.

4.3.4 Statistical Analyses

We restricted our analysis to the first observation for each individual among persons tested for both HIV and syphilis and for whom valid test results were available. Some inmates were arrested and screened multiple times throughout the four-year study period. Syphilis is fully curable and successfully treated cases are at risk for re-acquiring syphilis each time they re-enter the community. This is not true, however, for HIV which is the primary focus of this study. For each of the two outcomes (HIV infection vs. HIV infection or new syphilis diagnosis), we examined frequencies, distributions and unadjusted bivariate odds ratios for each covariate.

We used multivariable logistic regression to develop predictive models for each outcome. A "full" or reference model was developed using covariates with bivariate $p \leq 0.25$. Candidate variables were assessed for collinearity using eigenvalues and tolerances. We also created and tested interaction terms for the composite sexual

behavior variable (males reporting MSM, males not reporting MSM, women) and each covariate. If a model with the covariate and its interaction term was significantly different from the model with just the covariate using a likelihood ratio test at $p<0.05$, the interaction term was retained in the reference model.

We used a manual backward elimination procedure to create the final model. We examined likelihood ratio tests and the area under the receiver operating characteristic (ROC) curve for each model to ensure that the removal of each successive variable did not significantly reduce model performance. Backward elimination of variables continued until all variables remaining in the model had p values ≤ 0.05. All models were assessed for goodness of fit using the Hosmer-Lemeshow test.

The final models were used to create risk scores to serve as the basis for jail screening algorithms for HIV and syphilis testing[27-29]. The first set of scores directly used the β coefficients from the models. These "predicted probability" scores were closest to the final model but too complex to use in the field and were done for comparison only. The greatest degree of simplicity was achieved with the "unweighted" scores which assigned a value of 1 to each attribute and 0 to each referent. We also developed a "weighted" risk score after testing three methods of weighting to maintain some complexity and prediction based on the β, but providing some relative simplification from the full linear combination of the β coefficients. The three weighting methods included rounding the β coefficients to the nearest integer, dividing them by the smallest β coefficient and rounding, and multiplying by two and rounding. We examined the area under the ROC curves and the sensitivity and specificity of models using the scores in place of the original variables to guide our choice of which method to use. For both the

HIV outcome model and the HIV/syphilis model, rounding the β coefficients to the nearest integer produced the optimal result.

We then applied these risk scores to hypothetically test 50% of the total available screening population. For each of the two models we calculated the sensitivity and specificity of the risk scores in predicting each of three outcomes: HIV only, syphilis only, HIV or syphilis. Model coefficients, risk scores, sensitivity and specificity were all validated using bootstrap analyses in which the cohort was sampled 1000 times with replacement[30]. All statistical analyses were conducted using Stata SE version 8.0 (Stata Corporation, College Station, TX).

4.3.5 Costs Analysis

Using the North Carolina Syphilis Elimination jail screening program as a model for the new programs emphasizing HIV testing, the primary costs of jail screening are described. We present results for four hypothetical scenarios based on screening strategy (standard sample testing for HIV only, standard sample testing for both syphilis and HIV, targeted sample testing for HIV only, and targeted sample testing for both syphilis and HIV). Fixed costs include salaries for screening personnel and the cost of initial screening tests for all samples. Variable costs include quantitative and confirmatory testing performed on positive screening samples and are dependent upon the number of positive screening tests expected.

Disease prevalence estimates for the standard sample scenarios were taken directly from the screened study population because that was the method under which the data were collected. The standard screening method approximates a universal screening approach since testing is offered to all inmates equally. For targeted testing, estimates

were taken from the populations that would be screened using risk scores developed in this study. We assumed the number of samples requiring additional HIV testing to be equal to the estimated prevalence. We chose not to make any adjustments for false positives because the rate is known to be very low[31]. Estimates of personnel costs and the number of inmates that could be screened per shift were obtained from the North Carolina SEE jail screening project budgets. Estimated costs for laboratory tests were based on Medicaid reimbursement rates and were taken from an impact analysis performed by the North Carolina Division of Public Health in association with a change in HIV testing laws[32]. Costs per HIV case detected included the cost of HIV screening and confirmatory tests and all personnel costs because the HIV screening program is the funded entity. Since the addition of syphilis screening to the existing HIV program is in question, costs per case detected include only the cost of additional testing.

4.4 RESULTS

4.4.1 Study Population

During the study period, 5,441 samples were taken from inmates 18 years of age and older who were screened for syphilis in the two participating jails. Many individuals were re-arrested and screened more than once. We removed 128 observations for which no HIV test was performed, 419 with missing syphilis or HIV test results, and 30 not considered at risk (second HIV test, syphilis test of cure). Finally, we restricted the remaining sample of 4,864 to the first observation for each individual leaving 3,626 records for analysis.

Women represented 17.7% of the total inmates in the study (Table 4.1). The average age for both men and women was 33years. Screened inmates were primarily

black non-Hispanic (63.9%) and white non-Hispanic (27.9%). Hispanics made up 5.5% of the study population, more than all remaining race/ethnicity groups combined. For all of the risk categories that applied to both men and women, women were more likely to report than men.

Forty-six people (1.3% of the study population) were found to be HIV positive. Four of these individuals also had reactive syphilis tests yet none were found to have current syphilis disease upon followup. Most of the HIV cases were among men (n=34) but they had a lower positivity rate (1.1%) than women (n=12 cases, 1.9%). Similarly, there were 99 men with a reactive syphilis test. Of these, 22 were confirmed new cases of disease (0.74%). Among women there were 59 reactive tests and eight new syphilis cases (1.3%) (Table 4.1).

4.4.2 Results for HIV infection

Women (OR 1.8, 95% CI 0.92 - 3.5) and men who reported sex with other men (OR 28.5, 95% CI 7.5 - 108.5) were more likely than heterosexual men to have HIV infection (Table 4.2). The outcome was also associated with increasing age and with Hispanic/Black non-Hispanic race ethnicity (OR 3.9, 95% CI 1.5 - 9.9). None of the risk categories was predictive of disease with the curious exception of marijuana use which had an inverse effect (OR 0.33, 95% CI 0.08 - 1.4).

The full or "reference" model contained the composite sex variable, age, race/ethnicity, ever tested for HIV, and marijuana use (Table 4.3). After backward elimination, the final model included sex, age, race/ethnicity and ever tested for HIV. The ROC curves for the full and final models were similar (ROC_{ref} =0.7499, ROC_{final}

=0.7360, χ^2 p=0.34) and model fit was good (Hosmer-Lemeshow goodness of fit test p=0.85).

We created risk scores using the beta coefficients from the models directly (predicted probabilities) and indirectly (weighted and unweighted risk scores) (Table 4.3). These scores were applied to hypothetically screening 50% of the available population to create cutoffs (at or above the cutoff = screened, below the cutoff = not screened). The sensitivity and specificity of each cutoff to detect each of three outcomes (HIV, syphilis, either) was assessed (Table 4.5). The weighted risk scores had the same sensitivity and specificity as the model predicted probabilities. In other words, there was no loss in performance when scores were simplified by rounding the beta coefficients to the nearest integer. Performance of the unweighted risk scores was always inferior, sometimes markedly so. We will focus the rest of our discussion on the weighted risk scores.

For the HIV outcome model, the lowest scoring individual type would be a heterosexual man, age 18-24, never tested for HIV, with a race/ethnicity in the referent group (total score=0)(Table 4.3). The highest scoring individual would be MSM, age 25 or older, previously tested for HIV, and of Hispanic or Black non-Hispanic race/ethnicity (total score=6). A risk score cutoff of 3 or above will lead to screening less than 50% of the available inmate population. This scenario has good sensitivity for the detection of HIV (82.6%, 95% CI 71.2 - 94.0) which is not surprising since the model was built to do exactly that. Its ability to detect syphilis is inferior to HIV but still quite reasonable (sensitivity 73.3%, 95% CI 56.5 - 90.1)(Table 4.5). The weighted score model performed consistently when validated using 1000 bootstrap samples.

4.4.3 Results for HIV/Syphilis

Covariates associated with the HIV/syphilis outcome were very similar to those associated with HIV only. Women and MSM were more likely than other men to have HIV or syphilis (Table 4.2). Disease was also more likely among persons of black non-Hispanic or Hispanic ethnicity and those in older age groups. The combined disease outcome was different in that it was associated with reported cocaine use (OR 1.8, 95% CI 0.94-3.3).

The reference model was nearly the same as the one for HIV only but with cocaine use substituted for marijuana use. The model included the composite sex variable, age, race/ethnicity, ever tested for HIV, and cocaine use (Table 4.4). After backward elimination, the final model retained only the demographic variables sex, age, and race/ethnicity. The ROC curves for full and final models were similar (ROC_{ref} =0.7488, ROC_{final} =0.7453, χ^2 p=0.42) and the model fit the data (Hosmer-Lemeshow test p=0.82).

The weighted risk scores for the HIV/syphilis model ranged from zero for a heterosexual man, age 18-24, with a race/ethnicity in the referent group to 7 for MSM, age 35 or older, and of Hispanic or Black non-Hispanic race/ethnicity (Table 4.4). The cutoff for screening 50% would be a score of 4 or more. This algorithm has good sensitivity for the detection of syphilis (80.0%, 95% CI 64.8 – 95.2) but is much weaker for the detection of HIV cases (sensitivity 65.2%, 95% CI 50.9 – 79.5)(Table4.5). Performance was validated with a bootstrapping analysis of 1000 samples.

4.4.4 Cost Analysis

The North Carolina Syphilis Elimination Effort employed teams of two people to work in each participating county jail for screening. They ranged from phlebotomists (about $23,000 annual salary) to registered nurses (about $56,000)[33]. Assuming an average wage in the middle ($39,500), the annual salary cost for each jail program is ~$79,000. Given constraints previously described, a screening team could be expected to test a maximum of 30-40 inmates per day[34]. Estimating 30 inmates per day, five days a week, each program could possibly screen 7,800 per year. These assumptions are applied to four HIV/syphilis screening scenarios, shown in Table 5. Costs from screening tests are based on Medicaid reimbursement rates and are taken from a DPH impact analysis as previously described[32].

The four scenarios are based on an HIV testing model with the question of whether or not (a) HIV screening should be universal (volunteers as available) or targeted (volunteers based on a screening algorithm) and (b) whether or not syphilis screening should be added to the HIV testing program. Because the HIV screening component is a given (currently the funded programs are based on HIV screening), all personnel costs are applied to the HIV figures.

The cost for each scenario is dependent upon the expected number of positive screening tests that will require additional testing. As described above, the weighted risk scores for the HIV outcome model provide optimal performance in the detection of HIV (sensitivity 82.6%) and secondarily, syphilis (sensitivity 73.3%) (Table 4.5). When these risk scores are applied to a hypothetical situation in which 50% of the inmates are tested, the composition of the screened population has necessarily changed. The HIV and

syphilis prevalence in these "new" populations is by design higher than in the untargeted group. These targeted population prevalences for HIV (2.3%), syphilis reactive test (7.1%), and syphilis case (1.3%) are applied to the cost estimates for the targeted testing scenarios in Table 4.6. The prevalence estimates from the study data (Table 4.1) were applied to the universal screening scenarios in Table 4.6. This is appropriate because the Syphilis Elimination screening program from which the study data were collected employed a standard screening strategy of offering testing to all available inmates and screening volunteers as time permitted.

The higher prevalence of disease in the targeted scenarios contributes to higher overall program cost due to the higher number of necessary confirmatory tests (from $238,648 to $249,579 when screening for both HIV and syphilis). However, efficiency increases dramatically. The number of HIV cases detected goes from 101 to 179 (increase of 77%) and the cost per case drops from $2,189 to $1,262, (a decrease of 42%). The addition of syphilis testing to this algorithm adds very little total cost ($23,707) and would result in the detection of 101 new syphilis cases for a cost per case of just $235.

4.5 Discussion

Theoretically, a "universal" screening approach would mean that all people are screened whereas a targeted approach would have fewer persons screened. In practice, a similar number of inmates is likely to be screened under either approach. The jail screening experience in North Carolina has been that teams of two can generally screen a maximum of 30 inmates per day even though there are often far more than 30 new inmates booked in the jail per day. It is unlikely that additional staff will be hired to

screen more people and it is therefore desirable to target the available personnel and tests to those inmates most likely to have HIV infection or syphilis. The screening algorithm developed in this study can serve to better inform which 30 people will be screened.

The sensitivity of the algorithm with respect to HIV is the most important factor in choosing which risk score method should be used. The CDC estimates that one in four people infected with HIV is unaware of their status. The new screening efforts, including jail screening, aim to notify many of these people of their HIV status so that they can protect their own health through treatment and protect the health of others by taking steps to prevent transmission[25]. Poor specificity (the ability to correctly inform negative subjects that they are disease-free) is less of a concern and should not be used to reject a model with good sensitivity. Likewise, the sensitivity of the model for syphilis is important but remains subordinate to the need for good sensitivity for HIV.

We therefore recommend the use of the weighted risk scores (cutoff=3) developed from the HIV outcome model. Sensitivity for the detection of HIV is much better than that for the combined outcome model (82.6% vs. 65.2%)(Table 4.5). This model also has quite good ability to detect new syphilis cases (sensitivity 73.3%). This algorithm has been converted to a screening tool that could be used in the jail setting to guide selection for screening (Figure 4.1). It should be noted that while the screening cutoff of 3 was designed to screen less than 50% of the total inmates, for the study population, the algorithm actually results in screening 39.2% of men and 81.0% of women (46.6% of the study population). This is reassuring given the heightened concerns about perinatal HIV transmission and congenital syphilis in this population.

The benefits of the targeted screening approach are enhanced when the costs are analyzed. As described above, the same number of inmates is likely to be screened under either universal or targeted testing. The issue becomes the efficiency of the screening approach taken. For the cost scenarios presented in Table 4.6, overall program costs go up slightly under targeted testing due to the higher number of confirmatory tests performed. However, efficiency is greatly improved with more HIV cases detected (179 vs 101) and a lower cost per case detected ($2,189 vs. $1,262). The addition of syphilis testing to this scenario adds very little overall cost and would detect 101 new syphilis cases. We therefore recommend a targeted testing approach and testing for both HIV and syphilis.

The data for this study were collected as part of Syphilis Elimination program evaluation activities, not as a research project. Data were only available for inmates who accepted the offer of syphilis (and often HIV) testing. It is possible that inmates who refused testing differed on important characteristics from inmates who accepted testing. It would be particularly important to know about refusals if the goal of the study were to explain the factors associated with having a positive HIV or syphilis test. However, the goal was to build a tool for prediction. The sample we used were inmates who voluntarily agreed to be tested and the tool we developed is also likely to be applied to a similar target population of screening volunteers.

The fact that the screening algorithm includes race/ethnicity may make it politically difficult to implement. We considered this when we translated the risk scores to the algorithm, placing race/ethnicity last in the series of parameters (Figure 1). This means that most inmates will be assigned to screening or not based on other criteria. Age

and race/ethnicity are also pieces of information that are routinely recorded for each person as part of the booking process for the jails. The screener may be able to use this information without directly asking the person to report their race and ethnicity. Training of the screening personnel would have to include detailed discussion about how the algorithms were developed and why they are useful. It may be useful to point out that the CDC enhanced testing initiative under which the HIV jail screening programs are funded is designed specifically to address racial disparities in HIV testing[25].

Our treatment of HIV and syphilis screening costs was simplistic. We did not attempt to quantify certain other important fixed (overhead, office space) and variable (costs of treatment and sequelae) costs. Nor did we attempt to describe the savings associated with HIV and syphilis cases prevented. Our goal was merely to provide a framework for assessing the impact of universal vs. targeted screening and of adding syphilis screening to existing HIV testing programs. The conclusions we have drawn are relative and are likely to hold true, even if other costs were to be included in the calculations. Namely, targeted screening slightly increases overall program costs but with large gains in effectiveness (decreased cost per case detected). Also, the cost of adding syphilis screening to an already existing jail HIV screening program is very low and should be recommended in communities with incident syphilis cases.

We believe that the screening algorithm will perform well in the county from which the sample was drawn. Generalization to other communities in the Southern United States with similar demographics and rates of HIV and syphilis is also possible. We consider it a distinct strength of the study that syphilis cases were fully diagnosed and staged since a large proportion of people with positive syphilis screening tests do not

actually have current disease. The screening tools developed here can help improve the efficiency of jail screening. We hope that the algorithms and the cost assessment will encourage communities with funding for HIV screening to consider adding syphilis testing to their protocols.

Table 4.1: Characteristics of Inmates screened for HIV and syphilis in North Carolina jails 2002-2005

	Men N=2985 (82.3%)		Women N=641 (17.7%)		Total N=3626	
Characteristic	N	%	N	%	N	%
STD SCREENING						
Screened for HIV and syphilis	2985	82.3	641	17.7	3626	100.0
Ever tested for HIV before	1983	66.4	494	77.1	2477	68.3
HIV positive	34	1.1	12	1.9	46	1.3
Reactive syphilis test	99	3.3	59	9.2	158	4.4
Confirmed new syphilis case	22	0.74	8	1.3	30	0.83
Coinfected (HIV positive and confirmed new syphilis case)	0	0	0	0	0	0
Either disease (HIV positive or confirmed new syphilis case)	56	1.9	20	3.1	76	2.1
DEMOGRAPHICS						
Age						
18-24 years	740	24.8	114	17.8	854	23.6
25-34 years	916	30.7	256	39.9	1172	32.3
35-44 years	916	30.7	216	33.7	1132	31.2
45+ years	413	13.8	55	8.6	468	12.9
Race/ethnicity						
White non-Hispanic	752	25.2	259	40.4	1011	27.9
Black non-Hispanic	1975	66.2	343	53.5	2318	63.9
Native American non-Hispanic	32	1.1	11	1.7	43	1.2
Hispanic	180	6.0	21	3.3	201	5.5
Asian/Pacific Islander non-Hispanic	22	0.74	2	0.31	24	0.66
Other/unknown	11	0.36	2	0.32	13	0.36
Missing	13	0.44	3	0.47	16	0.44

Table 4.1: Characteristics of Inmates screened for HIV and syphilis in North Carolina jails 2002-2005 (continued)

	Men N=2985 (82.3%)		Women N=641 (17.7%)		Total N=3626	
Characteristic	N	%	N	Characteristic	N	%
RISKS						
Homeless	70	2.4	45	7.0	115	3.2
Men who have sex with men (MSM)	13	0.44	--	--	--	--
Multiple sex partners	430	14.4	134	20.9	564	15.6
STD diagnosis	152	5.1	73	11.4	225	6.2
Trade sex for drugs or money	131	4.4	108	16.9	239	6.6
Alcohol use	513	17.2	161	25.1	674	18.6
Marijuana use	328	11.0	103	16.1	431	11.9
Injection drug use	46	1.5	32	5.0	78	2.2
Cocaine use	205	6.9	148	23.1	353	9.7

Table 4.2: Odds ratios and 95% confidence intervals for the association between HIV and syphilis screening outcomes and predictor characteristics among inmates screened in two North Carolina jails 2002-2005

		HIV positive N=46				HIV positive or confirmed new syphilis case N=76			
Characteristic	N	OR (95% CI) Unadjusted	p	OR (95% CI) Adjusted	p	OR (95% CI) Unadjusted	p	OR (95% CI) Adjusted	p
Men (all others)	2972	Ref	--	Ref	--	Ref	--	Ref	--
Women	641	1.8 (0.92 – 3.5)	0.08	2.0 (0.98 – 4.0)	0.06	1.8 (1.1 – 3.0)	0.03	2.0 (1.2 – 3.6)	0.01
MSM	13	28.5 (7.5 – 108.5)	<0.01	38.9 (7.5 – 201.2)	<0.01	16.5 (4.4 – 61.8)	<0.01	21.6 (4.8 – 97.6)	<0.01
Ever tested for HIV	2477	2.6 (1.2 – 5.9)	0.02	2.3 (1.0 – 5.3)	0.05	1.6 (0.94 – 2.8)	0.08	1.3 (0.75 – 2.3)	0.33
Age									
18-24 years	854	Ref	--	Ref	--	Ref	--	Ref	--
25-34 years	1172	2.8 (0.91 – 8.3)	0.07	2.4 (0.79 – 7.5)	0.12	3.1 (1.2 – 8.2)	0.02	2.9 (1.1 – 7.7)	0.04
35-44 years	1132	3.8 (1.3 – 11.2)	0.02	2.8 (0.94 – 8.6)	0.06	4.8 (1.9 – 12.3)	0.01	3.7 (1.4 – 9.8)	0.01
45+ years	468	3.2 (0.94 – 11.1)	0.06	2.7 (0.76 – 9.5)	0.13	7.2 (2.7 – 19.4)	<0.01	6.0 (2.2 – 16.6)	<0.01
Race/ethnicity									
White/all other	1091	Ref	--	Ref	--	Ref	--	Ref	--
Black NH/Hispanic	2519	3.9 (1.5 – 9.9)	0.01	3.5 (1.4 – 8.9)	0.01	5.2 (2.2 – 11.9)	<0.01	5.6 (2.4 – 13.1)	<0.01
RISKS									
Homeless	115	0.68 (0.09 – 4.9)	0.70	0.72 (0.09 – 5.9)	0.76	1.3 (0.39 – 4.1)	0. 70	1.0 (0.29 – 3.8)	0.94
Multiple sex partners	564	0.97 (0.43 – 2.2)	0.95	1.0 (0.32 – 3.1)	1.00	0.92 (0.48 – 1.8)	0.79	0.86 (0.35 – 2.2)	0.76
STD diagnosis	225	1.1 (0.32 – 3.4)	0.93	0.74 (0.20 – 2.7)	0.65	1.3 (0.56 – 3.0)	0.54	0.84 (0.33 – 2.1)	0.72
Trade sex for drugs or money	239	0.98 (0.30 – 3.2)	0.99	0.68 (0.14 – 3.2)	0.63	1.2 (0.52 – 2.8)	0.64	0.80 (0.26 – 2.4)	0.69
Alcohol use	674	0.92 (0.43 – 2.0)	0.83	1.1 (0.36 – 3.1)	0.82	0.90 (0.49 – 1.6)	0.74	0.75 (0.32 – 1.7)	0.50
Marijuana use	431	0.33 (0.08 – 1.4)	0.13	0.26 (0.05 – 1.3)	0.09	0.63 (0.27 – 1.5)	0.28	0.63 (0.23 – 1.7)	0.37
Injection drug use	78	--	--	--	--	1.2 (0.30 – 5.1)	0.77	1.6 (0.36 – 7.5)	0.52
Cocaine use	353	1.4 (0.59 – 3.3)	0.45	1.8 (0.53 – 6.1)	0.29	1.8 (0.94 – 3.3)	0.08	2.1 (0.85 – 5.3)	0.11

Table 4.3: Odds ratios and risk scores of prevalent HIV infection by predictor characteristics among inmates screened in North Carolina jails 2002-2005.

	Reference model N=3610 ROC Area = 0.7499		Final model N=3610 ROC Area = 0.7360			
Characteristic	OR (95% CI)	β (p)	OR (95% CI)	β (p)	Weighted Score*	Unweighted Score
Men (all others)	Ref	Ref	Ref	Ref	0	0
Women	2.0 (1.0 – 4.0)	0.70 (0.05)	1.9 (0.95 – 3.7)	0.64 (0.07)	1	1
Men who have sex with men (MSM)	36.4 (8.3 – 159.4)	3.59 (<0.01)	26.0 (6.4 – 105.5)	3.26 (<0.01)	3	1
Ever tested for HIV before	2.4 (1.0 – 5.4)	0.86 (0.04)	2.3 (1.0 – 5.2)	0.83 (0.05)	1	1
Age						
18-24	Ref	Ref	Ref	Ref	0	0
25-34	2.5 (0.80 – 7.6)	0.90 (0.12)	2.7 (0.88 – 8.3)	0.99 (0.08)	1	1
35-44	2.9 (0.98 – 8.7)	1.07 (0.05)	3.3 (1.1 – 9.8)	1.19 (0.03)	1	1
45+	2.8 (0.79 – 9.6)	1.01 (0.11)	3.2 (0.91 – 11.0)	1.15 (0.07)	1	1
Race/ethnicity						
White/all other	Ref	Ref	Ref	Ref	0	0
Hispanic or Black/non-Hispanic	3.5 (1.4 – 9.1)	1.26 (0.01)	3.5 (1.4 – 9.1)	1.26 (0.01)	1	1
Marijuana use	0.28 (0.06 – 1.3)	-1.28 (0.01)	--	--	--	--

* Weighted score = β coefficient rounded to the nearest integer

Table 4.4: Odds ratios and risk scores of disease outcome (prevalent HIV infection or confirmed new syphilis case) by predictor characteristics among inmates screened in North Carolina jails 2002-2005.

	Reference Model N=3610 ROC Area=0.7488		Final Model N=3610 ROC Area=0.7453			
Characteristic	OR (95% CI)	β (p)	OR (95% CI)	β (p)	Weighted Score*	Unweighted Score
Men (all others)	Ref	Ref	Ref	Ref	0	0
Women	2.0 (1.1 – 3.4)	0.68 (0.02)	2.1 (1.3 – 3.6)	0.76 (0.01)	1	1
Men who have sex with men (MSM)	14.9 (3.7 – 60.0)	2.70 (<0.01)	15.8 (4.0 – 61.8)	2.76 (<0.01)	3	1
Ever tested for HIV before	1.3 (0.77 – 2.3)	0.29 (0.31)	--	--	--	--
Age*						
18-24	Ref	Ref	Ref	Ref	0	0
25-34	3.1 (1.1 – 8.2)	1.12 (0.03)	3.2 (1.2 – 8.6)	1.16 (0.02)	1	1
35-44	4.2 (1.6 – 11.1)	1.44 (<0.01)	4.6 (1.8 – 11.9)	1.52 (<0.01)	2	1
45+	6.9 (2.5 – 18.9)	1.93 (<0.01)	7.4 (2.7 – 20.1)	2.00 (<0.01)	2	1
Race/ethnicity						
White/all other	Ref	Ref	Ref	Ref	0	0
Hispanic or Black/non-Hispanic	5.3 (2.3 – 12.3)	1.66 (<0.01)	5.3 (2.3 – 12.2)	1.66 (<0.01)	2	1
Cocaine use	1.3 (0.68 – 2.6)	0.28 (0.41)	--	--	--	--

* Weighted score = β coefficient rounded to the nearest integer

Table 4.5: Performance of selective screening criteria characteristics among inmates screened in North Carolina jails 2002-2005.

	HIV positive model N=3610			HIV positive or confirmed new syphilis case model N=3610		
Outcome tested Scoring method	Risk score cutoff	Sensitivity 95% CI	Specificity 95% CI	Risk score cutoff	Sensitivity 95% CI	Specificity 95% CI
HIV only						
Predicted prob.	0.009	82.6 (71.2 – 94.0)	53.9 (52.3 – 55.5)	0.029	65.2 (50.9 – 79.5)	64.3 (62.7 – 65.8)
Weighted score	3	82.6 (71.2 – 94.0)	53.9 (52.3 – 55.5)	4	65.2 (50.9 – 79.5)	64.3 (62.7 – 65.8)
Unweighted score	3	80.4 (68.5 – 92.3)	53.9 (52.3 – 55.5)	3	23.9 (11.1 – 36.7)	91.2 (52.3 – 55.5)
Syphilis only						
Predicted prob.	0.009	73.3 (56.5 – 90.1)	53.6 (52.0 – 55.3)	0.029	80.0 (64.8 – 95.2)	64.2 (62.7 – 65.8)
Weighted score	3	73.3 (56.5 – 90.1)	53.6 (52.0 – 55.3)	4	80.0 (64.8 – 95.2)	64.2 (62.7 – 65.8)
Unweighted score	3	73.3 (56.5 – 90.1)	53.7 (52.1 – 55.3)	3	20.0 (4.8 – 35.2)	91.1 (90.2 – 92.0)
HIV or syphilis						
Predicted prob.	0.009	79.0 (69.6 – 88.3)	54.1 (52.5 – 55.8)	.029	71.1 (60.6 – 81.5)	64.6 (63.0 – 66.2)
Weighted score	3	79.0 (69.6 – 88.3)	54.1 (52.5 – 55.8)	4	71.1 (60.6 – 81.5)	64.0 (63.0 – 66.2)
Unweighted score	3	77.6 (68.1 – 87.2)	54.1 (52.5 – 55.8)	3	22.4 (12.8 – 32.0)	91.3 (90.4 – 92.2)

Table 4.6: Costs of Screening for Syphilis and HIV in jail settings under four screening strategy scenarios

	Universal screening*		Targeted screening **	
	Screen for HIV only	Screen for HIV and syphilis	Screen for HIV only	Screen for HIV and syphilis
ASSUMPTIONS				
Individuals to be screened	7800	7800	7800	7800
HIV case prevalence	101 (1.3%)	101 (1.3%)	179 (2.3%)	179 (2.3%)
Syphilis screen prevalence (reactive screening test rate)	--	343 (4.4%)	--	554 (7.1%)
Syphilis case prevalence (confirmed cases)	--	65 (0.83%)	--	101 (1.3%)
HIV screening tests (EIA)	7800	7800	7800	7800
HIV confirmatory tests (WB) (HIV prevalence * 7800)	101	101	179	179
Syphilis screening tests	--	7800	--	7800
Syphilis quantitative tests (Syphilis screen prevalence * 7800)	--	343	--	554
Syphilis confirmatory tests (Syphilis screen prevalence * 7800)	--	343	--	554

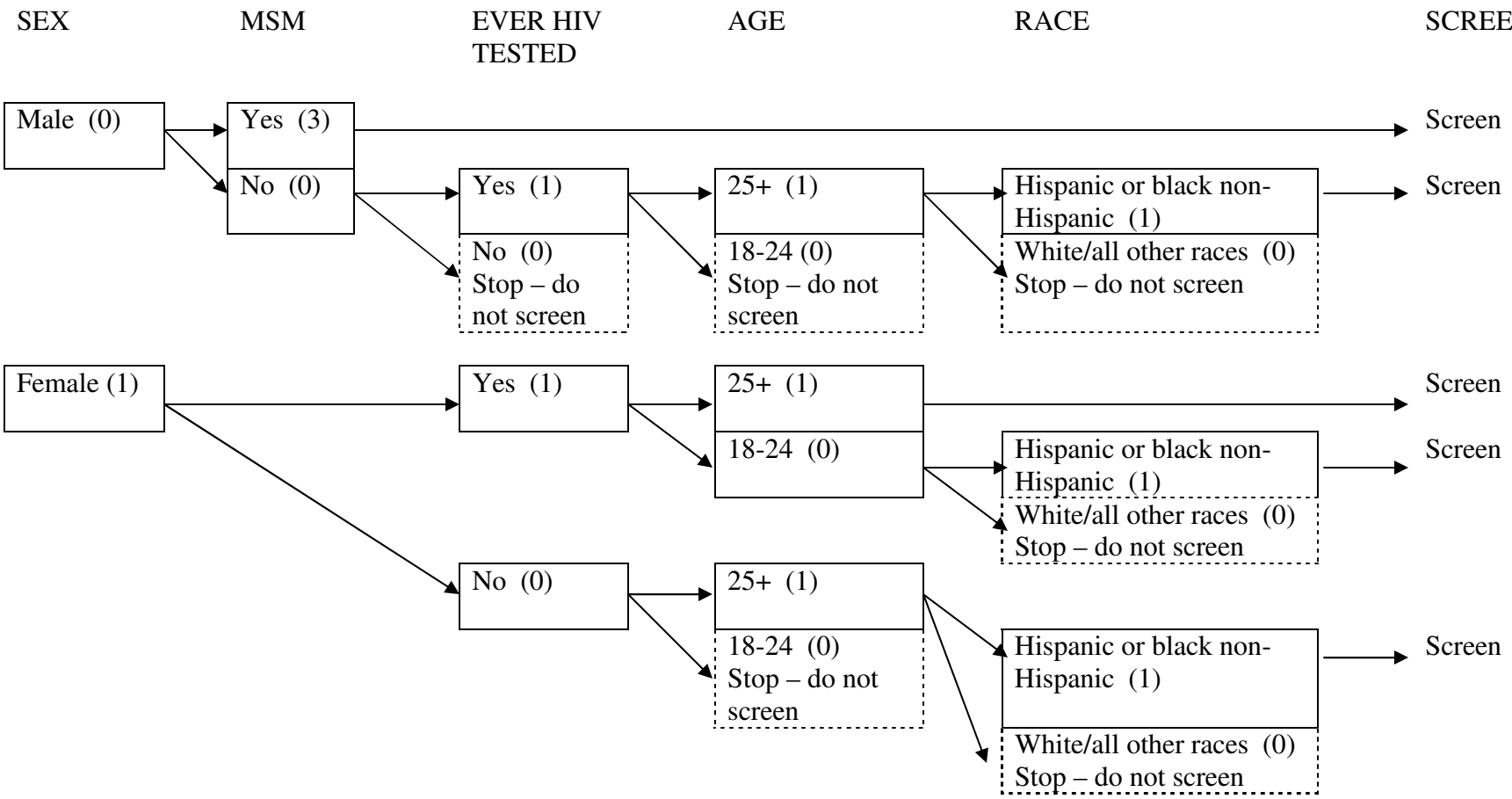
continued

Table 4.6: Costs of Screening for Syphilis and HIV in jail settings under four screening strategy scenarios

	Universal screening*		Targeted screening **	
	Screen for HIV only	Screen for HIV and syphilis	Screen for HIV only	Screen for HIV and syphilis
COSTS				
Personnel (2 employees)	$79,000	$79,000	$79,000	$79,000
HIV screening tests ($17.41 per EIA test)	$135,798	$135,798	$135,798	$135,798
HIV confirmatory tests ($17.41 x 2 repeat EIA and $27.05 per WB test)	$6,249	$6,249	$11,074	$11,074
Syphilis screening ($0.98 per stat RPR screening test)	$0	$7,644	$0	$7,644
Syphilis confirmatory tests ($6.22 per quantitative RPR test and $22.81 per confirmatory test – MHATP or FTA-ABS)	$0	$9,957	$0	$16,083
Total program cost	$221,047	$238,648	$225,872	$249,579
Cost/HIV case detected (cases/(personnel + HIV testing costs))	$2,189	$2,189	$1,262	$1,262
Cost/syphilis case detected (cases/syphilis testing costs)	--	$271	--	$235

* Universal screening = volunteers on a first come basis. Disease prevalence estimates taken from study population (Table 1).
** Targeted screening = volunteers from screening algorithm based on weighted risk scores from the model for HIV infection only (Table 4). Disease prevalence estimates taken from populations that would be screened if selected using those risk scores.

Figure 4.1: Algorithm for screening jail inmates for HIV infection



Screening algorithm applies weighted risk scores from the model predicting HIV infection to the hypothetical scenario of screening <50% of the jail population. The individual score for each attribute is listed in parentheses to the right. A cumulative score of 3 or more directs individuals to screening. Those with scores of 2 or less should not be screened.

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V. DISCUSSION

5.1 SCOPE OF THE PROBLEM

This dissertation sought to improve the efficiency of jail screening for syphilis and HIV through the development of algorithms for targeted screening and the examination of program costs.

North Carolina is a state disproportionately affected by both syphilis and HIV. From 1993-2003, North Carolina ranked in the top 10 states in primary and secondary syphilis rates and in the top 20 for congenital syphilis rates. When the NC primary & secondary syphilis rate peaked in 1992, it was nearly three times higher than the national rate that year (36.2 vs. 13.3/100,000)[1]. This coincided with the state's HIV epidemic. New HIV disease (first report of HIV infection) reports in North Carolina were highest from 1992-1995, averaging over 2000 reports per year[2]. Syphilis also disproportionately affects minority populations in North Carolina. The vast majority of HIV disease and early syphilis cases were among non-Hispanic blacks (approximately 70% per year, 2000-2006) though they make up only 22% of the State's population[2].

When the Centers for Disease Control and Prevention (CDC) launched its Syphilis Elimination Effort (SEE) in 1999, five of the 28 funded counties were in North Carolina. In the 1999 publication "The National Plan to Eliminate Syphilis from the United States"[3], the CDC outlined the rationale for undertaking something so ambitious. The elimination of syphilis was deemed important for two major reasons: to reduce racial/ethnic health disparities and because syphilis infection may contribute to the transmission of HIV.

One of the many strategies recommended by CDC was screening of jail inmates for both syphilis and HIV. All six SEE counties (one was added later) in North Carolina

participated in this effort, though only one added the HIV screening component. To ensure access to inmates before they are able to post bond (half will do so within two days of arrest[4]), screening took place at intake whenever possible. Most of the time, screening was done by teams of two, one to interview inmates and complete paperwork and one to draw blood samples for testing. Despite these best efforts, most of the participating jails screened less than 10% of the total inmates booked into the jail[5]. While it may be possible to improve this percentage with some operational changes, the bottom line is that the resources do not currently exist to screen all of the inmates in the SEE county jails for syphilis and HIV.

The Syphilis Elimination Effort was a success in many ways. Primary and secondary syphilis rates dropped steeply. With this came dramatic reductions in funding[6]. In North Carolina, nearly all of the jail screening staff positions were lost in these cuts. Fortunately, the CDC launched another new initiative, this one regarding the expansion of HIV testing, including jail screening[7]. The end result has been that the former syphilis jail screening projects were converted to HIV screening projects. This dissertation sought to address the issue of the continued relevance of syphilis screening in this new environment. This was done through the development of targeted screening algorithms and the assessment of program costs.

The identification of previously undiagnosed syphilis and HIV cases through jail screening has benefits at several levels. It is estimated that one in four people infected with HIV is unaware of their status[7]. Knowledge of HIV infection can help people protect their own health through treatment and protect the health of others by taking steps to prevent transmission. This is particularly true for pregnant women since treatment can

dramatically reduce perinatal transmission[8]. Identification and treatment of early syphilis cases also reduces transmission and helps control outbreaks. When late cases are diagnosed, the primary benefit is to the patient in the prevention of serious sequelae of late syphilis. Because women can transmit syphilis to their infants in utero up to eight years past the initial date of their own infection, finding female syphilis cases at any stage is critical to the prevention of congenital syphilis cases[9, 10].

5.2 FINDINGS

Screening algorithms with good sensitivity were produced for both syphilis and HIV. In the first study, syphilis screening data from all seven jails was modeled to create weighted risk scores and a screening algorithm for predicting new syphilis cases in men. The model included age, race/ethnicity, and reporting an STD diagnosis in the last six months and the resulting algorithm had a sensitivity of 82.7%. The same data did not yield a useful model for predicting syphilis in women. After model reduction, only cocaine use was retained in the final model and this single predictor was not effective for predicting new syphilis cases among female jail inmates (sensitivity 64.9%).

The second study sought to address the new programmatic changes in NC jail screening by focusing on screening for HIV. To address the issue of small cell sizes and the different outcome, a single model for both male and female inmates was developed. The final model contained sex, age, race/ethnicity and history of HIV testing and the resulting algorithm had sensitivity of 82.6% for the detection of HIV and 73.3% for the detection of syphilis.

The model results of the second study were applied to cost scenarios for universal vs. targeted screening for HIV only and HIV plus syphilis. Costs were compared under the assumption that that the same number of inmates would be screened under non-targeted vs. targeted selection. Targeted screening resulted in higher overall cost due to the larger number of confirmatory tests required. Selective screening improved efficiency in terms of the number of cases detected (increase 77% under targeted screening) and the cost per case detected (42% lower under targeted screening).

Both studies make major contributions to the jail screening literature by filling in gaps in both geography and epidemiology. For this dissertation, a comprehensive review of the literature was conducted. Nineteen studies[11-29] in which incarcerated subjects were screened for syphilis and 13 in which subjects were screened for HIV[11-14, 18, 19, 22, 28, 30-34] were identified (Appendix A and Appendix B). Of the nineteen syphilis studies, only 3 used a complete case diagnosis approach to measuring syphilis as was done here. Only six studies included information on risk behaviors and just six included facilities located in southern states. Among the thirteen HIV studies, only three were conducted in the southeast. Our study is the only one to apply screening results to a cost analysis.

5.3 LIMITATIONS

Because the data were collected as part of health department program evaluation activities and not as part of a research project, no provision was made to track those who were offered syphilis testing but refused. There was, however, data to show that over 98% of inmates who were offered HIV testing did accept it, among persons who had already agreed to be tested for syphilis. It is certainly possible that inmates who refused

syphilis testing were different from those who accepted which could bias our descriptive results. However, our main goal was to develop algorithms for use in future jail screening. Our study sample included volunteers who accepted the offer of testing. The population to which the screening algorithm would be applied would also be volunteers, minimizing the impact of possible bias.

Likewise, there is no way to know how truthful the respondents are regarding the self-reported behavioral risks. If the goal was to explain the role of these risks in predicting infection, this would be a valid concern. However, when the risk algorithms are applied in the field, risk behaviors reported will be self-reported. It is therefore reasonable to base the algorithm on data collected in the same fashion.

The cost assessment performed was by design, simplistic. A full accounting of fixed and variable costs of the screening program scenarios was not attempted. The goal was to examine the relationships between universal and targeted screening and of adding syphilis screening to existing HIV testing programs. While the true cost per HIV case diagnosed might not be exactly as we have calculated, we expect that the relative position of this cost when compared to another scenario would remain the same.

The most serious concern to emerge from the studies presented here is the issue of using race/ethnicity as a screening criterion. Incarcerated populations and persons with sexually transmitted diseases are already marginalized groups. Adding race to the equation may prove too sensitive to implement. County syphilis rates were examined as a possible substitute for race/ethnicity in the syphilis predictive model. Unfortunately, the performance of the resulting screening algorithm was substantially inferior to the

algorithm derived from the model that incuded race/ethnicity (sensitivity (73.4% vs. 82.7%).

Despite the possible problems associated with race/ethnicity as screening criteria, we recommend the use of the HIV and syphilis screening algorithms developed here. One way to address the issue is to structure the algorithm such that the subject is somewhat shielded from the knowledge that race/ethnicity is playing a role in selection for screening by incorporating data already collected by the jail booking process and/or placing race/ethnicity last in the list of criteria for screening. In either case, those implementing the protocol will be aware that race/ethnicity is part of the screening process. The rationale for using the criteria should be well covered in employee training, and should mention that both Syphilis Elimination and the expanded HIV testing programs were conceived by CDC specifically to address racial disparities in STDs[3, 7].

5.4 NEXT STEPS

The findings from this dissertation are of direct benefit and use to the jail screening programs operated by the North Carolina Division of Public Health. The screening algorithms will likely perform well in the counties from which the samples were drawn. The SEE counties had high syphilis rates when they were chosen for Syphilis Elimination in 1999. Generalization to other counties with much lower rates of syphilis may be more problematic. It is reasonable to expect that the algorithms may translate well to jail screening programs in other high prevalence counties in the Southeast where inmate demographics may be similar.

Due to the changes in the CDC funding climate, HIV screening may become the norm for jails that conduct any STD screening. If so, the syphilis screening algorithm for men may be a bit too late to arrive on the scene although it has the advantage of having been based on a much larger sample from six counties. It is therefore anticipated that the algorithm built from the model for HIV infection will be of the most interest to jail screening programs seeking to improve the efficiency of their screening efforts.

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APPENDIX A
SYPHILIS SCREENING STUDIES

Appendix A: Summary of syphilis screening studies in incarcerated US adults (n=19)

Author, Year, Ref	Data year(s)	Location	Facility	Gender, n	Syphilis case definition	Syphilis %	Other outcome measures	Behav. risks	Arrest Info	Notes
Altice, (2005)[1]	1994-1996	CT	Jail/ Prison combo	F (3,315)	RPR+, confirm FTA-ABS +, Self report	Serology (6.2%) Self report (8.5%)	HIV (7.5%) Other STDs by self report	Yes Assoc w. HIV	No	Syphilis assoc w. HIV+ status: Serology OR 3.2 (2.1-5.0) Self report OR 2.2 (1.5-3.3)
De Ravello, (2005)[2]	1998-1999	GA	Prison	F (3,636)	RPR≥1:8, confirm FTA-ABS +	RPR+ (9.7%) RPR≥1:8 (2.6%)	HIV (4.0%) Gc (0.7%) Ct (5.9%) Trich (8.2%) TB (10.5%) Pregnant (4.3%)	No	No	Retrospective chart abstraction
Solomon, (2004)[3]	2002	Baltimore MD	Jail and Prison	M (3,343) F (571)	RPR+, confirm FTA-ABS +	Jail (0.1%) Prison (1.8%)	Jail HIV (7.4%) HCV (31.1%) HBV (11.4%)	Limited Assoc w. HCV	Limited Jail: 46.1% drug charge Prison: 28.9%	Main focus HCV screening
Chen, (2002)[4]	2000	Los Angeles CA	Jail	M (811) all MSM	Full case diagnosis & staging. New vs. previously treated	New (1.1%) Prev Tx (3.6%)	HIV (9.0%) Ct (2.5%) Gc (0.9%)	Limited Prevale nce only	No	Screening in section of jail housing self-identified MSM

Author, Year, Ref	Data year(s)	Location	Facility	Gender, n	Syphilis case definition	Syphilis %	Other outcome measures	Behav. risks	Arrest Info	Notes
Finelli, (2002)[5]	1996-1999	LA, MS, SC, TX	Jails	M (67,756) F (12,202)	RPR+, RPR≥1:8	M RPR+ (5.2%) RPR≥1:8 (1.9%) F RPR+ (11.1%) RPR≥1:8 (4.1%)	None	No	No	Reported P&S syphilis case rates in community compared to % RPR≥1:8 No strong assoc.
Kahn, (2002)[6]	1994-1998	Baton Rouge, LA	Jail	M (32,573) F (6,156)	RPR+, confirm VDRL+, MHATP+, Tx and interview if available for staging	M (1.1%) F (2.5%)	None	No	Yes See notes	Nested case control to examine arrest info (n=165) M: Felony theft OR 4.3 (1.5-13.6) F: Prostitution OR 7.0 (1.5-39.3)
Mertz, (2002)[7]	1996-1999	AL, AZ, CA, GA, IL, MA, NY, RI	Jails (n=23)	M Range (3,560-94,137) F Range (512-13,741)	RPR+, RPR≥1:8	Median, range M RPR+ 2.5 % (1.0-7.8) RPR≥1:8 0.6% (0.1-2.9) F RPR+ 8.2 % (0.3-23.8) RPR≥1:8 1.7% (0.0-7.4)	None	No	No	Also screened for Ct, Gc in juvenile facilities

Author, Year, Ref	Data year(s)	Location	Facility	Gender, n	Syphilis case definition	Syphilis %	Other outcome measures	Behav. risks	Arrest Info	Notes
Arriola, (2001)[8]	2000	FL	Jails	M, F (918)	No information provided, assume RPR+, possibly with confirmatory	Positive 2.0%	Ct [screen in GA, MA] (6.5%) Gc [screen in GA] (3.1%) HIV [screen in FL, NJ, NY] (16.8%)	No	No	
Rich, (2001)[9]	1992-1998	RI	Jail/ Prison combo	F (6,249)	RPR+, confirm FTA-ABS+ Tx and interview if available for staging	New staged cases 1.4%	HIV+ assoc with new syphilis case OR 2.7 (p=.04)	Yes Hx STD OR 5.3 (p<.01) Hx IDU OR 2.3 (p=.04)	Yes Drug charge OR 2.6 (p<.01) SexDM chg	Nested case control study to look at behavioral risks, arrest info, n= 258
Silberstein (2000)[10]	1993-1995	Long Island, NY	Jail	M (16,690) F (1,752)	RPR+, confirm FTA-ABS+, Tx history if available	M RPR+ (2.6%) New case (1.1%) F RPR+ (9.4%) New case (3.8%)	None	No	No	Cost benefit study of screening program

Author, Year, Ref	Data year(s)	Location	Facility	Gender, n	Syphilis case definition	Syphilis %	Other outcome measures	Behav. risks	Arrest Info	Notes
Blank, (1999)[11]	1993-1997	New York, NY	Jail	F (3,579)	If no syph Hx at baseline: RPR+, confirm MHATP+ If syph Hx at baseline: Titer increase of ≥2 dilutions ≥1 month after adequate Tx	Incidence rate 6.5/ 100,000 person-years 289 of 3,579 women (8.1%)	None	No	No	Cohort study of women with multiple jail admissions, incident syphilis Women RPR+ at baseline were more likely to have new infection OR 1.5 (1.2-1.9)
Altice, (1998)[12]	1993	CT	Prison	M (975)	RPR+, confirm FTA-ABS+,	M 4.2%	HIV (6.1%)	Yes (assoc w. HIV)	Limited	Syphilis assoc. with HIV+ status serology OR 4.5 (1.8-10.8) self-report OR 7.6 (3.3-12.1)
Blank, (1997)[13]	1993	New York, NY	Jail	F (727)	RPR+, Tx history from Health Dept record search Vs. RPR+, confirm MHATP+	Need Tx 22.7% New cases 15.8%	None	No	No	Evaluation of treatment protocols Stat RPR+ alone was similar to standard
Beltrami, (1997)[14]	1993	New Orleans, LA	Jail	M (4,105) F (652)	RPR+, confirm MHATP+, VDRL+	M 1.5% F 3.1%	LET M 13%	Yes, prevalence only	Limited	

Author, Year, Ref	Data year(s)	Location	Facility	Gender, n	Syphilis case definition	Syphilis %	Other outcome measures	Behav. risks	Arrest Info	Notes
Heimberger (1993)[15]	1989-1990	Long Island, NY	Jail	M, F (9,797)	Full case dx and staging ART+, confirm FTA-ABS+, Tx history from Health Dept record search	ART+ and FTA-ABS+ 2.5% New cases 1.7%	None	No	No	Nested case control (n=481) New syph cases Female OR 5.8 (3.4-10.0) Black race OR 4.6 (2.7-8.1)
Cohen, (1992)[16]	1989	Los Angeles, CA	Jail	M (6,214)	Full case dx and staging RPR+, confirm MHATP+ and VDRL, physical exam, patient interview, tx history from Health Dept record search	RPR+ 4.9% New case 2.1%	None	Yes See notes	Yes No assoc w. syphilis	≥3 Sex PN OR 3.5 (1.5-8.3) Crack cocaine OR 2.1 (1.2-3.7) Hx Syph OR 2.2 (1.0-4.7) Hx STD OR 1.7 (1.1-2.6) Age, Race
Bickell, (1991)[17]	1988	New York, NY	Jail	F (114)	RPR+, confirm FTA-ABS +	Serology 22.2%	HPV (35.1%) Gc (7.2%)	No	No	
Weisfuse, (1991)[18]	1989	New York, NY	Jail	M (1,690) F (546)	RPR+, confirm MHATP+	M RPR+ (9.8%) confirmed (5.7%) F RPR+ (24.0%) confirmed (19.8%)	M HIV+ (16.1%) F HIV+ (25.8%)	Yes Assoc w. HIV	No	Syphilis assoc w. HIV+ status: M OR 2.1 (1.6-5.8) F OR 2.0 (1.3-5.4)

Author, Year, Ref	Data year(s)	Location	Facility	Gender, n	Syphilis case definition	Syphilis %	Other outcome measures	Behav. risks	Arrest Info	Notes
Farley, (1990)[19]	1983-1988	CT	Jail/ Prison combo	F (9,923)	RPR or VDRL+, confirm FTA-ABS+, clinical diagnosis	1983 (1.3%) 1988 (5.4%)	None	No	Yes See notes	Among women incarcerated for Sex DM (n=461), syphilis 10%, Among women incarcerated for drug charges (n=113), syphilis 7%

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APPENDIX B
HIV SCREENING STUDIES

Appendix B: Summary of HIV screening studies in incarcerated US adults (n=13)

Author, Year, Ref	Data year(s)	Location	Facility	Gender, n	HIV %	Other outcome measures	Behav. risks	Arrest Info	Notes
MacGowan (2007) [1]	2003-2006	FL, LA, NY, WI	Jail	M (26,294) F (6,916)	M (0.8%) F (1.0%)	None	M MSMIDU, IDU, MSM, Risky partner, No Risk F Risky Partner	No	Rapid HIV testing
Altice, (2005)[2]	1994-1996	CT	Jail/ Prison combo	F (3,315)	(7.5%)	Syphilis Serology (6.2%) Self report (8.5%)	IDU OR 5.9 (3.6-9.7) Herpes self report OR 3.1 (1.7-5.5) CSW OR 3.1 (2.4-4.0) Sex w. IDU OR 3.4 (2.2-5.2) more	No	Syphilis assoc w. HIV+ status: Serology OR 3.2 (2.1-5.0) Self report OR 2.2 (1.5-3.3)
De Ravello, (2005)[3]	1998-1999	GA	Prison	F (3,636)	(4.0)	Syph (2.6%) Gc (0.7%) Ct (5.9%) Trich (8.2%) TB (10.5%) Pregnant (4.3%)	No	No	Retrospective chart abstraction
Macalino (2004)[4]	1998-2000	RI	Prison	M (3,932)	(1.8%)	HBV (20.2%) HCV (23.1%)	IDU OR 10.1 (6.0-17.0)	Limited Recidivism (no assoc. with HIV)	Nested HBV, HCV incidence study.
Solomon, (2004)[5]	2002	Baltimore MD	Jail and Prison	M (3,343) F (571)	(7.4%)	Jail Syph (0.1%) HCV (31.1%) HBV (11.4%)	Limited Assoc w. HCV	Limited Jail: 46.1% drug charge Prison: 28.9%	Main focus HCV screening
Chen, (2002)[6]	2000	Los Angeles CA	Jail	M (811) all MSM	(9.0%)	Syph (1.1%) Ct (2.5%) Gc (0.9%)	Limited Prevalence only	No	Screening in section of jail housing self-identified MSM

Author, Year, Ref	Data year(s)	Location	Facility	Gender, n	HIV %	Other outcome measures	Behav. risks	Arrest Info	Notes
Arriola, (2001)[7]	2000	FL, NJ, NY	Jails	M, F (1,020)	(16.8%)	Syphilis [screen in FL] (2.0%) Ct [screen in GA, MA] (6.5%) Gc [screen in GA] (3.1%)	No	No	
Kassira, (2001)[8]	1998	MD	Prison	M (4,613) F (670)	M (3.1%) F (4.6%)	None	% of prison HIV cases M IDU (64%) Hetero (37%) F IDU (69%) Hetero (31%)	No	MSM only 1% of male prison HIV cases
Rich, (2001)[9]	1992-1998	RI	Jail/ Prison combo	F (6,249)	Not provided	Syph (1.4%) HIV+ assoc with new syphilis case OR 2.7 (p=.04)	Yes Assoc w. Syphilis	Yes Assoc w. Syphilis	Nested case control study to look at behavioral risks, arrest info, n= 258
Sabin, (2001)[10]	1992-1998	US	Jails and Prisons	M (344,085) F (113,494)	M New (1.9%) Prevalent (3.3%) F New (2.1%) Prevalent (3.8%)	None	As % of testers and % of positives. IDU MSM MSM/IDU	No	CDC counseling and testing data from US correctional facilities.
Thiede, (2001)[11]	1998-1999	Seattle, WA	Jail	M (262) F (86)	(2.3%)	None	Yes Lots of IDU detail Prevalences only	Yes Prevalence only	Newly arrested IDUs only. Primarily a behavioral survey

Author, Year, Ref	Data year(s)	Location	Facility	Gender, n	HIV %	Other outcome measures	Behav. risks	Arrest Info	Notes
Altice, (1998)[12]	1993	CT	Prison	M (975)	(6.1%)	Syph (4.2%)	Hx STD OR 2.4 (1.3-4.3) Mult PN OR 3.1 (1.6-6.2) Crack OR 4.4 (1.3-15.4) IDU OR 16.7 (6.1-45.5) more	L imited	Syphilis assoc. with HIV+ status serology OR 4.5 (1.8-10.8) self-report OR 7.6 (3.3-12.1)
Weisfuse, (1991)[13]	1989	New York, NY	Jail	M (1,690) F (546)	M (16.1%) F (25.8%)	M Syph (5.7%) F Syph (19.8%)	M Heroin use OR 3.9 (1.4-11.0) F Heroin use OR 7.8 (2.8-21.7)	No	Syphilis assoc w. HIV+ status: M OR 2.1 (1.6-5.8) F OR 2.0 (1.3-5.4)

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APPENDIX C
DATA COLLECTION INSTRUMENTS

SYPHILIS SCREENING FORM

ATTENTION: This form is for Syphilis Screening Serology. Use DHHS 3445 to request confirmatory syphilis testing. Please see back of this form for instructions.

1. Last Name
[1] First Name MI

2. Patient Number (Soc. Security No.) – – – H

4. Date of Birth (mm,dd,yyyy)

3. Address

Apt. City Zip Code

5. Race 1. White 2. Black 3. American Indian 4. Asian/Pacific Islander 5. Other 6. Unknown

6. Hispanic Ethnicity: 1. Yes 2. No 3. Unknown

7. Sex 1. Male 2. Female

8. Co. of Residence

9. Medicaid Client No Yes, Enter# –

10. Family Planning or EPSDT patient? If yes, please check box:

STATE LAB NO/DATE REC'D

[3] ESSENTIAL PATIENT DATA

Collection Date: MM DD YY

- Routine screening
- Prenatal
- Neonatal screening
- Premarital, state _____
- Past history of syphilis
- Contact to a known case
- Suspicious lesion
- Secondary symptoms/signs
- Treatment follow-up
- Other _____

North Carolina Department of Health and Human Services
Division of Public Health
HIV/STD Prevention and Care Branch

Syphilis Elimination Project

Phone: (919) 733-7301
Fax: (919) 733-1020

UNSATISFACTORY SPECIMEN

- No name on specimen
- Broken, leaked
- Specimen mislabeled
- Quantity not sufficient
- Laboratory accident
- Other _____

[2]

PUT RETURN ADDRESS ON ALL COPIES

FEDERAL TAX NO.: _____

_____

_____

_____ Zip Code _____

PART 1 (White): NCSEP
PART 2 (Pink): PATIENT'S RECORD
PART 3 (White): STATE LABORATORY

STATE LABORATORY RESULTS: (only)

Reactive 1: (CPT #86593)

Nonreactive (CPT# 86592)

Comments: _____

Report Date *(if not same date of receipt)*: MM DD YY

SYPHILIS SCREENING SEROLOGY (TRUST)

AKAs _____

Home Phone _____

Emergency Contact _____

Emergency Phone _____

Employment/Phone _____

Other Locating _____

_____

Y N Transgender
Y N Married (optional)
Y N Pregnant
Y N Pregnancy in last year *(other than current preg.)*

Client Information: *(in last 6 months)*

- Homeless
- Multiple Sex Partners
- Previous STD
- PLWHA
- Sex for D/M
- Partner of sex for D/M
- Domestic Violence
- MSM
- Alcohol (any)
- Crack
- IDU
- Other_____
- None

Diagnosis:

- 710 (primary)
- 720 (secondary)
- 730 (early latent)
- Not a case
- Other

Confirmatory Results:

- TP-PA
- FTA-ABS
- NR
- R
- Unsat
- Not done

Site Type: NTS SEP Other

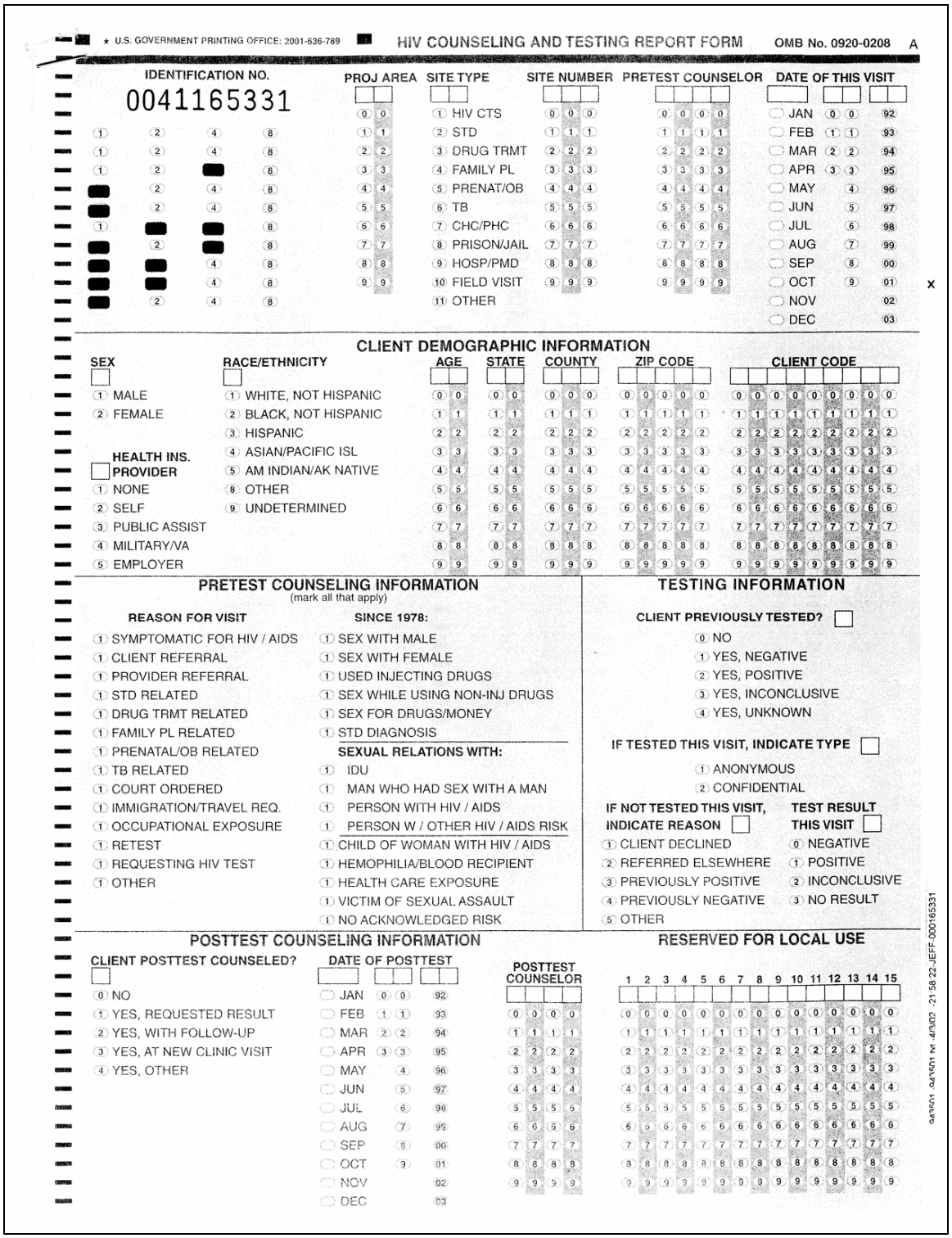
Submitting County Code

Location:

- Adult Bookstore
- Bar
- Barber/Beauty Shop
- CBO Facility
- Church/Faith Based
- Client's Residence
- College/University
- Community Center
- Convenience Store
- Crack House
- Detox
- Emergency Department
- Jail Intake
- Jail Pod
- Jail Referral
- Jail Medical
- Mobile
- Motel
- Park
- Prison
- Shelter
- Soup Kitchen
- Street
- Sub. Abuse RX Center
- Tattoo Parlor
- Transitional Housing
- Other

DHHS T1507(11/01)
HIV/STD Review (11/02)

HIV SCREENING FORM



★ U.S. GOVERNMENT PRINTING OFFICE: 2001-636-789

HIV COUNSELING AND TESTING REPORT FORM

OMB No. 0920-0208 A

IDENTIFICATION NO. 0041165331

PROJ AREA

SITE TYPE
1 HIV CTS
2 STD
3 DRUG TRMT
4 FAMILY PL
5 PRENAT/OB
6 TB
7 CHC/PHC
8 PRISON/JAIL
9 HOSP/PMD
10 FIELD VISIT
11 OTHER

SITE NUMBER

PRETEST COUNSELOR

DATE OF THIS VISIT
JAN 92
FEB 93
MAR 94
APR 95
MAY 96
JUN 97
JUL 98
AUG 99
SEP 00
OCT 01
NOV 02
DEC 03

CLIENT DEMOGRAPHIC INFORMATION

SEX
1 MALE
2 FEMALE

HEALTH INS. PROVIDER
1 NONE
2 SELF
3 PUBLIC ASSIST
4 MILITARY/VA
5 EMPLOYER

RACE/ETHNICITY
1 WHITE, NOT HISPANIC
2 BLACK, NOT HISPANIC
3 HISPANIC
4 ASIAN/PACIFIC ISL
5 AM INDIAN/AK NATIVE
8 OTHER
9 UNDETERMINED

AGE

STATE

COUNTY

ZIP CODE

CLIENT CODE

PRETEST COUNSELING INFORMATION
(mark all that apply)

REASON FOR VISIT
1 SYMPTOMATIC FOR HIV / AIDS
1 CLIENT REFERRAL
1 PROVIDER REFERRAL
1 STD RELATED
1 DRUG TRMT RELATED
1 FAMILY PL RELATED
1 PRENATAL/OB RELATED
1 TB RELATED
1 COURT ORDERED
1 IMMIGRATION/TRAVEL REQ.
1 OCCUPATIONAL EXPOSURE
1 RETEST
1 REQUESTING HIV TEST
1 OTHER

SINCE 1978:
1 SEX WITH MALE
1 SEX WITH FEMALE
1 USED INJECTING DRUGS
1 SEX WHILE USING NON-INJ DRUGS
1 SEX FOR DRUGS/MONEY
1 STD DIAGNOSIS

SEXUAL RELATIONS WITH:
1 IDU
1 MAN WHO HAD SEX WITH A MAN
1 PERSON WITH HIV / AIDS
1 PERSON W / OTHER HIV / AIDS RISK
1 CHILD OF WOMAN WITH HIV / AIDS
1 HEMOPHILIA/BLOOD RECIPIENT
1 HEALTH CARE EXPOSURE
1 VICTIM OF SEXUAL ASSAULT
1 NO ACKNOWLEDGED RISK

TESTING INFORMATION

CLIENT PREVIOUSLY TESTED?
0 NO
1 YES, NEGATIVE
2 YES, POSITIVE
3 YES, INCONCLUSIVE
4 YES, UNKNOWN

IF TESTED THIS VISIT, INDICATE TYPE
1 ANONYMOUS
2 CONFIDENTIAL

IF NOT TESTED THIS VISIT, INDICATE REASON
1 CLIENT DECLINED
2 REFERRED ELSEWHERE
3 PREVIOUSLY POSITIVE
4 PREVIOUSLY NEGATIVE
5 OTHER

TEST RESULT THIS VISIT
0 NEGATIVE
1 POSITIVE
2 INCONCLUSIVE
3 NO RESULT

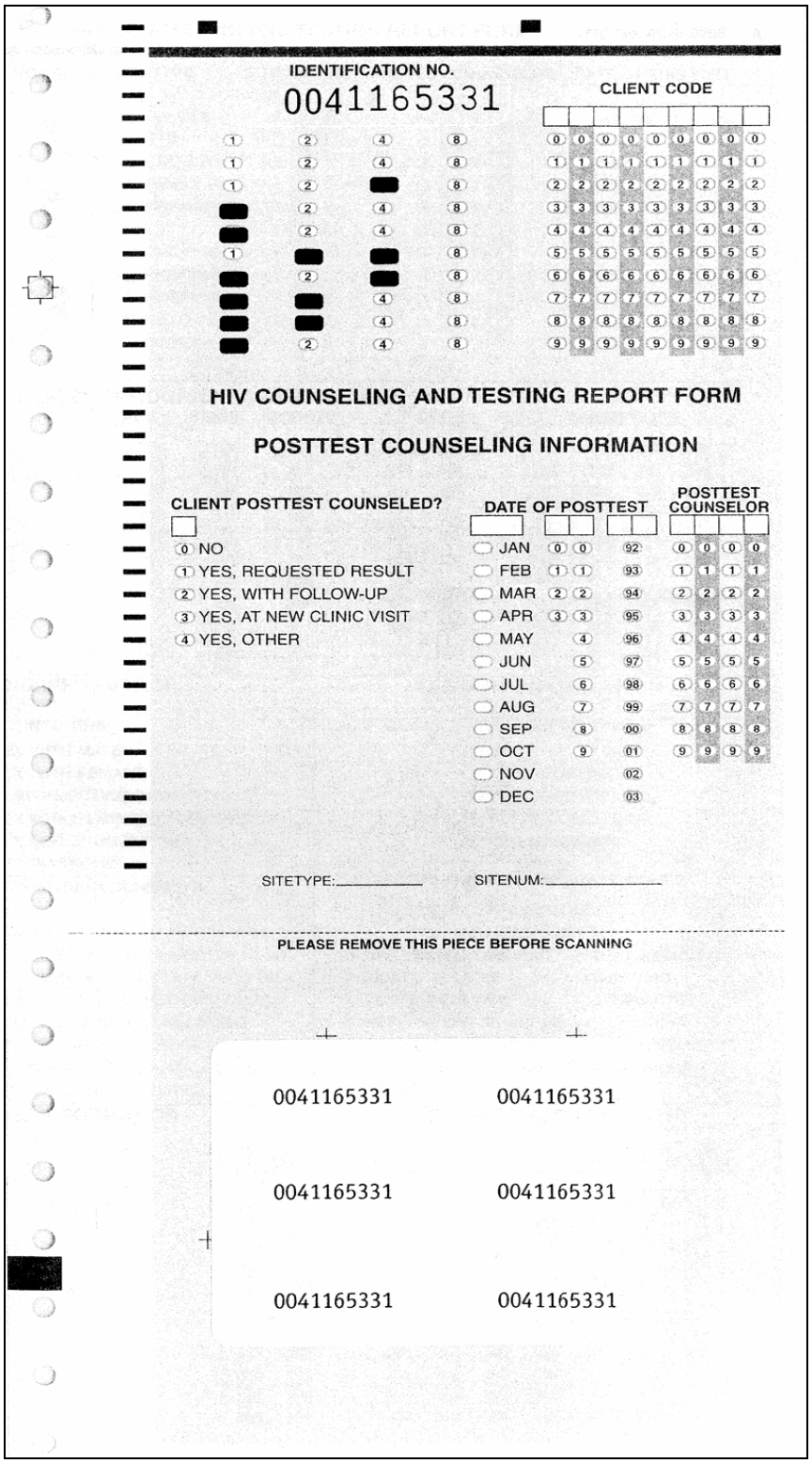
POSTTEST COUNSELING INFORMATION

CLIENT POSTTEST COUNSELED?
0 NO
1 YES, REQUESTED RESULT
2 YES, WITH FOLLOW-UP
3 YES, AT NEW CLINIC VISIT
4 YES, OTHER

DATE OF POSTTEST
JAN 92
FEB 93
MAR 94
APR 95
MAY 96
JUN 97
JUL 98
AUG 99
SEP 00
OCT 01
NOV 02
DEC 03

POSTTEST COUNSELOR

RESERVED FOR LOCAL USE
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15



IDENTIFICATION NO.

0041165331

CLIENT CODE

HIV COUNSELING AND TESTING REPORT FORM

POSTTEST COUNSELING INFORMATION

CLIENT POSTTEST COUNSELED?

0 NO
1 YES, REQUESTED RESULT
2 YES, WITH FOLLOW-UP
3 YES, AT NEW CLINIC VISIT
4 YES, OTHER

DATE OF POSTTEST

JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC

92 93 94 95 96 97 98 99 00 01 02 03

POSTTEST COUNSELOR

SITETYPE:_____ SITENUM:_____

PLEASE REMOVE THIS PIECE BEFORE SCANNING

0041165331 0041165331

0041165331 0041165331

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