EPIDEMIC SYPHILIS IN ROBESON COUNTY, NORTH CAROLINA: ACTUAL OR ARTIFACT?

A SURVEILLANCE SYSTEM EVALUATION, 1999-2001

by

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Introduction-

Dramatically declining incidence of infectious syphilis in the United States in recent years prompted the Centers for Disease Control and Prevention (CDC) to pursue syphilis elimination in this Country. "Elimination of syphilis would have far-reaching public health implications because it would remove two devastating consequences of the disease—increased likelihood of HIV (human immunodeficiency virus) transmission and compromised ability to have healthy babies due to spontaneous abortions, stillbirths, and multi-system disorders caused by congenital syphilis acquired from mothers with syphilis." [1] A leader in the field said control of this disease is a national priority because of the ravages of congenital infections.[2]

Syphilis is coded 001-139 under the infectious and parasitic diseases heading of the ICD-9 scheme. The first set of syphilis diagnoses is Congenital. Code 090.0, Early congenital syphilis, includes choroiditis, chronic coryza, heaptomegaly, mucous patches, periostitis, splenomegaly, epiphystitis, osteochondritis, pemphigus, and any congenital syphilitic condition specified as early or manifest less than two years after birth. Codes 090.1-090.3 include Latent early congenital syphilis, Unspecified early congenital syphilis, and Syphilitic interstitial keratitis, respectively.[3] Stillbirths and spontaneous abortions due to vertical transmission are among the sequelae of this preventable and curable sexually transmitted disease (STD).

"...Kassowitz's law (states): The longer the duration of the untreated infection before the pregnancy, the less likely it is that the fetus will be stillborn or infected. Thus, pregnancy while the mother is in the primary or secondary stages of infection frequently terminates in a stillbirth, whereas pregnancy occurring during the later stages of syphilis

may result in a clinical spectrum from a fulminating fatal congenital syphilis to an uninfected child."[4] Monitoring incidence of congenital infections is, therefore, useful in syphilis surveillance because of the temporal relationship between expectant mothers' recent inoculations and adverse pregnancy outcomes. Surges in congenital case reports typically follow increasing incidence of lesion cases. The CDC received 529 congenital case reports during the year 2000 from across the Nation, for a rate of 13.4 per 100,000 live-born infants. This compares to 27.8 in 1997, for a 51.8% decrease during this four-year period. This decrease is evidence of national progress toward elimination. However, the South had the highest year 2000 rate of congenital cases at 18.8 per 100,000 live-born. [5]

The national plan to eliminate syphilis

Syphilis elimination at the national level is defined as "...the absence of sustained transmission in the United States. At the local level, syphilis elimination is defined as the absence of transmission of new cases within the jurisdiction except within 90 days of report of an imported case...the national goal, therefore, is to reduce primary & secondary (P&S) syphilis cases to 1,000 or fewer and to increase the number of syphilis-free counties to 90% by 2005."[6] Syphilologists assume the infecteds became inoculated while sex partners had primary lesions. A painless ulcer at the infection site characterizes the primary stage of this systemic disease. Symptoms of secondary infection "...include but are not limited to skin rash, mucocutaneous lesions, and lymphadenopathy."[7] While relapses of secondary symptoms occur, these manifestations typically appear following a brief period of early latency. Thus, the significance of tallying P & S cases is apparent.

Patients so diagnosed were infected and potentially infectious within weeks to months before diagnosis date. The occurrence of P & S cases is clear evidence of sustained propagation.

To meet the criteria for an early latent syphilis diagnosis, the patient with reactive nontreponemal and treponemal serology must have an epidemiologic link to a known primary or secondary case, a history of symptoms suggestive of primary or secondary syphilis within the twelve months prior to the reactive tests, or a confirmed history of a nonreactive serology within the preceding year. Clinicians presumptively diagnose early latent infection by observing a two-dilution nontreponemal test titer increase between sequential tests in the absence of treatment.[8] To improve robustness of this study, early latent diagnoses were merged with P & S. The sum of P & S cases plus those meeting the criteria for early latent diagnoses comprised early syphilis cases.

Robeson County, population 123,399, is experiencing epidemic early syphilis. This contrast with national and state incidence renders Robeson a High Morbidity Area (HMA). An HMA is defined as "...(an area) with continuing syphilis transmission, usually signaling the need to improve preventive access to clinical and laboratory services."[9] If this rural county continues to experience epidemic conditions, it will be left behind when CDC meets its goal of national level elimination. Further, "...continuing current STD prevention and control efforts, alone, will not be sufficient. New strategies are also required. Combining intensified traditional approaches with innovative approaches can generate new synergy and enhance the effectiveness of syphilis elimination efforts."[10] A look at national incidence follows, narrowing to that of North Carolina (NC), and then to Robeson County.

Distribution of early syphilis by time

The crude case count of infectious syphilis in the US decreased approximately 20% per year since the most recent national epidemic in the early 90's, with the rate of decrease flattening to just 5% from '98 to '99. Distribution by time since 1996 revealed a similar picture. 31,575 (11,388 P&S plus 20,187 early latent) cases were reported in 1996, down to 18,334 (6,657 P&S plus 11,677) in 1999 for a 42% decrease in early syphilis during this four-year period. The Southeast US continued to experience high rates of early syphilis relative to the other three US regions.[11]

Zooming in on North Carolina (NC), one observes how this state contributed to historically low national incidence despite NC's distinction as a state with disproportionately high rates. The nearly 2-fold decline in early syphilis across the country during the late 90's was exceeded in NC.[12] During 1996, 2,121 (29.0 cases/100,000 population) cases of primary, secondary, and early latent syphilis were reported in this State. This figure fell to 1,104 cases (14.2 cases/100,000 pop.) in the year 2000, for a 48% decline from 1996's rate. During the period 1996-2000, Robeson County appeared to be the most intractable of the State's five HMA's.[13]

This county's syphilis experience met the definition of epidemic. Epidemic is defined as "The occurrence in a community...of cases of an illness...with a frequency clearly in excess of normal expectancy...; epidemicity is thus relative to usual frequency of the disease in the same area."[14] The number of primary, secondary, and early syphilis cases among Robeson County residents increased from 65 in 1996 to 144 cases in 2001. Thus 2001's incidence was 122% greater than that of 1996. This jurisdiction without any metropolitan areas had the country's highest early syphilis incidence rate in the year

2000, and 2001's case count was even higher yet. The rate of increase appears to be flattening. For the period under examination, 1999-2001, ordinary least squares regression was employed to test for a trend of increasing incidence. Please refer to Figure 1.

Alternative methods to detect the presence of epidemics

How does one know when epidemic conditions are present? "An epidemic, or outbreak, is the occurrence of a disease in members of a defined population clearly in excess of the number of cases usually or normally found in *that* population." [15] The increase in reported cases during the late 1990's represents an aberration in time in terms of Robeson County residents' syphilis experience. Beyond case counts, this analysis of surveillance data considered the impact of varying screening intensity on incidence. "Perhaps the most fundamental question suggested by the analysis of a surveillance system is...When does the value of reported events signal a change in process from past patterns?"[16] Janes *et al* describe four techniques for detecting aberrations from baseline by comparing current reports to historical data. Detection of aberrations from baseline, in turn, prompts public health action. At the national level of surveillance, such techniques can detect the presence of epidemics. States are obligated to customize thresholds for outbreak detection within their jurisdictions. In the local setting of Robeson County, sharply increasing incidence prompted forceful intervention.

P&S cases are more useful than those reported as early latent as a marker for evidence of ongoing transmission also because unreliable staging is more likely with early latent diagnoses. The ratio of P&S to early latent diagnoses in Robeson County

reversed in direction from 1996's 1:1.5 to the first half of 2001's ratio exceeding 2:1. The proportionate increase in P&S is cause for alarm because of these diagnoses' association with sustained transmission and congenital infections.[17] Before activating the Klaxon, however, one may consider the significance of discovering lesion cases; by reaching patients during the infectious stages, controllers minimize the duration of infectiousness. Therefore, a temporary surge in P&S reports could signal success.

The more we looked for infections, the more we found?

Burgeoning annual case reports generated consensus among agencies combating syphilis in this county that an epidemic was underway. Yet, the more cases found, the more ardently controllers sought new cases by intensifying contact tracing efforts with more Disease Intervention Specialists (DIS), increasing community screening during a Rapid Intervention Outreach Team (RIOT's) mobilization, promoting increased screening among private providers, campaigning with innovative health education events with mass media and community outreach. Much of this activity was embedded in the North Carolina Syphilis Elimination Project, part of CDC's *National Plan to Eliminate Syphilis.*

North Carolina's Department of Health and Human Services' (NC DHHS) sustained response to increased incidence was designed to increase screening of the population at risk for acquiring and transmitting syphilis. Increased reported incidence in the presence of intensified traditional approaches and innovative case finding efforts suggested, "...other than the disease process itself...other factors could cause (the observed increase)."[18] The other factor of interest herein is specimen collection history. Data from

the pre-epidemic period capturing the number of specimens collected were unavailable, so this analysis was confined to that portion of the epidemic period bounded by Jan 1 1999 through Dec 31 2001.

Objectives and rationale behind experimental approach

The purpose of this project is to elucidate epidemic syphilis in Robeson County, one of this country's few remaining geographic areas where syphilis transmission is concentrated. Taking population size into account, no other U.S. county has incidence rates as high. This project closely examined efforts to find new cases in an attempt to more fully explain the observed increase in incidence. Increased incidence "...may, in part, reflect improved reporting and case finding resulting from the national...effort. However, the increases also may be attributed to increases in populations that have been difficult to reach..."[19]

The central thesis question: Is this HMA is in the midst of a true epidemic or has an artifactual epidemic been caused by improved ascertainment? While epidemiologic dynamics are complex with complete explanations elusive, two measures of interventionists' effects on incidence may provide a partial answer to this query. One measure will capture how intensely cases are sought, and the other will capture how effectively they are found.

In the presence of sustained and aggressive screening, as is the case among Robeson County residents, the proximate measure of declining *hit rate* through time can couple with the distal outcome of declining incidence as signs that the current epidemic is abating. Alternatively, steady or increasing hit rates would suggest that victory is by no

means at hand. In addition to more accurately characterizing recent trends in this HMA, exploring associations in this manner may yield a novel way to evaluate success within and between sexually transmitted disease (STD) programs from the local to national levels. This evaluation could supplement routinely gathered registry data to monitor progress toward elimination.

Those whose job entails controlling and preventing bacterial STD may be viewed as case finders. Successful control of STD's such as syphilis is achieved to the extent that new infections are sought, found, and cured. For this project, the distal predictor of incidence, *intensity* (*I*), is defined as the number of serologic tests for antibodies to *Treponema pallidum* performed per unit time. Additional measures that could supplement a composite intensity measure were considered. However, other candidates for inclusion in a novel measure, more elaborate than as defined herein, were too distal and interrelated to be useful. One could hypothesize that incidence is roughly proportionate to the number of residents screened within the HMA. Yet, screening in an effort to eliminate syphilis is without effect to the extent that it fails to detect new infections. Therefore, this project also attempted to quantitatively measure effectiveness of case finding.

A second measure called e*ffectiveness* (*E*) was primarily the number of hits, as defined below. The number of included cases, or "hits," was the proximate predictor of incidence; each hit contributed to this study's case counts. *Hit rate* is the percentage of reactive serologies resulting in diagnoses of early syphilis per unit time; this effectiveness measure quantified *impact*, facilitating intra-site and inter-site comparisons. Holding i*ntensity* (the number of patients tested) constant, improved e*ffectiveness* (the number of

tests yielding early diagnoses) can drive incidence upward. Against a background of decreasing transmission of new infections, and assuming constant risk among the screened, hit rates decline through time. These measures have the following mathematical relationships:

Equation 1. GM's formula for case finding evaluation

$$\textit{Hit rate (impact)} = \frac{E}{I}$$

A similar phenomenon has been described in the context of US DHHS's Reg X Chlamydia Project. That sustained intervention, built on widespread screening among young women and other selected subpopulations, was successful as measured by declining prevalence; this measure was calculated by dividing the number of positive tests by the number of tests performed. Distribution of prevalence by time suggested programmatic success. Prevalence is analogous to this study's *hit rate.*

An alternative explanation for decreasing prevalence among those screened for *Chlamydia trachomatis* was lesser risk among the screened through time. Adjusting for risk among the screened was beyond the scope of this project. Robeson County's recent experiencewas one of increasing reported incidence, so hit rates might have been expected to increase with time. This expectation is consistent with true epidemic conditions, as opposed to an epidemic generated by intensified screening in the presence of endemic early syphilis. A clear association existed between increased reporting of chlamydia infections through time and increasing incidence at the national level. As more states mandated reporting, a national epidemic was observed.[20] Emerging

infections are not confined to recent introduction of pathogens to human reservoirs; *C. trachomatis*' immunotypes D through K had a dimly understood history of propagation between human hosts before extensive, pathogen-specific screening was established. While the U.S. pool of infecteds may be expanding through time, the current epidemic of urogenital chlamydia infections could be characterized as manufactured, or artifactual, from this perspective.

Despite the appearance of an increasing rate at which infection was reproducing, a positive association between changes in intensity and effectiveness would suggest Robeson County's epidemic was at least partially an artifact of our interventions. The term "endemic" may more accurately describe syphilis morbidity in this setting.[21] Distribution of early syphilis by reason for exam could shed light on the thesis question more simply. For example, if symptomatic volunteers inundated the STD clinic and the hospital emergency room, compelling surveillance data suggestive of a climbing rate at which infection was reproducing would have been available. The same conclusion could be drawn from increasing incidence of congenital cases, although as an echo of the previous year's inoculations. While the illustrious Dr King Holmes' *Rho* is a heuristic device rather than measurable in a community, subtracting that portion of increased incidence attributable to intensified screening could illumine *Rho*'s direction in this setting.[22] Because *hit rates* incorporate specimens collected and cases found, a straightforward way to measure the intensity-effectiveness connection is to look at changes in hit rate over time.

From a case finder's perspective, screening in the absence of detecting early infections is devoid of impact. From a surveillance perspective, case counts alone can lead to

erroneous inferences partly because case counts are too subject to changes in screening practices (i.e.: intensity differences). Seroprevalence is even less meaningful in that this measure merges newly infecteds with their previously treated counterparts. The proportion, yield among reactors, is similarly invalid as a detector of where this County's morbidity trend is going because the denominator increases with time; that is, as the number of persons with a history of infection increases, yield among reactors decreases even in the presence of steady or moderately increasing incidence.

Evidence suggesting that increasing incidence is attributable to intensified screening can be found by measuring the association between differences in *intensity* and differences in the number of *hits*. Increasing hits through time from increasing specimen collections answers the thesis question affirmatively, as do decreasing hits from decreasing collections and steady hits from unchanging collections. A finding of discordance between collections and hits answers the thesis question negatively. How closely does the observed increase in incidence correspond to the actual state of affairs?[23]

Bound by its limitations, this study will have explained Robeson's aberrational epidemic to the extent that it finds positive associations between *intensity* and *effectiveness*.

Benediction

Syphilis will not have been eliminated by the year 2005 using current strategies unless naturally occurring10-year cycles and risk behaviors conspire favorably with the intensity and effectiveness of our efforts.[24] This project attempts to illumine our efforts' impact on the goal of elimination as these efforts relate to reported incidence in the setting of

Robeson County. The following methodology was employed to determine to what extent, if any, the observed increase in incidence was attributable to increased screening.

Methods-

Intensity of screening for antibodies to *T. pallidum* was quantified by counting specimens collected during the period 1999 through 2001 from patients seen at three major service sites. *Effectiveness* of the screening effort was quantified by counting hits. A *hit* is defined as a reported diagnosis of primary, secondary, or early latent syphilis. The sum of hits comprised *study case counts*, a subset of all reported cases within this jurisdiction. The association between *intensity* and *effectiveness* was measured by calculating an impact measure called *hit rate*. These measures--*intensity*, *effectiveness*, and the association between them as measured by *hit rate*-- were compared between and within sites through time.

Statistical manipulations and package used

All statistical results were generated by EpiInfo 2000.[25] A database of 10 summary "observations" was created including the following variables: service site; year of specimen collection; number of specimens collected; number of reactive tests; and number of hits. Dr Del Williams of NC DHHS provided confidential NC Syphilis Registry data in the form of an Excel spreadsheet. This spreadsheet, containing all Robeson County residents reported with early syphilis diagnoses during the period of interest, was the only material used in this study available in modern database form. Please refer to Appendix 3 for a listing of data fields from this Excel document.

Ordinary least squares regression was employed to determine if trends of increasing annual registry case counts and study case counts were statistically significant. This was accomplished by using the "analysis" program's "regress" command, and selecting the variable "year of collection" and registry case counts, and again by regressing "year" against "number of hits". *F* statistics from these regressions were then compared to a *t* value table as published in *Biometrika Tables for Statisticians*. In the absence of statistically significant trends, further statistical analysis would be without meaning.

To test for intra and inter site *intensity* differences, the "epitable calculator" program was employed. Selecting "compare", "proportions", and "goodness of fit", the number of specimens collected at each site was entered as actual values while the three-year mean served as expected values. This procedure produced values for the chi squared goodness of fit test. Values for chi squared and p-values were automatically generated by the program. In the absence of statistically significant intensity differences, the hypothesized link between *intensity* and *effectiveness* could not be explored meaningfully with this study's methodology.

To test for intra and inter site *effectiveness* differences, values for *hit rate* and number of specimens collected were entered into the appropriate fields of the package's epitable calculator. This procedure assumed equal categories and produced values for the chi squared test for homogeneity. Values for chi squared and attendant p-values were again generated by the program. Inter site differences quantified distribution of *impact* by site. Intra site differences quantified distribution of *impact* by time.

Three service sites as surrogate for universe of the screened

Sites excluded from this study included private practices within Robeson County using laboratories other than SRMC's, private practices outside Robeson County serving county residents, public health care sites (i.e. health departments, correctional facilities) located outside the county where Robeson residents received serologic tests for syphilis, and non-STD clinic public health care sites within the county (i.e. RCHD's Prenatal and Adult Health Clinics, state correctional facilities located within the county). The number of specimens collected at these excluded sites is unknown.

Initial interest in SRMC, the only hospital in Robeson County, was based on the belief that emergency room encounters contributed importantly to reported incidence.[26] SRMC's Laboratory not only ran serologic tests for syphilis for SRMC patients wherever these patients may have been encountered within the hospital, but also for patients screened at many private provider offices across the County. Thus, *intensity* and *effectiveness* of small office settings was folded into SRMC data and measured as well.

While the total number of specimens collected for serologic testing among Robeson County residents during this three-year period was unknown, three service sites collected a total of 28,880 specimens during the period 1999 through 2001. These three sites accounted for 70% (271/386) of all primary, secondary, and early latent case reports recorded in the North Carolina Syphilis Registry. The magnitude of specimens collected at these sites coupled with the sites' large proportionate contribution to early case reports led to confinement of this study to Robeson County Health Department (RCHD), Southeast Regional Medical Center (SRMC), and Robeson County Jail (RCJ). Because

no attempt was made to randomly select subjects from whom specimens were obtained, the patients comprised a convenience sample.[27]

The sum of *hits* at these three service sites, referred to herein as *study's case counts,* served as a surrogate for total incident cases in this jurisdiction. Had this project captured all county residents screened and all reported morbidity, the number of hits would have been the total number of incident cases. Least squares regression was again employed to test for an increasing trend of *study case counts*. Please refer again to Figure 1, noting concordance between registry and study case counts.

Quantifying intensity

RCHD maintains specimen collection histories in a set of logbooks. Laboratory personnel manually recorded patient names, serologic test dates, and test results. One book contained names and serologic results from all patients seen in the health department's Communicable Disease Clinic; this binder captured all specimens collected from patients presenting to the STD specialty clinic. Another book contained patient names and tests ordered for all patients screened at RCJ. A third book contained names and results from all patients encountered in the community during the RIOT events of August 2001. Please refer to Appendix 2 for sample form used by lab staff.

From these logs, the number of specimens collected, dates of collection, patient names, and test results were recorded. Rather than grouping all RCHD specimens together, only the STD clinic and RIOT data were examined. Test results of non-STD clinic patients were not recorded in the logbooks, so other RCHD clinics (i.e.: prenatal, orthopedic) were excluded from this study. *Hit rate* was hypothesized to differ between

RCHD clinics due to greatest risk among STD clinic attendees, but this wasn't explored due to unavailability of RCHD's non-STD clinic patient data.

The third component of the health department's specimen collection history came from Rapid Intervention Outreach Team (RIOT) efforts of Aug 17-18, and Aug 24-25 2001. RCHD laboratory staff logged the names, dates of specimen collection, and serologic results of all patients from whom specimens were collected during the RIOT. The number of specimens collected during this event spanning two weekends was counted.

While SRMC laboratory personnel recorded specimen collection history differently from their public sector counterparts, the number of specimens collected per month was systematically recorded on DHHS Form #1393; please refer to Appendix 1. These forms also include line listings of patients with reactive nontreponemal or treponemal tests. The number of specimens collected per month was tabulated, and then monthly were compressed into annual tallies.

In addition to calculating changes in numbers of annual specimen collections, the chi-squared goodness of fit test was employed to seek statistically significant intensity differences within sites by year and between sites within a given year. Please refer to the first numeric column of Tables 2 through 8 for distributions of *intensity* by site and year.

Quantifying effectiveness

Having tallied and tabulated the number of specimens collected at each site under examination, the number from each site resulting in reactive nontreponemal and treponemal serologies as documented on SRMC's DHHS form 1333 and RCHD's three

logbooks was counted. Biologic false positives (BFP's), defined as a reactive nontreponemal tests in the presence of nonreactive treponemal tests, were excluded from this analysis. All BFP's were classified as nonreactive.[28] Specimens with reactive STS included patients with confirmed histories of having been adequately treated for syphilis in the past were tabulated. Only those reactive STS resulting in new diagnoses of primary, secondary, or early latent syphilis, however, were tabulated under the tables' *hit rate* column heading. The sum of *hits* comprised *study case counts.*

In calculating proportions of patients with reactive serologies, the number of reactive STS was divided by the number of specimens collected as recorded on the prescribed form and log books; this proportion is *seroprevalence.* An additional proportion of peripheral interest was *yield among reactors*; this measure was obtained by dividing the number of early diagnoses by the number of reactive tests. Please refer to the second and fourth numeric columns of Tables 1 through 8 for *seroprevalence* and *yield among reactors.*

Quantifying impact, a measure of effectiveness

The value for *hit rate* as defined herein is an impact measure. This measure adjusts for *intensity* changes, thereby allowing easily interpretable relationships between varying screening effort and attendant changes in cases found. Hinman described four types of evaluation, including that of "impact". "Evaluation should take place at all stages in the...application of such interventions, whether preventive or therapeutic." [29] *Hit rate* quantified how much of an impact screening efforts had on case finding. The number of *hits* is the number of specimens resulting in early diagnoses. *Hit rate* is the number of

hits divided by the number of specimens collected. Please refer to the third numeric columns of Tables 1 through 8 for *hit rates*.

Screening for syphilis in the county jail

To quantify the proportion of inmates screened at RCJ, the number of inmates admitted per unit time was tabulated. RCJ staff provided annual reports of inmate admissions. These reports detailed how many inmates had been admitted to RCJ by month. The number of inmates receiving serologic tests for syphilis (STS) was counted and tabulated. This setting is the only one for which patient census was rigorously considered, although universal screening is standard procedure at the STD clinic. Please refer to Figure 3.

The proportion of inmates screened was calculated by dividing the number of specimens collected per month by the number of inmates admitted per month. Monthly tallies were then compressed into annual counts. These proportions quantified how closely the goal of universal screening was met at RCJ. They also measured to what extent "...opportunities for syphilis treatment... among this transient population" were seized. [30] *Intensity*, *effectiveness*, and other measures were calculated, tabulated, and manipulated as they were for RCHD and SRMC.

Distribution of effectiveness by service site & and by time

With *hit rate* calculations in place, the next step in this analysis was to observe how *hit rates* compared within and between service sites. Was there a difference between *hit rates* at RCHD's STD clinic, SRMC, RCJ, and the RIOT setting in a given year? How

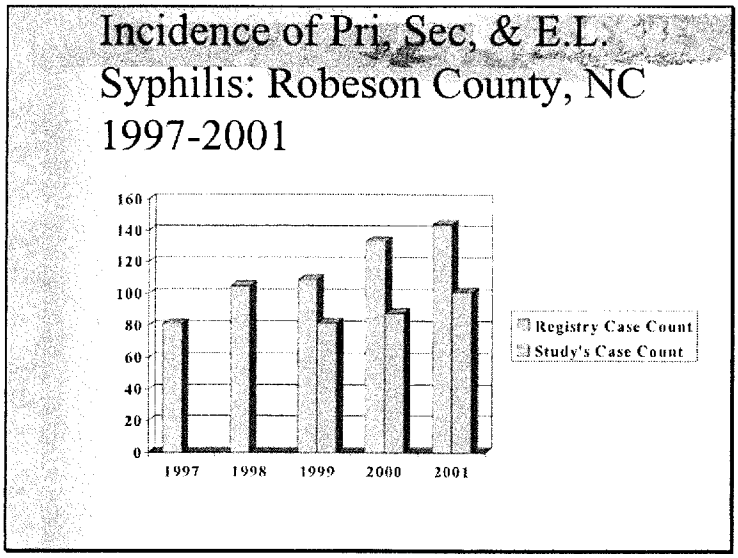
did each site's *hit rate* change over time? To measure how *effectiveness* may have varied within and between sites, distribution by time of *hits* and *hit rate* at each setting was explored, as was distribution of *effectiveness* by service site. An attempt was made to discover an association between the number of specimens collected and the number of early diagnoses found. To what extent, if any, were changes in the number of specimens collected associated with changes in the study's case count? This question was answered by quantifying the association between intensity and hits.

Results-

Distribution of early syphilis by time

Annual incidence of primary, secondary, and early latent syphilis increased each successive year during the period 1997-2001. The number of reported early cases increased from 109 to 144 (32.1%) during the study period--1999-2001. From 1999 to 2000, incidence increased from 109 to 133 reported cases (22.0%). Incidence then rose further from 2000's 133 cases to 2001's 144 (8.3%). While the rate of increase decelerated between 2000-2001 in comparison to the period 1999-2000, the epidemic continued on its course. Please refer to Figure 1.

Figure 1. Incidence of primary, secondary, & early latent syphilis: registry case counts 1997-2001 and study case counts 1999-2001, Robeson County, NC



Least squares regression was employed to test for a statistically significant difference between annual case counts. Simple linear regression of number of cases by year yielded the following tables (Table A and Table B), reproduced from EpiInfo's output:

Table A. Least squares regression of registry case counts by year, 1999-2001

correlation coefficient r=0.98, r-squared=0.96

Source	Df	SS	MS	F-statistic
Regression	1	612.5000	612.5000	21.75
Residuals	1	28.1667	28.1667	
Total	2	640.6667		

With a correlation coefficient of 0.98, the number of cases reported annually (dependent variable), was highly correlated with year of report (independent variable). To determine if the registry case count increased significantly through time, a test for a nonzero slope of this plot was performed. The t-test yielded the same results as the F-test in this application because just one independent variable was considered. Multivariate analysis would have led to use of F-distribution tables. The null hypothesis states that beta=0, that the slope of this plot is equal to zero. With an F-statistic of 21.75 and 1 degree of freedom, the t-value at the 0.05 level of significance was 6.314. Since 21.75>6.314, the null was rejected; the alternative hypothesis, that the slope of registry case counts versus year of report was not equal to zero, was accepted. Registry case counts increased to a statistically significant degree through time.

Table B. Beta coefficients for least squares regression of registry case counts by year, 1999-2001

Variable	Mean	B coefficient	95% C.I.'s		Standard Error	Partial F-test
			Upper	Lower		
Year	2000	17.50	-30.18279	65.18279	3.75278	21.7456
y-intercept		-34871.3334				

The partial F-test statistic of 21.7456 is equal to that found in table A because this regression included just one "predictor" variable. The most meaningful information gleaned from Table B is the beta-coefficient of 17.50. This value is interpreted thusly: for each successive year, the number of total incident cases increases by nearly 18. From another perspective, 17.50 was simply the mean difference in registry case counts between years. A statistically significant increasing trend is apparent. Confidence

intervals crossed zero; additional years of observations could tighten this wide disparity between upper and lower bounds.

Distribution of study case counts by time

Of the specimens collected during 1999 at the three sites under examination, 82 yielded diagnoses of primary, secondary or early latent syphilis. 2000's collections yielded 88 new cases, and 2001's 101. This study captured 75% (82/109) of 99's early syphilis morbidity, 66% (88/133) of 2000's, and 70% (101/144) of 2001's, or 70% (271/386) of the cases reported during the three-year period. The study's case count increased by 23.2% from 1999 through 2001, a muted increase in comparison to the 32% rise observed in registry case counts during the same period. Please refer again to Figure 1. Was this subset of all reported cases, herein referred to as *study case counts*, characterized by a statistically significant increasing trend?

To answer this question, least squares regression was again used to determine if the increasing trend of *study case counts* was significant. Similar results were found. Regressing annual *study case counts* by year, EpiInfo yielded Tables C and D.

Table C. Least squares regression of study case counts by year, 1999-2001

correlation coefficient: r=0.98, r-squared=0.96

Source	df	SS	MS	F-statistic
Regression	1	180.5000	180.5000	22.10
Residuals	1	8.1667	8.1667	
Total	2	188.6667		

As seen in table C, *study case counts* were highly correlated with year of report as revealed by a correlation coefficient of 0.98 and r-squared of 0.96. The null hypothesis states that the slope of the line describing this association is zero, while rejection of the null leads to the alternate hypothesis of a nonzero slope. With an F-statistic of 22.10 and 1 degree of freedom, the t-value at the 0.05 level of significance was 6.314. Since 22.10>6.314, the null was rejected. A statistically significant trend of increasing *study case counts* existed.

Table D. Beta coefficients for least squares regression of study case counts by year, 1999-2001

Variable	Mean	Beta coefficient	95% C.I.'s		Standard Error	Partial F-test
			Lower	Upper		
Year	2000	9.5000	-16.17538	35.175378	2.020729	22.1020
y-intercept		-34871.3334				

Table D includes a beta coefficient for the regression line's slope of 9.5; for each successive year, nearly 10 additional cases were found. Less sophisticated analysis finds 9.5 as simply the mean difference between years in *study case counts*. While confidence intervals around this coefficient are tighter than found for registry case counts, they too cross zero.

Distribution of intensity & effectiveness by time, combined sites

In 1999, 9,640 specimens were collected for serologic testing for antibodies to *T. pallidum* at the service sites included in this study. These sites included Southeast

Regional Medical Center (SRMC), the Robeson County Jail (RCJ), the Rapid Intervention Outreach Team (RIOT, 2001 only), and Robeson County Health Department's Communicable Disease Clinic (RCHD). 9,463 specimens were collected during 2000, for 1.84% *fewer* specimens collected in comparison with the previous year. With 9,777 specimens tested during 2001, collections increased by 3.32% in comparison to 2000. With a total of 28,880 total specimens collected during the period of interest, the annual mean was 9,627. Please refer to Table 1.

Table 1. Specimen collection history & hit rate, combined sites 1999-2001

Specimen Collection Hx & Hit Rate, Combined Sites 1999-2001

Year	Number of Specimens Collected	Number of Reactors/ (Sero-prevalence)	Number of Hits/ (Hit Rate)	Yield among Reactors
1999	9640	286 (2.97%)	82 (0.85%)	28.67%
2000	9463	315 (3.33%)	88 (0.93%)	27.94%
2001	9777	393 (4.02%)	101 (1.03%)	25.70%

Was the difference between annual number of specimens collected statistically significant? Using EpiInfo to conduct a chi-squared goodness of fit test, assuming all categories were equal, the value for chi-squared was 5.15 with 2 degrees of freedom, yielding a p-value > 0.05. A statistically insignificant difference between annual number of specimens collected at combined sites was apparent.

Early cases identified among patients seen at included sites increased by 7.32% from 1999's 82 cases to 2000's 88. The cases so identified increased 14.77% from 2000's 88 to 2001's 101. The number of cases identified at included sites increased by 23% during the period 1999-2001. *Hit rates* at all sites combined hovered around 1% through the period of interest. In 1999, the *hit rate* was 0.85%, rising to 0.93% in 2000, and higher yet to 1.03% in 2001. A chi-squared test for homogeneity was conducted to compare these proportions. The chi-squared value was 1.75 with 2 degrees of freedom, yielding a p-value > 0.05. *Hit rates* between years among combined sites did not differ to a statistically significant degree.

Distribution of intensity & effectiveness by site, 1999

With 1999's 45 hits among STD Clinic patients, this clinic yielded more early cases than SRMC (21) and RCJ (16) combined. This STD Clinic's yield was even more impressive considering that collections among SRMC patients were over 3-fold greater than among STD clinic patients. Please refer to Table 2.

Table 2. Specimen collection history & hit rate, all sites 1999

Specimen Collection History & Hit Rate, All Sites 1999

Service Site	Number of Specimens Collected	Number of Reactors/ (Sero-prevalence)	Number of Hits/ (Hit Rate)	Yield Among Reactors
SRMC	5791	90 (1.55%)	21 (0.36%)	23.33%
RCJ	2027	75 (3.70%)	16 (0.79%)	21.33%
RC STD Clinic	1832	121 (6.60%)	45 (2.46%)	37.19%

A gradient of seroprevalence is evident between these three sites. RCJ's seroprevalence was 3.70%, over 2-fold greater than SRMC's 1.55%. The STD clinic's seroprevalence of 6.60% was, in turn, nearly twice that of RCJ's. Unsurprisingly parallel to this gradient is that of *hit rate.*

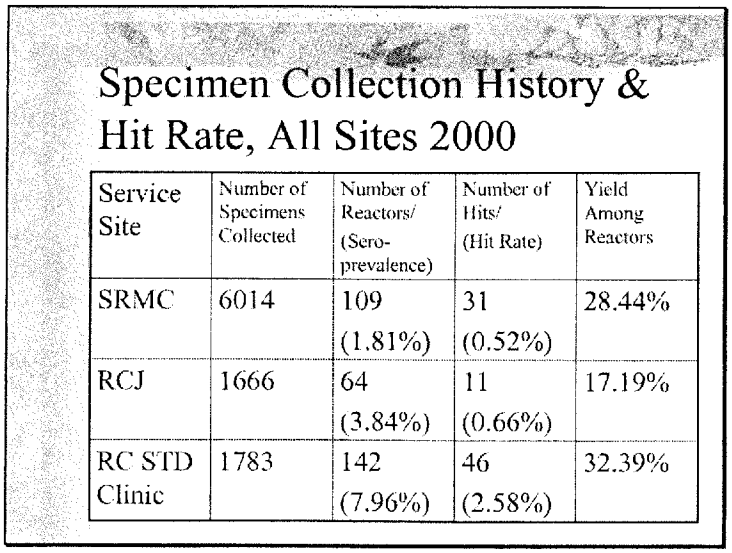
RCHD was the site characterized by maximum *effectiveness* with 45 hits from 1,832 specimens collected for a *hit rate* of 2.46%. RCJ's *hit rate* of 0.79% with 16 early cases discovered from 2,027 specimens collected revealed that the Jail had less than half the *hit rate* of RCHD. The lowest *hit rate*, 0.36%, from 21 cases detected of 5,791 specimens collected, was among SRMC patients. RCHD's *hit rate* was over 7-fold greater than that of Southeast Regional (SRMC). Employing the chi-squared test for homogeneity to compare these proportions, the value for chi-squared was 72.52; with 2 degrees of freedom, the resultant p-value was well below 0.05. In the year 1999, a statistically significant difference between *hit rates* by site existed.

Yield among reactors was also greatest at the STD Clinic (RCHD), with 45 *hits* among 121 reactive tests (37.19%). The yield among reactors at SRMC (23.33%) and RCJ (21.33%) were comparable to each other.

Distribution of intensity & effectiveness by site, 2000

In the year 2000, RCHD again produced more early cases than SRMC and RCJ combined. Southeast Regional again collected more specimens than RCJ and RCHD combined. Please refer to Table 3.

Table 3. Specimen collection history & hit rate, all sites, 2000



Specimen Collection History & Hit Rate, All Sites 2000

Service Site	Number of Specimens Collected	Number of Reactors/ (Sero-prevalence)	Number of Hits/ (Hit Rate)	Yield Among Reactors
SRMC	6014	109 (1.81%)	31 (0.52%)	28.44%
RCJ	1666	64 (3.84%)	11 (0.66%)	17.19%
RC STD Clinic	1783	142 (7.96%)	46 (2.58%)	32.39%

Consistent with the previous year, a gradient of increasing seroprevalence was evident from SRMC's 1.81% (109 reactive tests/6,014 specimens collected), to the Jail's 3.84% (64 reactive tests/1,666 specimens), to the Health Department's 7.96% (142 reactive tests/1,783 specimens).

Similarly, *hit rates'* relationships between sites parallel the seroprevalence gradient. The greatest *hit rate*, 2.58% (46 early diagnoses/1,783 tests), was among Health Department patients. Patients screened at Robeson County Jail contributed 11 early diagnoses to the *study case count* in 2000, with a *hit rate* of 0.66% (11 cases/1,666 tests). With a hit rate of 0.52% (31 early diagnoses/6,014 tests), SRMC had the lowest proportionate yield of early diagnoses among these three sites. Using a chi-squared test for homogeneity to compare *hit rates* between sites during the year 2000 revealed findings similar to that of the previous year. The value for chi-squared comparing these three sites was 65.22 with 2 degrees of freedom for a p-value well below 0.05. If RCHD were excluded, the difference between RCJ and SRMC's *hit rates* would fade to

statistical insignificance; comparing RCJ and SRMC's *hit rates* with one degree of freedom, the value for chi-squared was 0.50 with an attendant p-value > 0.05.

Distribution of intensity & effectiveness by site, 2001

As was the case in previous years, Southeast Regional collected more specimens in 2001 than all other sites combined. A fourth setting was added to sites under consideration—the Rapid Intervention Outreach Team (RIOT) of August 2001. The deployed RIOT team collected 706 specimens primarily for syphilis antibody testing; this quantity was nearly half the number of specimens collected at the Jail during the entire year.

At 3.54% (25 reactive tests/706 specimens collected), the RIOT's seroprevalence fell between that of the Jail and the Health Department. The seroprevalence gradient measured from the year 2000 held during 2001, with SRMC's at 2.29% (130/5,687), RCJ's at 3.39% (48/1,417), and RCHD's at 9.66% (190/1,967). Please refer to Table 4.

Table 4. Specimen collection history & hit rate by site, 2001

Specimen Collection History & Hit Rate, All Sites 2001

Service Site	Number of Specimens Collected	Number of Reactors/ (Sero-prevalence)	Number of Hits/ (Hit Rate)	Yield Among Reactors
SRMC	5687	130 (2.29%)	22 (0.39%)	16.92%
RCJ	1417	48 (3.39%)	8 (0.56%)	16.67%
RIOT	706	25 (3.54%)	5 (0.71%)	20.00%
RC STD Clinic	1967	190 (9.66%)	66 (3.36%)	34.74%

RCHD again contributed more early cases to the study's case count than all other sites combined. With 66 cases found among nearly 1,967 patients tested, the Health Department's *hit rate* of 3.36% exceeded that of the other sites. The RIOT's yield was 0.71% (5/706), nearly 5-fold less than that of the Health Department. The Jail's *hit rate* was 0.56% (8 cases/1,417 specimens). Having screened far more patients than any other site, Southeast Regional contributed 22 (22%) cases to the 2001 study case count; SRMC's *hit rate* was 0.39% (22 cases/5,687 specimens), once again the lowest proportionate yield of any setting considered. Comparing these *hit rates* by site during the year 2001, the now familiar relationships between service sites was observed. The proportion of early cases from RCHD exceeded that of SRMC by over 8-fold.

How did these effectiveness measurements differ in statistical terms? With three degrees of freedom, the chi-squared value from a test for homogeneity was 130.76 and the attendant p-value less than 0.05. A statistically significant difference between *hit rates* was evident. Were the public STD clinic excluded, all *hit rates* would be less than 1% and no statistically significant differences would emerge; excluding RCHD, with 2 degrees of freedom, the chi-squared value was 1.98 with an attendant p-value greater than 0.05.

Distribution of intensity & effectiveness by time, SRMC

SRMC consistently processed more specimens than any other site. SRMC performed an annual mean of 5,831 serologic tests for syphilis from 17,492 specimens collected during the three years under examination. The chi-squared goodness of fit test was employed to determine if annual collections from SRMC patients differed significantly.

The value for chi-squared was 9.57 with 2 degrees of freedom, yielding a p-value < 0.05. A statistically significant difference between annual SRMC collections was apparent. Please refer to Table 5.

SRMC consistently had the lowest seroprevalence and *hit rates* in comparison to its public setting counterparts. Seroprevalence steadily increased from 1999 through 2001. 1.55% (90 reactors of 5,791 tests) of all tests were reactive in 1999, 1.81% (109/6,014) 2000, and 2.29% (130/5,687) in 2001.

Table 5. Specimen collection history & hit rate, SRMC 1999-2001

Specimen Collection History & Hit Rate, SRMC 1999-2001

Year	Number of specimens collected	Number of Reactors/ (Sero-Prevalence)	Number of Hits/ (Hit Rate)	Yield Among Reactors
1999	5791	90 (1.55%)	21 (0.36%)	23.33%
2000	6014	109 (1.81%)	31 (0.66%)	28.44%
2001	5687	130 (2.29%)	22 (0.39%)	16.92%

With more specimens collected in 2000 than the previous or following year, this site detected the maximum number of cases in 2000. 31 cases were discovered in 2000, compared to 21 in the previous year, and 22 in the following year. While 2000's number of specimens collected increased by just 3.9% over 1999's, the number of cases increased by fully 47.6% between these two years. *Hit rates* followed this pattern of a maximum in the year 2000. With 5,791 tests among SRMC patients in 1999, 21 early diagnoses

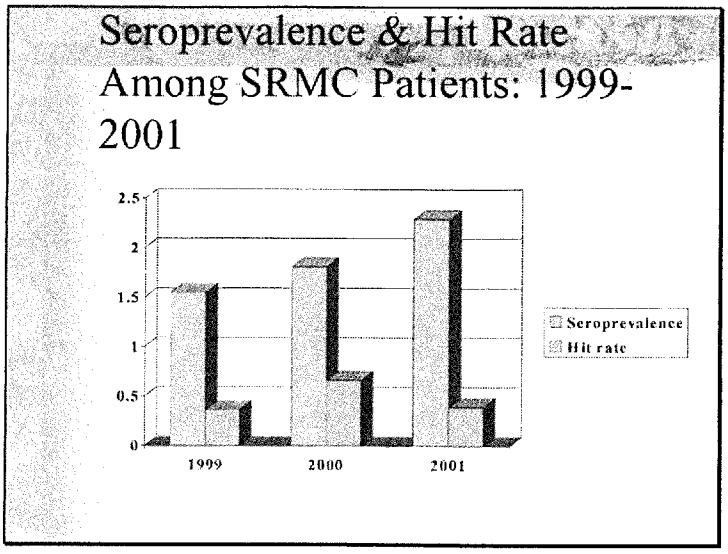
emerged; 21 cases/5,791 tests yielded a *hit rate* of 0.36%. This site's 6,014 tests in the year 2000 yielded 31 hits for a *hit rate* of 0.66%--nearly 2-fold greater than in the previous year. 22 hits from 5,687 tests in the year 2001 resulted in a *hit rate* of 0.39%.

Comparing this distribution of SRMC *hit rates* by time using a chi-squared test for homogeneity, the chi-squared value was 7.09 with 2 degrees of freedom, yielding a p-value < 0.05. A statistically significant difference between SRMC's *hit rates* was evident. The spike in hits in the presence of a surge in collections in the year 2000 rendered *effectiveness* differences significant. SRMC was the sole site under examination with observed *hit rate* heterogeneity through time.

Relationship between seroprevalence & hit rate, SRMC

In 1999 at SRMC, just 1.55% of all screened patients had reactive tests. The proportion of positive tests rose to 1.81% in 2000. This figure climbed yet further in 2001 to 2.29%. Through this 3-year period, a 32% increase in reactive tests among those screened at the hospital and private providers' offices across the county was observed. While seroprevalence increased steadily from 1999-2001, the *hit rate* spiked in 2000 at 0.66%, and then decreased to 0.39% in 2001. Please refer to Figure 2 from Table 5's data for a graphic depiction of this relationship.

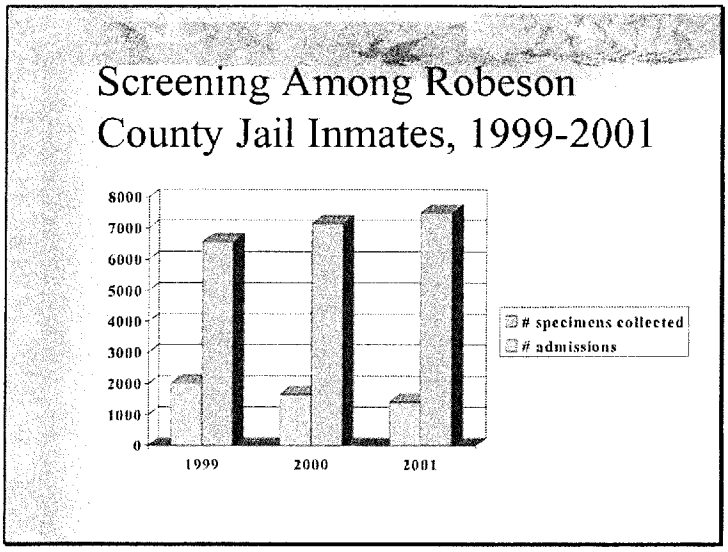
Figure 2. Seroprevalence & hit rate among SRMC patients, 1999-2001



Declining intensity at the county jail through time

Testing among Robeson County Jail inmates decreased throughout the period of interest. A total of 2,027 specimens were collected from this population in 1999. This figure declined to 1,666 in the following year, and yet further to 1,418 in 2001. 30.8% of admitted inmates were tested in 1999, 23.3% in 2000, and 18.9% in 2001. Average monthly collections decreased from 169 per month in 1999 to 139/mo in 2000, and fell further to 118/mo in 2001. Please refer to Figure 3.

Figure 3. Screening among RCJ inmates, 1999-2001



Distribution of intensity & effectiveness by time, RCJ

Fewer specimens were collected each year from Robeson County Jail inmates. Collections declined from 2,027 to 1,666 between 1999 and 2000, for a decrease of nearly 18%. Collections declined yet further in 2001 with just 1,417 tests, for a decrease of nearly 15% compared to 2000's efforts to find new cases. The 3-year decline in collections was about 30%. A chi-squared goodness of fit test was used to determine if the trend in declining specimen collection was significant. The value for chi-squared was 110.45 with 2 degrees of freedom, yielding a p-value well below 0.05. A statistically significant difference between annual RCJ specimen collections was apparent. Please refer to Table 6.

Table 6. Specimen collection history & hit rate, RCJ 1999-2001

Specimen Collection History & Hit Rate, RCJ 1999-2001

Year	Number of Specimens Collected	Number of Reactors/ (Sero-prevalence)	Number of Hits/ (Hit Rate)	Yield Among Reactors
1999	2027	75 (3.70%)	16 (0.79%)	21.33%
2000	1666	64 (3.84%)	11 (0.66%)	17.19%
2001	1417	48 (3.39%)	8* (0.56%)	16.67%

*Excludes 4 found through RIOT-related SCR

Seroprevalence values between years were virtually unchanged, ranging from 3.39% to 3.84%. The number of annual hits followed the trend of declining collections. Fewer early cases were discovered among County Jail inmates each year. 16, 11, and 8 early cases were found in 1999, 2000, and 2001, respectively, among this transient population. The case count declined by over 31% from 1999-2000, and by 27% from 2000-2001. Comparing 1999 to 2001, the number of hits from this site decreased by 50%. Consistent with RCJ's decreasing contribution to annual *study case counts*, *hit rate* steadily declined through the period of interest. Each year, less than 1% of tests yielded early cases. *Hit rate* dropped from 0.79% (16 cases/2,027 tests) in 1999 to 0.66% (11 cases/1,666 tests) to 0.56%(8 cases/1,417 tests) in 2001. Similarly, yield among reactors decreased from over 21% in 1999 to nearly 17% in 2001. Comparing *hit rates* through time in the setting of RCJ with a chi-squared test for homogeneity, EpiInfo's package generated a chi-squared value of 0.64. This value had an attendant p-value greater than 0.05, leading to the

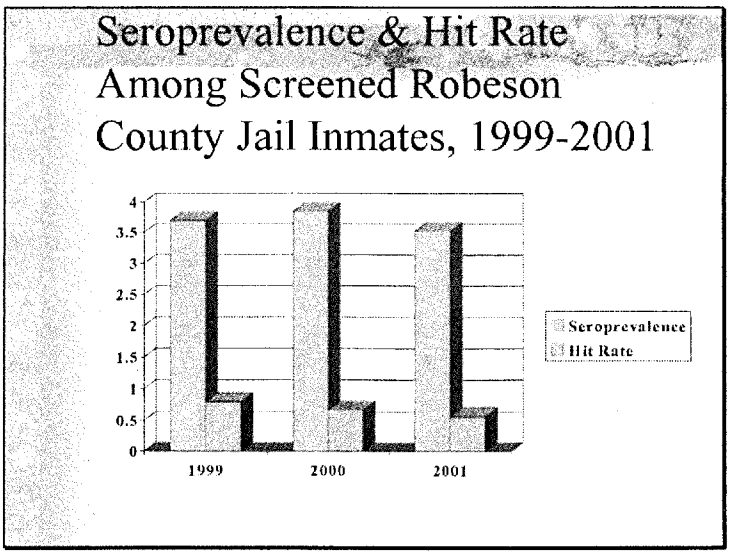
conclusion that a statistically significant difference in *hit rates* at RCJ through the period of interest did not exist.

Relationship between seroprevalence & hit rate, RCJ 1999-2001

In 1999, 3.7% (75 reactive tests/2,027 specimens) of all specimens collected from Robeson County Jail inmates were reactive for antibodies to *T. pallidum.* This figure rose to 3.84% (64/1,666) in 2000 and then fell to 3.53% (50/1,418) in the year 2001. Please refer to Figure 4.

During 1999, the year of minimum incidence with 109 early cases reported among Robeson County residents, the RCJ *hit rate* was at a 0.79% maximum. *Hit rate* fell to 0.66% in 2000, when total incidence increased to 133 reported cases. The *hit rate* declined further in 2001 to 0.56%, when the number of registry case counts was greatest at 144. The yield of early cases among those screened at the County Jail decreased from 1999 (0.79%) through 2001 (0.56%). The decrease over this 3-year period was nearly 30%. Please refer to Figure 4, extracted from data presented in tabular form at Table 6.

Figure 4. Seroprevalence & hit rate among screened RCJ inmates, 1999-2001



Intensity and effectiveness of Robeson County RIOT, 2001

Of 706 specimens collected, 25 (3.54%) tests were reactive for antibodies to *T. pallidum*. 5 (0.71%) tests resulted in early syphilis diagnoses. With 5 early diagnoses out of 25 positive tests, 20% of all reactive tests yielded cases of early syphilis. Please refer to Table 7.

Table 7. Specimen Collection History & Hit Rate, RC RIOT 2001

Specimen Collection History & Hit Rate, RC RIOT 2001

Number of Specimens Collected	Number of Reactors/ (Sero-prevalence)	Number of Hits/ (Hit Rate)	Yield Among Reactors
706	*25 (3.54%)	5 (0.71%)	20%

*Includes 2 from patients not yet located at this writing

Distribution of intensity & effectiveness by time, RCHD

Table 8 summarizes the results of three years of syphilis screening among patients at Robeson County's Communicable Disease Clinic. The vast majority of patients seen in this setting received services related to sexually transmitted diseases. No clear trend in specimen collection was apparent, although more tests were performed in 2001 than in either of the previous years. 1999 and 2000's screening *intensities* were nearly equal, as were these years' numbers of hits and *hit rates*. Please refer to table 8.

Table 8. Specimen collection history & hit rate, RCHD 1999-2001

Specimen Collection History & Hit Rate, RCHD 1999-2001

Year	Number of Specimens collected	Number of Reactors/ (Sero-prevalence)	Number of Hits/ (Hit Rate)	Yield Among Reactors
1999	1832	121 (6.60%)	45 (2.46%)	37.19%
2000	1783	142 (7.96%)	46 (2.58%)	32.39%
2001	1967	190 (9.66%)	66 (3.36%)	34.74%

Intensity of casefinding was at maximum during 2001. 1,832 specimens were collected in 1999, 1,783 in 2000, and 1,967 in 2001. A chi-squared goodness of fit test was conducted to determine if the differences between these *intensities* were statistically significant. The value for chi-squared was 9.76 with 2 degrees of freedom, yielding a p-value < 0.05. A statistically significant difference between annual specimen collections at RCHD was evident.

Seroprevalence at the Health Department increased steadily during the period 1999-2001. While 121 (6.60%) tests were reactive among 1999's 1,832 specimens collected, 142 (7.96%) were reactive in 2000. Seroprevalence climbed further yet in 2001, when 190 (9.66%) were reactive out of 1,967 specimens collected.

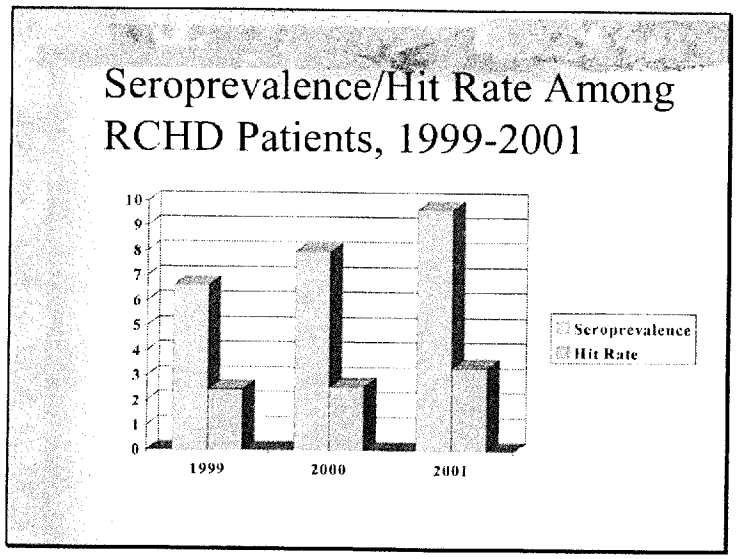
The contributions to *study case counts* from this site through time unsurprisingly followed reported incidence, although this relationship did not hold at SRMC or RCJ. RCHD produced 45 early cases in 1999, 46 in 2000, and 66 in 2001. The *hit rates'* climb from 2.46% (45 cases/1,832 tests), to 2.58% (46 cases/1,783 tests), to 3.36% (66

cases/1,967 tests) fell short of statistical significance. Comparing *hit rates* over time at the STD Clinic with a chi-squared test for homogeneity, the value for chi-squared was 3.32 with 2 degrees of freedom. This test yielded a p-value greater than 0.05.

Relationship between seroprevalence & hit rate among RCHD patients

As was the case among SRMC patients, seroprevalence among those screened at the Health Department increased through the study period. In 1999, 6.60% of the 1,832 tests were reported as positive. Seroprevalence increased to nearly 8% among the 1,783 tests performed in the year 2000. Among 2001's 1,967 tests, 9.66% were reactive. Please refer to Figure 6, based on data from Table 8.

Figure 6. Seroprevalence & hit rate among RCHD patients, 1999-2001



Seroprevalence rose more rapidly than *hit rate* through this 3-year period. *Hit rates* were 2.46%, 2.58%, and 3.36% in 1999, 2000, and 2001 respectively, while seroprevalence rose to nearly 10% by 2001.

Discussion-

Population growth's possible contribution to the epidemic

Where routine STD surveillance data are used, incidence rates expressed as

Equation 2. Standard formula to calculate incidence rates

$$\frac{\text{(number of cases reported annually)}}{\text{(estimated mid-year population size)}} \times 100{,}000 \text{ population}$$

are the conventional measurements used to compare STD morbidity burdens between years within a jurisdiction over time or synoptically between geographic areas. Adjusting for population size in this way raised Robeson County's early syphilis burden to infamy despite its small number of inhabitants relative to places such as similarly troubled Detroit. However, US Census data estimates from Census 1990 combined with Census 2000's population count provided misleading denominator values with respect to this project. Basing its projections on pre-1990 growth rates, the Census Bureau underestimated Robeson County's 1999 population size. Consequently, users of this unaltered data calculated erroneously high incidence rates for the period of the late nineties and erred on the low side with Census 2000's population count.

The estimated size of Robeson's population as of Jul 1 1999 was 116,597 residents. Census 1990 counted 105,179 residents. Therefore, the rate of growth as estimated from 1990's census was 1,269 [(116,597-105,179 residents)/9 years] additional souls per year.

The actual number of inhabitants as tallied by Census 2000 was 123,339. The official estimates for Jul 1 2001 based on the most recent decennial census were unavailable at this writing. Mean annual population growth as calculated by subtracting 1990's count from 2000's was 1,816 [(123,339-105,179 residents)/10 years] additional residents per year. Subtracting the mean estimated annual additions from the actual number of additional residents results in an underestimate of growth of 547 residents per year. Estimated growth based on 1999 projections was 1.2% while actual growth based on inter-decennial difference was 1.7%. From here, this project could have employed customized population estimates for 1999 and 2001.

However, these denominators were excluded in favor of stalwart case counts. This analysis relied on case counts without taking population size or growth into account. Beyond the previously discussed reason for omitting incidence rates, denominators ideally include only those people at risk for the condition under examination. Because the subset of total inhabitants at risk for acquiring syphilis is unknown, even accurate census data is of less than optimal utility in this application. Surveillance data from special studies would provide more meaningful incidence rates for a detailed look at the local level such as undertaken herein. While leaving this piece of the discussion, one notes that population growth could have "caused" up to 1.7% of the observed annual case count increases.

Statistically significant increasing incidence

You don't need a weatherman to know which way the winds of incidence blow in The Tarheel State.* Non-statisticians in NC DHHS and from CDC have responded attentively to rising incidence in this High Morbidity Area. Entrenched syphilis transmission in Robeson County led to locally managed intervention efforts, a unique configuration within the State. The other 99 counties are under the operational control of seven regional DHHS supervisors. The trend of increasing incidence during the study period, apparent in NC Syphilis *Registry case counts*, is less pronounced in *study case counts*.

As illustrated at Tables A and B, the *registry case counts'* 17.50 beta-coefficient for the regression line's slope was greater than the *study case counts'* 9.50. The trend of increasing registry case counts is nearly 2-fold stronger than that of study case counts. This project accurately characterized the trend's direction while failing to fully capture its strength. Had the total number of specimens collected from all county residents during the period of interest been obtained, complete *hit rates* could have been computed using registry case counts as numerator rather than the 70% subset of reported cases. Observed differences between annual study case counts "explained" by differences between annual specimen collections could change from that reported herein had all tests and all reported cases been included rather than a subset of those cases and tests.

Factors driving an actual STD epidemic and its abatement

Rather than uncritically accepting the premise that an epidemic caused by ever-increasing propagation among residents was proceeding apace, this project explored an

* The author is a former U.S. Air Force meteorologist and early Dylan fan.

alternate explanation. Dr King Holmes mathematically captured the essence of STD propagation in any setting with the following equation:

Equation 3. Dr Holmes equation heuristically describing STD burden.

$$R = B \times C \times D$$

"Rho is the rate at which infection is reproduced. A rate of 1 would represent a stagnant situation; if Rho was greater than 1 the infection was spreading and an epidemic was underway. The *B*...stood for the mean efficiency of transmission of the microbe per sexual contact. If *B* was a low number it signified that the microbe wasn't terribly contagious and the odds of becoming infected through a single act of intercourse were low."[31] *C* is the mean number of sex partners per day, and *D* is the duration of infectiousness. The elements of syphilis control's armamentarium explored in this project were: a) testing (true screening pooled with selective testing) and b) curative therapy administered to those found to be infected. Thus, the duration of infectiousness, Dr Holmes' *D*, is the factor curtailed by each *hit* achieved. While public health-minded social engineers can reduce *B* through increased uptake of condom use among those at risk and *C* theoretically can be reduced, *D* appears to be that link of the epidemiologic chain most alterable by biomedical intervention.

The very essence of syphilis elimination is decisive interruption of indigenous propagation. In the elimination campaign, driving *Rho* downward through intervention is essential. However, rising incidence alone does not equate to $R>1$. The alternative

impetus, explored herein, for rising incidence is that of increasing *intensity* and/or *effectiveness* of case finding efforts among Robeson County residents through time.

Increasing incidence in this HMA has been drawing ever-increasing fiscal and human resources aimed at reducing indigenous propagation. This study explored the possibility that all or part of the epidemic had been manufactured via intensified case finding efforts. This dynamic phenomenon is what the illustrious Dr Morton described as an "administrative epidemic" in the context of chlamydia surveillance data.[32] In popular media discussions of the chlamydia epidemic, few references are made to the pre-epidemic absence of a specific assay. Even within the epidemiology community, this pathogen is among so-called emerging infectious diseases. As uptake of screening for *C. trachomatis* increased concurrently with increasingly more states mandating reports of chlamydiosis, an epidemic was manufactured. This illustrates how erroneous inferences can be drawn from observed burgeoning incidence.

While interventions in this HMA include traditional and innovative approaches to reducing morbidity, the proximate means of discovering new cases is to perform serologic tests for syphilis (STS). While screening is conventionally understood as testing of asymptomatic individuals for the presence of infection, this term was used herein to describe testing of patients irrespective of clinical profile. This study sought and found statistically significant differences in distribution of specimen collections (*intensity*) by time at each of the three sites. This study sought statistically significant differences in *hit rates* to distinguish between a true epidemic and one of our own making, and found such a difference only at SRMC. In general, more collections were accompanied by more *hits*, consistent with the artifactual epidemic concept.

Distribution of intensity & effectiveness by time at combined sites by time

Statistically significant differences between the numbers of specimens collected annually were found at each of the three sites under examination. By contrast, such a difference through time was not discovered when SRMC's, RCJ's, and RCHD's tallies were combined. The number of annual hits from combined sites steadily increased through time.

Adjusting for changing *intensity*, *hit rates* among combined sites increased through time, demonstrating increasing effectiveness. However, differences between years' *hit rates* were statistically insignificant. While the increasing proportion of specimens collected yielding early diagnoses during these three years appeared unsettling with annual *hit rates* of 0.85%, 0.93%, and 1.03%, the lack of statistically significant differences in *hit rates* tempered concern about runaway propagation.

Since the number of specimens collected decreased by nearly 2% from 1999-2000 in the presence of a greater than 7% increased case count, none of the observed increase in hits was "explained" by changing *intensity*. Factors other than intensified specimen collection efforts must have accounted for the increased case count during this two-year period. By contrast, over 3% more specimens were collected during 2001 in comparison to the previous year; in the presence of a nearly 15% case count increase from 2000-2001, intensified specimen collection between these two years period could explain up to 22.5% (3.3% specimen collection increase/14.8% case count increase) of the observed increase in case counts during this period, assuming a linear relationship between *intensity* and *effectiveness*. Nearly 80% of increased incidence during the period 2000-

2001 remains wholly unexplained by this analysis. Factors other than intensified screening account for at least 77.5% of the 2000-2001 increase.

A subtle trend is apparent in the form of decreasing yield among reactors. As the proportion of reactors resulting in early diagnoses approaches zero in the presence of aggressive case finding efforts, one may infer that Holmes' R does as well. Yield among reactors is adjunctive to the central measures under examination. Among 1999's 286 reactive tests, over 28% resulted in early diagnoses. Among 2000's 315 reactive tests, nearly 28% were deemed early. This proportion decreased to less than 26% from 2001's 393 reactors.

This decreasing trend of reactive tests resulting in early diagnoses could be due to slowly diminishing R, but victory doesn't appear to be at hand. A more obvious explanation for slightly declining yield among reactors is the increasing proportion of reactive tests among those who previously received adequately treatment for this infection. Another plausible explanation for the declining trend in reactive tests yielding early diagnoses is that an increasing proportion of the infecteds were diagnosed with Late Syphilis, Unknown Duration or Late Latent Syphilis. As provisional 2002 data mounts, early latent cases comprised an increasing proportion of total reported early syphilis.

Distribution of intensity & effectiveness by site, 1999

An *intensity* gradient was evident between sites. A very different *effectiveness* gradient was observed. While the Hospital collected the most specimens (5,791), it had the lowest *hit rate* (0.36%). While the STD clinic collected the fewest specimens, it experienced the greatest *hit rate*; 2.46% of 1,832 tests were hits. The Jail had 16 hits

from 2,027 tests; *hit rate* here (0.79%) fell between those of the two other sites. Distribution of *intensity* and *effectiveness* by service site were found to be statistically significant. Please refer to Table 2.

SRMC implements much true screening such as testing among the pregnant to help cover the "O" in the TORCH mnemonic. Syphilis is among the "other" infectious diseases of concern for those who provide prenatal care; the remaining pathogens in this scheme are *Toxoplasma gondii*, the Rubella virus, Cytomegalovirus (Human Herpes virus 5), and Herpes simplex virus. As evidenced by repeatedly appearing patient names among reactors, SRMC also does a lot of serologic follow-up among those previously diagnosed and treated, in accordance with CDC Treatment Guidelines. Repeat customers were found at the other service sites as well. Because of this rather shotgun approach to case finding, SRMC collects many specimens but finds few cases among its patients. Based on the hospital's consistently low *hit rate*, one can infer that the SRMC population is at lower risk for acquiring syphilis than its RCJ and RCHD counterparts.

Collections from the jail population would have exceeded those of the other sites had universal screening been achieved. The number of hits, in turn, would have increased by an unknown amount but resulting in an estimated *hit rate* of less than 1% . The *hit rate* at RCJ is higher than that of SRMC because of the presumably greater risk factors among the incarcerated group in comparison to their hospital counterparts. Crack cocaine possession, manufacturing, or distribution, for example, are common reasons for arrest. Property crimes stemming from the criminogenic characteristics of prohibited drug use also land Robesonians in jail.[33] Further, disease investigators occasionally locate contacts to known cases in the Jail, and then arrange for testing in this setting. For these

reasons, Jail *hit rates* exceeded those of SRMC. Downward pressure on RCJ *hit rates* comes from screening anyone who is admitted, irrespective of clinical profile, thus merging low with high-risk detainees into the same pool.

Collections from STD clinic patients were dependent on patient census. With few exceptions, all patients presenting to this specialty clinic received tests for syphilis. With just 1,832 specimens collected during 1999, 45 hits yielded a *hit rate* of 2.46%. These relatively impressive effectiveness measures stem from this population's characteristics. Uninsured patients seek care at the Health Department due to lack of other access options. The STD clinic is a well known source of specialized services among county residents, so patients often present voluntarily. DIS referred exposed and otherwise high-risk patients to this clinic oftentimes even when other care options existed, taxiing known contacts and suspects to and from the clinic when necessary. These rides often helped to establish rapport between investigators and their patients, resulting in epidemiologically important exchanges of information on the fly.

Distribution of intensity & effectiveness by site, 2000

Similar to 1999's findings, SRMC collected the most specimens while achieving the lowest *hit rate* (0.52%) of the three sites considered. Once again, the Jail had an intermediate *hit rate* (0.66%) and the Health Department had the highest (2.58%). This difference between sites' effectiveness measures was found to be statistically significant. RCHD's relatively high *hit rate* pushed the statistical test past the level of significance. Variations in *intensity* and *effectiveness* between sites are at least partly attributable to factors explained above. Please refer to Table 3.

As was the case at all sites in all years, calculation of the proportion of reactive tests yielding early diagnoses revealed that most patients with positive test results were either previously treated or diagnostically staged as other than early syphilis. However, a substantial proportion (RCJ's 17% ranging to RCHD's 32%) of reactive specimens yielded early diagnoses. Patients presenting to RCHD clearly weren't the worried well.

Distribution of intensity & effectiveness by site, 2001

Please refer to Table 4. Generally, seroprevalence and *hit rates* corresponded with yield among reactors. The greater the *hit rate*, the greater the proportion of reactive tests resulting in early syphilis diagnoses. This correspondence suggests that *hit rate* and yield among reactors--proportion of early diagnoses among reactive tests--are useful adjuncts to routinely collected surveillance data in monitoring progress toward syphilis elimination in this county. The apparent utility of these two measures is among the most important findings of this project, even though the primary objective was to measure the association between case finding *intensity* and *effectiveness*. If NC DHHS management were to routinely monitor *hit rates* and yield among reactors, a more elaborate surveillance data collection and analysis system would be needed.

In Spring 2002, a major effort was undertaken to routinely capture the type of data presented in this thesis project. This study attempted to augment routinely collected surveillance date, thereby distinguishing between an actual epidemic and one of our own making. The focus of the DHHS initiative, by contrast, is active surveillance with an attempt to increase the sensitivity of the state's system. This promotion of active surveillance across the state is a key objective toward the goal of syphilis elimination.

Distribution of intensity & effectiveness by site, 2001

SRMC persisted in screening more patients than the other three sites combined. This difference between sites' collections was again found to be statistically significant. The STD Clinic's case finding impact as measured by *hit rate* was 3.36%, exceeding previous years' RCHD rates and several-fold greater than each of the other three sites in 2001. The RIOT's collections were impressive (706), while its *hit rate* fell between the Jail and the STD Clinic's, and well above SRMC's. Please refer to Table 4.

A major component of the RIOT included screening Robeson County Jail inmates. This was deemed necessary because screening had ceased among inmates due to staffing difficulties. The RIOT's seroprevalence and *hit rate* were driven higher by inmates' contributions; fully 80% (4/5 early cases discovered in 2001's RIOT) were found in this population. In terms of case finding effectiveness, the RIOT's degree of success was greatly attributable to Jail screening.

In an effort to corroborate this study's findings from the RIOT, a discrepancy was discovered between *effectiveness* as measured in this study and as tallied by DIS staff. *Hit rate* in the RIOT setting as reported herein should therefore be considered conservatively as a minimum. A more accurate *hit rate* appears to be at least 0.99% (7 cases/706 specimens). Additionally, any iterative cases generated by interviews of RIOT reactors were counted as STD clinic patients. Further, social marketing via radio spots and print advertisements in advance of the RIOT, diffusion of risk reduction messages throughout the County generated by outreach team members, and post-event media coverage may have favorably and significantly, yet immeasurably using this project's

methodology, affected syphilis elimination in this HMA. The full impact of the RIOT is therefore understated by these data.

Distribution of intensity & effectiveness by time, SRMC

17,492 specimens were collected from SRMC patients during the study period. More specimens were collected in 2000 than in either of the other years. With 6,014 tests during the year 2000, a statistically significant difference was found between years' intensities. The maximum *hit rate* (0.66%) observed in 2000 similarly rendered *hit rate* differences at this site statistically significant. 2001's *hit rate* was nearly equal to 1999's 0.36%. While this equality suggested little progress toward syphilis elimination in the HMA, it did not suggest burgeoning propagation either. *Intensity* and *effectiveness* rose and fell synchronously. Please refer to Table 5.

Assuming a linear relationship between collections and number of hits, factors other than intensified screening explained most of increased incidence in 2000 at SRMC. At most, 8.2% (3.9% specimen collection increase/47.6% increase in number of hits) of the increased study case count was due to intensified screening. Because the year 2000 spike in hits at SRMC was not observed at the other sites, scant evidence existed for a year 2000 outbreak within the broader pattern of increasing incidence by time. The remaining 91.8% of the increased case count from 1999-2000 was apparently due to increased propagation in the community, increased index of clinical suspicion among private providers using SRMC's laboratory, increased awareness of risk and symptoms followed by care seeking among Robeson County residents, some combination of these factors, or additional factors not considered.

Similar comments can be made about the decreases emerging in the year 2001 relative to the previous year. While the number of specimens collected in 2001 (5,687) decreased by just 5.4% from the previous year's 6,014 specimens, the number of early diagnoses decreased by 29.0%. Apparently, declining collections did not explain much of the observed decline in hits. At most, fewer collections "explained" just 18.6% (5.4% decline in specimen collections/29.0% fewer hits) of declining case counts at this site during 2001 in comparison to the previous year.

A parallel trend emerged from the proportions of reactive tests resulting in early diagnoses. A spike of 28.44% (21 early diagnoses/90 reactive tests) was apparent during 2000, the year of this study site's maximum case count. This compared with 23.33% in 1999 and 16.92% in 2001. Again, the correspondence between *hit rate* and proportion of positive tests with early diagnoses suggests that *hit rate* and yield among reactors are useful adjuncts to case counts and incidence rates for monitoring progress toward syphilis elimination. Substantial barriers to routine monitoring of *hit rates* exist however. While reactors are routinely entered into a database by name, thereby allowing easy calculation of yield among reactors, only a fraction of the nonreactors are routinely entered by name. Therefore, accurate and complete seroprevalence and *hit rate* values can only be monitored by capturing the number of specimens and their test results as executed herein.

The correspondence between *hit rates* and yield among reactors observed at SRMC was also evident among all sites combined through the period 1999-2001, further suggesting that these measures were of value to those interested in the epidemic's course. Based on these data, one can infer that *hit rate* and the proportion of reactive tests yielding early diagnoses will decline before or concurrently with any future decline in

reported incidence. *Hit rate's* stability during this three-year period, hovering around 0.4%, suggests little movement toward zero; predictions of imminent elimination would appear to be premature as the year 2005 approaches ever closer.

Seroprevalence's relationship to hit rate, SRMC 1999-2001

The most meaningful trend discernable from these data is that of increasing seroprevalence among SRMC patients. Seroprevalence can vary asynchronously with hit rate. The 41% decline in hit rate from 2000-2001 suggests that the pathogen's propagation in Robeson County had reached a 3-year maximum in 2000. However, as discussed above, the other service sites did not experience this spike, so such an inference is tenuous. Please refer to Figure 2, based on data presented at Table 5.

Missed opportunities for case finding at RCJ

Fewer annual specimen collections occurred in the presence of growing annual admissions. The difference between specimens collected and detainees admitted represented missed opportunities for screening. With a total of 21,225 men and women having passed through this facility's entrance gate during the period of interest, a total of 5,111 specimens were collected—no trivial specimen collection effort, but less than 25% of the potential maximum. Please refer to Figure 3. At this writing, Mr Pete Moore of CDC is retrospectively examining RCJ's case finding efforts with a focus on cases allowed through missed opportunities for screening. When the author served as a consultant to the National Coalition of STD Directors during the summer of 2000, he formally recommended universal screening at RCJ.

Recently published literature abounds with positive associations between the dual risk factors of using crack cocaine and/or exchanging sex for money and/or drugs and the outcome of interest—recently acquired syphilis infection. For example, "Patients during the epidemic period were more likely to have used illicit drugs at some time...and to have exchanged sex for drugs or money during the preceding year."[34] Similarly, Fleming *et al* found that "Persons with syphilis more frequently had...crack-using sex partners... and history of incarceration."[35]

In Oregon, seroprevalence sank so low during the late nineties at State correctional facilities that routine screening was halted based on fiscal considerations. "The prevalence of infection above which we should screen is based mostly on economic grounds, but is undetermined. We intuitively recognize such a threshold, however, when we use epidemiologic markers to restrict our efforts to groups in whom we think the yield is worth the effort."[36] The legal prohibition against prostitution and selected drug use combined with law enforcement agencies' efforts make Robeson County Jail a suitable screening site as long as *hit rates* remain impressive. DIS follow up on all reactors with detainee interviews; when hits are achieved in RCJ, these interviews generally lead to evaluation and curative or preventive treatment of exposed sex partners and others at risk for infection.

A striking feature of the World Health Organization's successful campaign to remove Variola virus from the human experience was the inverse relationship between incidence and fiscal cost per case found. As the haystack of humanity grew, the needles of infected individuals became fewer. With due respect to Dr Oxman of Oregon, War is too important to be left to the accountants.[37] In the context of Syphilis Elimination with its

hunt for an increasingly rare disease, even relatively low *hit rates* could justify continued screening in the corrections setting.

The goal of universal screening among Robeson County Jail (RCJ) inmates was unrealized. Barriers to universal screening included: brevity of inmate stays, particularly following weekend bookings when medical staff are unavailable; insufficient nursing/phlebotomist staff burdened with competing priorities; absence of a dedicated STD troop at RCJ; challenges of getting buy-in from RCJ personnel; inmate unwillingness to submit to venipuncture; fiscal costs of overcoming these barriers.

Declining intensity & effectiveness at the jail

The drop from over 2,000 specimens collected in the first year of study to less than 1,500 in the final year was statistically significant. By contrast, *hit rates'*--consistently less than 1%-- decline was found to be statistically insignificant. Although *hit rates* did not change meaningfully in statistical terms, the number of hits was sensitive to increased screening *intensity*. In addition to tandem decreases in number of specimens collected and hits achieved, the RIOT supplemented a finding of such sensitivity. RIOT-related screening among detainees found at least 4 early cases in addition to the 8 discovered through routine screening during the year 2001. The RIOT was considered as a fourth site. Please refer to Table 6.

Because universal screening among jail patients was attempted, greatly independent of clinical suspicion and patient or investigator initiative, data from this setting provided evidence in support of the thesis's central question. The hypothesis supposed that more collections at any site would accompany more hits, thereby driving incidence upward.

Fewer collections accompanied fewer hits at RCJ. *Hit rates* also decreased with time, but their near-equality in statistical terms suggested endemicity across the county. Since the study case count declined by 50.0% and the number of tests declined by 30.1%, one could say that over 60% (30.1%/50.0%) of decreased contribution to study case counts was attributable to fewer annual collections. Thus, RCJ data offered compelling evidence of the surveillance system's sensitivity to *intensity* of case finding efforts.

The correlation between *hit rates* and declining yield among reactors, observed in all sites combined and at SRMC, further supported the surveillance utility of these measures. Parenthetically, RCJ's seroprevalence was 3.8% in the year 2000. This proportion was about 3-fold greater than that found at NC State & County correctional facilities in 2000.[38]

Discordance between of RCJ hit rate and incidence

The decreasing RCJ *hit rate* stood ironically in contrast to increasing incidence through the period of interest. This 30% decline in *hit rate* at the County Jail could suggest that propagation of syphilis infection in Robeson County has been decreasing over the last three years. This interpretation is based on the distinctive characteristics of the inmate population. Of the four populations under study in this project, arrestees comprise the screened group perhaps least subject to case finder bias. That is, efforts to universally screen inmates irrespective of their clinical status differed from efforts in private practice where decisions to test were guided by clinical presentation (ie: presence of suspicious lesions) and other factors. Please refer to Figure 4.

Seroprevelance's meaning and utility

Changes in seroprevalence through time did not necessarily reflect changes in the pathogen's propagation or varying *effectiveness*. Seroprevalence was only loosely related to propagation in the community; seroprevalence can remain high or even increase in the presence of a waning epidemic. In a decreasingly naive population such as that of Robeson County's, seroprevalence's utility as a surveillance tool diminishes with time. *Hit rate* was more informative for monitoring the epidemic's course because it excluded those with a history of adequate treatment, and it excluded the infecteds who failed to meet the criteria for early syphilis.

RIOT, anyone?

The RIOT was a major effort involving most of the NC HIV/STD Branch's Field Staff, augmented by Robeson County Health Department personnel, and others. This event involved intensively targeted screening of neighborhoods known to have recently produced lesion cases.

Disease Intervention Specialists (DIS) from across the State joined forces under NC Department of Health and Human Services leadership and support staff, along with CDC field staff and RCHD clinic personnel to plan and execute this outreach operation. Planners called this campaign "Syphilis Makes Awareness Robeson's Target" (SMART). A prominent feature of this innovative event was collection of specimens from those residing in neighborhoods where evidence of recent transmission abounded. North Carolina has a consistent history of pronounced decreases in incidence following RIOTs in high morbidity counties. A plan exists for another Robeson RIOT while we watch for evidence of similar success in this County. Targeted neighborhoods, including a mobile

home park frequented by prostitutes, are called "hot spots" by those engaged in syphilis control.

A temporal association exists between NC RIOT events and subsequent dramatic declines in incidence of early syphilis. Whether this association is one of cause and effect is open to question, but the RIOTs' efficacy in driving incidence downward is plausible and stands as an article of faith among NC DHHS staffers. The RIOT remains a tool of major importance among NC's syphilis control strategies, most recently executed in Guilford County in May of 2002. That event uncovered evidence of ongoing propagation where reported incidence had been on the decline through the late nineties. While we watch for similar success in the wake of Robeson's 2001 RIOT, another Robeson RIOT is in the planning stage.

Nash/Edgecombe County's 1993 RIOT was followed by a marked decline in incidence, as was Guilford's and Wilson's of 1996, and Montgomery's of 2000. Alternative explanations for decreasing incidence in these jurisdictions include events unrelated to RIOT activities. Where hits among RIOT patients don't contribute substantially to annual incidence in a given county, an inference of cause and effect between a RIOT and decreasing incidence appears dubious. Another possible explanation for declining incidence is post-RIOT diminished case finding *intensity* and/or *effectiveness*, and/or greater pre-RIOT *intensity* and/or *effectiveness*.

Intensity & effectiveness of Robeson County RIOT, 2001

The Rapid Intervention Outreach Team collected specimens from Robeson County residents in their homes and at strategically chosen places of business, with team

members going door-to-door in neighborhoods characterized by high syphilis morbidity, high prostitution and cocaine activity, or both. The RIOT team also screened as many Robeson County Jail inmates as possible during two weekends in August 2001; this setting demanded the Team's attention due to understaffing at the Jail. Consequently, the RIOT's *hit rate* was inflated by the contribution of early diagnoses from this incarcerated population. Four of the RIOT's five early cases discovered were among RCJ inmates. Please refer to Table 7.

An alternative way to study *hit rate* by setting is to incorporate RIOT-related RCJ case finding efforts into RCJ's 2001 specimen collection history rather than considering the RIOT independently. This alternative methodology, if used, would have inflated RCJ's *hit rate* while greatly reducing the RIOT's. Comparing the RIOT's seroprevalence, *hit rate*, and yield among reactors to RCJ's, consistency between these two sites was unsurprisingly observed as shown in Table 6.

While increased community awareness and other favorable results of the RIOT may have occurred, such impacts are difficult to measure. With respect to case finding, it would be difficult to characterize the RIOT as highly successful in the absence of greater yield among non-RCJ patients. Time will tell whether a temporal association between this RIOT and decreasing incidence in Robeson County will appear.

Distribution of intensity & effectiveness at RCHD by time

Many patients treated at RCHD received screening at private medical doctor sites, predominantly at Southeast Regional Hospital and offices using SRMC's laboratory. These individuals were reclassified as SRMC patients because treatment of infections

from this group did occur at RCHD but case discovery occurred at private service sites. Because these infections were discovered at non-HD sites, the credit for case finding went to SRMC even though the NC Registry indicated RCHD as the provider. Had reporting source not been changed thusly, SRMC's effectiveness measures would have been artificially deflated and RCHD's inflated.

While comparatively high *hit rates* over time did not change significantly as measured by the chi-squared test, the increasing number of hits at RCHD was noteworthy. *All* of the year 2000-2001 increase in *registry case counts* (133 cases vs 144 cases)—just 11 cases—was due to improved case finding at RCHD. The near equality between RCHD's 1999 and 2000's collections and yields supports the hypothesis of incidence's sensitivity to screening *intensity*; unchanging collections yielded unchanging study case counts. RCHD case finding effectiveness as measured by *hit rate* has been increasing. Notwithstanding the failure of *hit rate* differences to reach statistical significance, the 20 case difference (44% increase) in RCHD's contribution to *study case counts* between the years 2000 and 2001 was impressive. This difference illustrated this surveillance system's hard-won increased sensitivity. Please refer to Table 8.

The year 2001 maximum specimen collection occurred in the presence of sustained and increased DIS labor, leading to 1,967 tests. Not only did this clinic census receive a boost from two *dedicated* Disease Intervention Specialists (Ms Constance Jones and Ms Vonetta Bethea), but also from the contributions made by an ever-present temporary duty DIS. Further, two CDC Syphilis Elimination Rapid Response team members strongly contributed to the case finding effort during the last quarter of 2001. Collections from

patients in the field comprised an increasingly large proportion of RCHD's *intensity* measures.

Because nearly universal screening of RCHD patients held throughout the period of interest, and degree of clinical suspicion remained consistently acute, this increasing *hit rate/study case count* at RCHD was further evidence of incidence's sensitivity to case finding intensity. This association was also conversely evident in the Jail setting; at RCJ, fewer annual specimen collections yielded fewer annual cases. It appears that increasing case finding *intensity* at RCHD helped to artifactually sustain the epidemic. Based on findings at RCJ, one can infer that a closer approximation of universal screening in that setting would have fuelled incidence as well. Beyond the realm of inference, RIOT-related screening among RCJ inmates did, in fact, achieve more hits than would have been the case without this supplemental screening.

The free STD specialty clinic setting is something of a stacked deck in terms of yield. In addition to patients self-referring due to known exposure or presence of symptoms, many patients presented to the STD clinic because DIS referred them as contacts or suspects to known cases. Non-study data in support of this phenomenon came from consultant Mr Muth of Quintus-ential Solutions. This social network researcher looked at distribution of early syphilis in Robeson County and said, "Such data supporting the Wasserheit epi phase picture would be well received." [39] While not all contacts to known cases presented to RCHD, most did so.

The most striking feature of this part of his analysis was the growing proportion of syphilis cases found by epi-referrals—notification of the exposed followed by evaluation yielding early diagnoses. Among women, laden as they were with reproductive

implications, the number of syphilis cases discovered through notification steadily increased since 1998; by 2001, more cases were found among women by this method than by either screening or volunteering. Among men, a similar picture emerged. From 1999-2001, the proportion of cases found through screening diminished as the contribution made through notification steadily grew. By 2001, the number of cases (all diagnoses) ascertained through contact notification and referral exceeded the number of cases found through either the screening or volunteer method. These data powerfully and simply answer this thesis' central question of whether our efforts increasingly fuel incidence. We ironically celebrate such increases in incidence, anticipating declining incidence caused by successful interruption of transmission.

When partner notification drives incidence upward, taking the pole position among methods of case detection, the epidemic becomes a celebratory trend. Rather than fretting over incidence independently spiraling upward, we know that effective DIS efforts are fuelling case counts. In this light, even the growing proportion of primary and secondary stage diagnoses can be viewed as a favorable trend. By rapidly identifying and treating lesion cases, transmission was interrupted by treating patients during the infectious stages rather than during post-lesion latency. Having shortened Dr Holmes' *D* among many of the infecteds, an imminent decline in early syphilis incidence can be predicted. An increasing proportion of early latent diagnoses among total early syphilis could also evidence successful interruption.

Seroprevalence's relationship to hit rate by time, RCHD

The statistically insignificant increasing RCHD *hit rate* could reflect increased propagation in the community, improved ascertainment (ie: DIS efforts) among those at greatest risk of infection, increased awareness of risk among county residents with resultant increased self-initiated voluntary presentation, some combination of these factors, or other reasons. Improved ascertainment through DIS efforts demonstrably increased the number of hits, driving *hit rates* upward. It would seem that the steady to modestly increasing *hit rate* in this setting gave little support for optimism about imminent declines in incidence. On the other hand, rather than seeing cause for alarm in this increasing *hit rate*, distribution of early diagnosis by reason for exam provided evidence of progress toward syphilis elimination rather than unchecked upwardly-spiraling incidence. Please refer to Figure 6.

Limitations

An important limitation of this study was its failure to capture observations from the pre-epidemic period. To gain a fuller understanding of how *intensity* and *effectiveness* variations relate to incidence, the methodology employed herein should be extended to cover a longer span of time. Additional years of observations would allow comparisons between pre-epidemic and epidemic period, improving the results' robustness.

Another limitation of this project was its exclusion of 30% of study period cases as recorded in the NC Syphilis Registry. The study design identified specific service sites, SRMC, RCJ, RIOT, and RCHD, as places where the preponderance of cases reported during the period 1999-2001 were discovered. These sites were then evaluated with respect to case finding *intensity*, *effectiveness*, and *impact*. Because no attempt was made

to examine excluded sites, the study ignored a substantial proportion of reported cases. To what extent this study's findings would comport with an analysis of efforts at excluded sites is unknown.

The method of data collection presents yet another limitation. The only data source already in modern database form was the NC Syphilis Registry. Numbers of specimens collected along with names of test recipients and their test results were painstakingly extracted from hand written log books. Laborious hand counts are prone to miscounting, although great attention was given to ensure accurate tallies. These books extended three years into the past, precluding extension of the study period earlier than 1999. For this methodology to be employed routinely to surveillance data, more thorough recording and more easily retrievable form of *intensity* data should be implemented prospectively.

Use of registry data presented a related limitation. Surveillance data as recorded in communicable disease registries are always provisional even after official morbidity reports are published, eternally subject to updates due to factors such as late reporting or reclassification of diagnoses. Any early syphilis cases reported after Dec 31 2001 among patients tested before this date were excluded from this study by default. Similarly, any early cases reported after Jan 1, 1999 among patients tested before this date were excluded. The date of specimen collection was the starting point for this analysis, not the date of case report. While these temporal bounds would tend to cancel each other out, no rigorous attempt was made to explore this how this limitation might change the results.

Summary and main findings

Study case counts increased annually, reflecting the comparatively stronger trend of increasing *registry case counts*. Both of these trends were statistically significant. This project hypothesized that increasing incidence, as measured by study case counts, was attributable to increasing specimen collections among the study population. *Intensity*, defined as the number of specimens collected annually, was explored as a distal predictor of study case counts. *Effectiveness*, defined as the number of early cases or *hits* discovered annually, contributed directly to study case counts. *Hit rate*, an impact measure defined as the result of *effectiveness* divided by *intensity*, quantitatively captured the surveillance system's sensitivity to variations in screening by time and by service site.

Results of this analysis did not reveal a close correspondence between increasing intensity and increasing case counts as expected, although some evidence of incidence's sensitivity to varying intensity was found. Inter-site differences in *intensity* and *effectiveness* were masked when combined sites were examined. Distribution of *intensity* by time at combined sites increased through time, but not steadily nor to statistically significant degree.

Examining each service site's distribution of *intensity* by time revealed statistically significant differences, but again in the absence of steadily increasing collections. SRMC's maximum *intensity* occurred during 2000, the year of maximum *effectiveness* at this site. RCJ's maximum occurred in 1999, the year of maximum cases found at this site; RCJ's steadily declining *intensity* accompanied ever fewer hits. RCHD's maximum *intensity* also occurred in 2001, when the greatest number of hits was achieved. Each service site's distribution of *effectiveness* by time paralleled its *intensity* distributions; this

association was further evidence of the surveillance system's sensitivity to varying specimen collection effort. Reported incidence was, therefore, partly a function of case finding *intensity* in the setting of this HMA. Yet, specimen counts proved a rather crude measure of casefinding intensity; impressive hit rates among health department patients revealed the power of traditional contact tracing to find early cases within the social networks of infecteds and their partners.

Whether this project's findings are generalizable to other settings is unknown, but presumed to be so. Analysis of national chlamydia surveillance data not only inspired the thesis idea, but also provided evidence of external validity of this project's findings. A study's power to detect associations is greatly dependent on sample size and, due to practical constraints, this study's sample size was not great. One would therefore expect to experience more difficulty discovering tight associations in a three-year analysis of a small geographic area's syphilis experience in comparison to a two-decade analysis of the entire country's chlamydia experience.

Excepting SRMC, *hit rate* heterogeneity through time was not observed at any service site. This absence of statistically meaningful within-site *hit rate* differences with simultaneously meaningful within-site *intensity* differences provided limited evidence for affirmatively answering the central thesis question--increasing incidence is at least partly explained by increasing specimen collections. Statistically insignificant increasing RCHD *hit rates* suggested that propagation was subtly increasing, case finding effectiveness was improving, some combination of these factors was occurring, other causes drove hit rate, or the increase was simply spurious. Possible forces behind statistically insignificant decreasing RCJ *hit rates* may be similarly described.

Concerning the surveillance utility of the primary measures employed in this project's methodology, *intensity*, *effectiveness*, and their association as quantified by *hit rate*, these measures appeared to comprise a useful way to measure success within and between service sites in the setting of Robeson County. Evaluating a program's impact in this way is not ecologically limited to this jurisdiction; such an analysis could be performed in any geographic setting where progress toward syphilis elimination is of interest. Just as service sites can be compared in this way, so can jurisdictions within a state or states to one another. These data revealed gradients of *intensity*, *effectiveness*, and *hit rates* between service sites.

In general, SRMC collected the most specimens, RCHD collected fewer, and RCJ the fewest. By contrast, RCHD consistently found the greatest number of cases, followed by SRMC, with RCJ finding the fewest. Statistically significant *hit rate* differences between sites followed another gradient; RCHD consistently had the greatest *hit rate*, followed by the Jail's, and SRMC had the lowest. Yield among reactors, and to a lesser degree, seroprevalence, were apparently useful adjuncts to routinely gathered surveillance data for monitoring an epidemic's course.

Synthesizing temporally varying case finding *intensity* and *effectiveness*, statistically significant differences in specimen collections were observed in the presence of statistically insignificant *hit rate* differences. Since impact as measured by *hit rate* remained fairly constant at all service sites through the period 1999-2001, endemic may characterize Robeson County's syphilis burden more accurately than epidemic. Our indefatigable leader, Ms Evelyn Foust, was among the first to describe local conditions

this way. This characterization appears valid despite observed increasing study and registry case counts during the study period.

This project's greatest value may lie in the method employed rather than in its results. The methodology employed herein could serve as the model for a component of surveillance system evaluation within and beyond North Carolina. The method is simple enough to avoid unwieldiness, yet sophisticated enough to generate useful information for those leading the fight toward interruption of indigenous transmission of *la gross verole.*

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