Epidemiology of Tuberculosis in North Carolina, 1966 to 1986: Analysis of Demographic Features, Geographic Variation, AIDS, Migrant Workers, and Site of Infection*

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ABSTRACT: We analyzed all cases of tuberculosis reported in North Carolina between 1966 and 1986, and related the incidence rate of tuberculosis (per 100,000 population) to age (0 to 4 years, 7.59; 5 to 14 years, 3.44; 15 to 24 years, 6.30; 25 to 44 years, 15.92; 45 to 64 years, 33.85; >65 years, 51.54), race (white 9.03, nonwhite 47.40), and gender (male 25.49, female 11.25). Over the 21-year study period the annual number of cases declined from 1,248 to 711 (43%), and the incidence rate from 25.56 to 11.25 (56%). Although the incidence rate of tuberculosis fell for all subgroups, nonwhites continued to have an incidence rate 3.2 to 22.5 times higher than whites, depending on age. The standardized morbidity ratio (SMR) (by age, race, and gender) of tuberculosis in the eastern region of North Carolina was nearly twice that of the western region and unexplainable by its demographics. Between 1983 and 1986 only a small percentage of cases of tuberculosis in North Carolina were accounted for by migrant farm workers (1.7% to 2.7%) and patients with the acquired immunodeficiency syndrome (<1%). Tuberculosis is increasingly a disease of the elderly, especially nonwhite men. Tuberculosis is a geographically and demographically focal disease in North Carolina, and preventive strategies should be appropriately targeted.

BOTH the number of cases and the incidence of tuberculosis in the United States has declined dramatically since the turn of the century, though accurate data have been available only since 1953, when uniform national reporting was implemented.[1-4] From 1966 to 1985, the incidence of tuberculosis in the United States declined an average of 4.9% per year. In 1986 22,768 cases of tuberculosis (9.4/100,000) were reported to the Centers for Disease Control. This represented an increase of 2.6% in the number of reported cases over 1985 totals and marked the first occurrence of an increase in indigenous tuberculosis morbidity since 1953.[2] However, provisional national data from 1987 reported 22,014 cases of tuberculosis, a decline of 3.3% from 1986.

Tuberculosis rates vary with age, gender, and race. Advancing age, male gender, and nonwhite race are all independently associated with an increased incidence of tuberculosis.[3,5-8] In addition, in the United States tuberculosis disproportionately afflicts certain subpopulations such as Hispanics,[9,10] American Indians/Alaskan Natives,[11] Asians/Pacific Islanders,[12-15] homeless populations,[16,17] blacks,[10,18] and persons infected with the human immunodeficiency virus (HIV-1) or having the acquired immunodeficiency syndrome (AIDS).[19-25]

Tuberculosis remains a major public health concern. In 1986 tuberculosis ranked sixth on the list of diseases reportable to the Centers for Disease Control, and among reportable communicable diseases it continues to cause the greatest mortality. To aid in public health intervention strategies for controlling tuberculosis we analyzed 21,115 cases of tuberculosis occurring in North Carolina between 1966 and 1986. We present here our data, which highlight changes in the incidence of tuberculosis over a 21-year period stratified by age,

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gender, and race. The effect of tuberculosis within the migrant worker population and among individuals infected with HIV-1 upon the overall state statistics for recent years is noted. Finally, we report a markedly increased incidence of tuberculosis in a band running north-south across eastern North Carolina, unexplainable by the age, gender, and racial makeup of the region.

METHODS

Case Ascertainment and Definitions

Tuberculosis has been a reportable disease in North Carolina since 1953. Criteria used in case ascertainment by the State of North Carolina have been similar to those used by the Centers for Disease Control.[26-28]

The current case definition was initiated in 1977. Only verified cases of pulmonary and extrapulmonary tuberculosis that meet the following criteria were counted to determine annual incidence. Generally, a positive culture was necessary to confirm the diagnosis of tuberculosis, though some cases were accepted for counting on the basis of a positive microscopic examination when a culture had not been or could not be obtained. In the absence of bacteriologic confirmation, cases in which the diagnostic process was completed were accepted as verified and were counted if there was evidence of tuberculous infection (indicated by a positive skin test), if there were other signs and/or symptoms compatible with tuberculosis (such as abnormal chest film or clinical evidence of disease), and if treatment with two or more antituberculous medications was recommended for at least five consecutive months. Persons whose treatment was recommended for preventive or prophylactic reasons only and whose infections showed no evidence of current activity were not accepted as cases. For statistical purposes, persons who had recurrent disease, who had been discharged from supervision more than 12 months earlier, or who had been lost to follow-up were counted as having a new case of tuberculosis. Cases ascertained at the time of death were counted in annual morbidity statistics, provided the person had current disease before death. To improve ascertainment of tuberculosis cases the state law was amended in 1980 to require all isolates of *Mycobacterium tuberculosis* by laboratories operating in North Carolina to be reported to the North Carolina Tuberculosis Control Branch.

In North Carolina, state tuberculosis control efforts have existed since the inception of public health in 1877. Presently the Tuberculosis Control Branch employs 20 full-time professionals. In addition, all local health departments have personnel dedicated to tuberculosis control, including about 200 persons in outreach programs. All cases reported by physicians or isolates of *M tuberculosis* reported by laboratories were verified by the local county health director, followed by verification at the Morbidity Unit/State Tuberculosis Control Office.

Our data include all cases of tuberculosis occurring in North Carolina between 1966 and 1986. Cases occurring from 1966 to 1972 were obtained from hardcopy files in the Central Files Office of the North Carolina Government. Case records from 1973 to 1986 were obtained from a tape provided by the North Carolina Tuberculosis Control Branch.

Population estimates for each county by age, gender, and race were provided by the North Carolina Demographics Branch. County population density and mean family income were based on United States census data.

Determination of Incidence Rates and Standardized Morbidity Ratios

Incidence data were always recorded as cases per 100,000 population based on the estimated midyear population of the cell. Standardized morbidity ratios were calculated using the indirect method ($\Sigma Ci/\Sigma RiNi$, where C = number of cases, i = age, race, gender cell, Ri = United States attack rate, Ni = estimated cell population). For hypothesis testing purposes, we obtained an approximate sampling variance for the SMR following the method of Keyfitz.[29]

Association of Tuberculosis and AIDS

Subjects meeting both the AIDS and tuberculosis case definitions currently used by the Centers for Disease Control were detected by matching names on both surveillance lists.

RESULTS

Effects of Race, Age, Gender

During the 21-year study period, 1966 to 1986, 21,115 cases of tuberculosis were reported in North Carolina. The incidence rate (per 100,000) of tuberculosis over the 21 years was 18.19. Univariate analysis revealed that this rate varied tremendously with race, gender, and age. Combining the data over the 21-year study period, the univariate incidence rates were as follows: race—white 9.03, nonwhite 47.40; gender—male 25.49, female 11.25; and age—0 to 4 years 7.59, 5 to 14 years 3.44, 15 to 24 years 6.30, 25 to 44 years 15.92, 45 to 64 years 33.85, and >65 years 51.54. Thus in North Carolina between 1966 and 1986, the incidence of tuberculosis was 5.25 times greater in nonwhite than in white individuals, 2.27 times greater in male than in female subjects, and

TABLE 1. Incidence of Tuberculosis in North Carolina (per 100,000) by Age, Race, and Gender

Time Intervals	Subgroups	Age (years) 0-4	5-14	15-24	25-44	45-64	≥65
1966-68	White male	3.2	1.2	4.3	17.0	44.1	71.2
	White female	6.3	2.2	4.7	6.1	9.8	21.9
	Nonwhite male	31.6	19.9	33.5	106.9	203.8	226.3
	Nonwhite female	21.9	19.1	37.3	56.5	50.3	95.7
1969-71	White male	5.1	0.9	4.7	13.2	37.1	53.7
	White female	4.5	1.5	3.9	5.7	7.5	19 0
	Nonwhite male	34.0	13.9	27.0	121.7	201.9	216 1
	Nonwhite female	20.7	14.5	25.6	47.8	35.7	105 8
1972-74	White male	3.5	0.7	3.3	8.2	28.8	49 8
	White female	2.2	0.9	2.2	3.1	6.5	15 4
	Nonwhite male	24.6	11.3	19.1	103.6	187.2	201.1
	Nonwhite female	17.7	12.6	15.6	37.5	46.5	88 4
1975-77	White male	1.7	1.0	2.3	9.1	33.0	60.7
	White female	2.3	0.7	1.8	4.4	8.5	19 1
	Nonwhite male	18.8	6.5	17.1	93.3	215.6	240 0
	Nonwhite female	19.6	11.1	20.2	32.3	51.3	97.3
1978-80	White male	1.9	0.6	1.5	6.8	25.5	53.2
	White female	2.0	0.8	1.7	3.3	8.2	17.9
	Nonwhite male	14.2	5.3	14.6	74.4	192.5	227.1
	Nonwhite female	21.4	6.1	12.7	27.5	40.6	87 5
1981-83	White male	2.1	0.4	0.8	4.6	20.7	40.1
	White female	2.2	0.4	0.4	2.5	5.3	16.5
	Nonwhite male	9.2	2.8	8.6	50.7	137.2	222.5
	Nonwhite female	8.3	4.1	9.0	19.1	36.0	71.8
1984-86	White male	1.1	0.3	1.1	3.6	13.1	32.1
	White female	1.7	0.2	1.0	1.5	4.4	12.7
	Nonwhite male	8.5	2.8	5.3	37.3	103.5	183.0
	Nonwhite female	8.3	2.6	6.5	15.4	28.0	70.5

14.98 times greater in individuals older than 65 than in individuals aged 5 to 14.

Stratification of tuberculosis incidence rates by race, gender, and age (Fig 1, Table 1) demonstrated that the incidence of tuberculosis was markedly higher in nonwhite than in white individuals regardless of age or gender. Depending on the specific age and gender subgroup, the

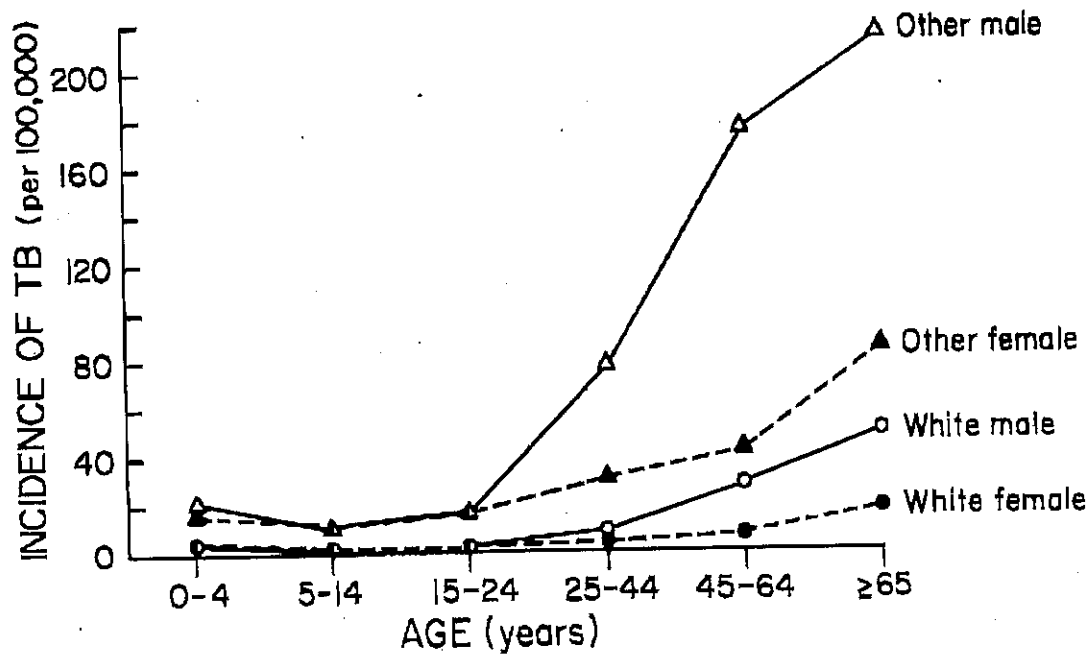

FIGURE 1. Incidence of tuberculosis in North Carolina (per 100,000) from 1966 to 1986 by gender, race, and age.

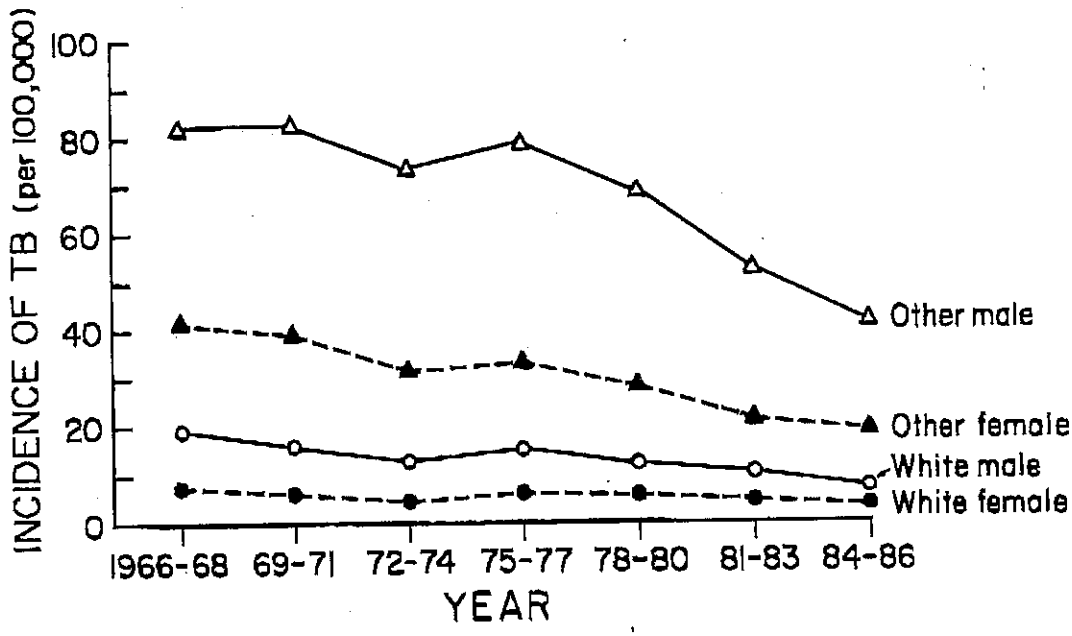

FIGURE 2. Incidence of tuberculosis in North Carolina (per 100,000) in three-year intervals from 1966 to 1986 by gender and race.

incidence of tuberculosis was 3.2 to 22.5 times higher among nonwhites than whites. Overall the incidence of tuberculosis was higher in male than in female subjects regardless of race, but this difference is highly age dependent. For the three age groups between 0 and 24 (ie, 0 to 4, 5 to 14, 15 to 24) the incidence of tuberculosis was similar regardless of gender. For the three age groups between 25 and more than 65 (ie, 25 to 44, 45 to 64, >65) the incidence of tuberculosis was consistently higher in men than in women regardless of race. Depending on the race and age subgroup, the incidence of tuberculosis in male subjects was 1.8 to 4.9 times greater than in female subjects.

Trends in Tuberculosis Incidence

The number of reported cases of tuberculosis in North Carolina has dropped 43% from 1,248 cases reported in 1966 to 711 cases reported in 1986 (Fig 2, Tables 1 and 2). Correspondingly,

TABLE 2. Incidence of Tuberculosis (per 100,000) and Standardized Morbidity Ratios (SMR) (Excess or Deficit Compared With Predicted) for Tuberculosis in North Carolina by Year and Region

		Incidence By Region			*SMR By Region*		
Year	*TB Cases*	*East*	*West*	*Total: NC*	*East*	*West*	*Total: NC*
1966	1,248	40.20	18.42	25.56	1.14 (+77)	0.67 (−299)	0.85 (−221)
1967	1,242	36.33	19.79	25.18	1.07 (+36)	0.75 (−214)	0.86 (−176)
1968	1,201	37.88	17.53	24.10	1.21 (+105)	0.72 (−224)	0.91 (−119)
1969	1,155	36.12	16.64	22.91	1.27 (+124)	0.76 (−185)	0.93 (−58)
1970	1,219	40.65	16.17	24.08	1.52 (+227)	0.79 (−149)	1.07 (+78)
1971	1,050	33.23	14.30	20.52	1.34 (+138)	0.75 (−166)	0.97 (−28)
1972	1,015	32.31	13.49	19.44	1.39 (+150)	0.77 (−147)	1.00 (+2)
1973	986	30.61	13.01	18.58	1.41 (+151)	0.79 (−124)	1.03 (+26)
1974	936	27.33	12.79	17.41	1.31 (+112)	0.81 (−111)	1.00 (+1)
1975	1,154	32.17	16.01	21.21	1.36 (+130)	0.89 (−70)	1.07 (+80)
1976	1,219	34.79	16.93	22.30	1.57 (+223)	0.97 (−18)	1.20 (+204)
1977	1,041	29.84	16.68	18.90	1.44 (+162)	0.87 (−74)	1.09 (+88)
1978	941	27.31	11.85	16.91	1.44 (+151)	0.81 (−102)	1.06 (+49)
1979	982	29.57	11.85	17.51	1.62 (+202)	0.85 (−79)	1.14 (+123)
1980	1,036	33.12	11.51	18.49	1.84 (+278)	0.85 (−81)	1.23 (+197)
1981	972	29.63	10.14	16.31	1.65 (+220)	0.76 (−134)	1.10 (+86)
1982	794	23.80	8.29	13.19	1.49 (+137)	0.66 (−172)	0.95 (−35)
1983	779	23.11	8.05	12.81	1.50 (+147)	0.70 (−146)	1.00 (+2)
1984	756	22.14	7.71	12.26	1.44 (+131)	0.67 (−162)	0.96 (−31)
1985	658	16.57	7.75	10.52	1.16 (+45)	0.73 (−123)	0.89 (−77)
1986	711	19.40	7.49	11.25	1.34 (+99)	0.70 (−141)	0.94 (−42)

the incidence (per 100,000) has decreased 56% from 25.56 to 11.25. Stratification of the data by race and gender revealed that among all four subgroups the incidence of tuberculosis has declined from 1966 to 1986 (Fig 2). The decrease in the incidence of tuberculosis was greatest for white male subjects (63%), followed by white female subjects (56%), nonwhite female subjects (55%), and nonwhite male subjects (50%). Although all four race and gender subgroups showed a significant decrease in tuberculosis rates between 1966 and 1986, the rank order of tuberculosis incidence at every time point remained nonwhite male > nonwhite female > white male > white female subjects.

Stratified analysis (Table 1) revealed that the incidence of tuberculosis declined for all racial, gender, and age subgroups. However, the degree of decrease was greater for individuals aged 0 to 24 years than for those older than 25. Although the incidence of tuberculosis has declined in both whites and nonwhites, the relative difference between the groups (about threefold to 23-fold) has remained approximately constant between 1966 and 1986.

Impact of Geographic Location

The incidence of tuberculosis varied significantly among the regions of the state (Fig 3, Table 2). The eastern section of North Carolina, depending on the study year, recorded an incidence of tuberculosis 1.8 to 2.9 times that of the western section of the state. This eastern predominance has remained relatively stable over the 21 years despite a decreasing incidence of tuberculosis in both regions.

In an attempt to evaluate the importance of age, race, and gender in explaining the eastern predominance of tuberculosis we calculated standard morbidity ratios (SMR) for each section of North Carolina, which took into account race, gender, and age within the regions (Table 2). North Carolina as a whole had an SMR of 1.01 over the study period, indicating the state is close to the rates expected for its race, age, and gender distribution based on data for the United States. Standardized morbidity ratios, however, revealed a marked eastern predominance of tuberculosis unexplained by the race, gender, or age distribution of the population. Over the 21-year study period, eastern North Carolina had an SMR of 1.38 while the western region had an SMR of 0.77. Thus eastern North Carolina had significantly more cases of tuberculosis than is explainable by its age, race, and gender distribution, while western North Carolina had significantly fewer cases. This eastern predominance occurs in a band

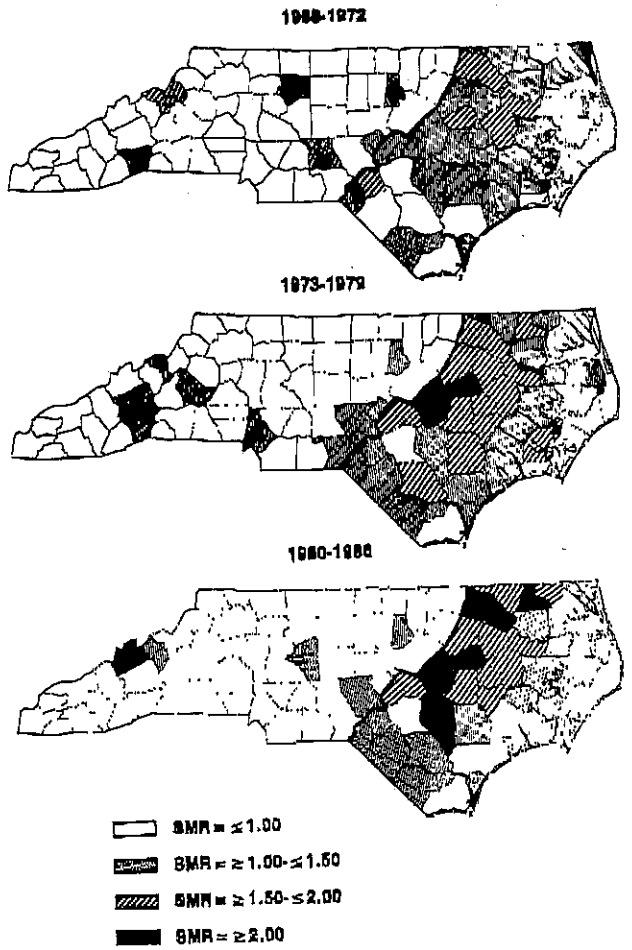

FIGURE 3. North Carolina standardized morbidity ratios (SMR) (by age, race, gender) for tuberculosis by county in seven-year intervals.

that spares the coastal counties (Fig 3).

Stratified analysis (Table 3) revealed a markedly higher incidence of tuberculosis in the eastern portion among individuals more than 25 years old in all time periods, and for all race and gender groups. However, a higher incidence of tuberculosis was not noted for individuals 24 years old or younger, regardless of time period studied, race, or gender. Further, the eastern section is becoming increasingly deviant from the remainder of the state (Fig 3).

Correlation of SMR by county with county population density or mean family income did not show a statistically significant relationship: 1969—county SMR versus population density, $P = .15$; county SMR versus mean family income, $P = .15$; 1979—county SMR versus population density, $P = .08$; county SMR versus mean family income, $P = .43$. However, the directionality was as expected; the incidence of tuberculosis increased as population density increased (Spearman's correlation: 1969 = 0.066, 1979 = 0.22), and as the mean family income decreased (Spearman's correlation: 1969 = −0.18, 1979 = −0.12).

TABLE 3. Incidence of Tuberculosis in North Carolina (per 100,000) by Race, Gender, Age, and Geographic Region

		1966-1968		1975-1977		1984-1986	
[illegible]	Age	East	West	East	West	East	West
White male	0-4	3.56	5.80	1.55	1.81	0.77	1.27
	5-14	0.99	1.27	0.73	1.07	0.38	0.29
	15-24	5.39	3.71	2.71	2.12	1.28	1.05
	25-44	22.57	14.92	12.48	7.87	4.70	3.13
	45-64	64.39	36.96	35.32	27.22	23.87	9.42
	>65	134.98	50.38	116.91	42.42	59.58	25.29
White female	0-4	7.46	5.80	4.95	1.27	1.54	1.68
	5-14	1.39	2.51	1.92	0.28	0.81	0.00
	15-24	9.09	2.97	2.46	1.59	1.30	0.95
	25-44	11.74	6.82	4.51	4.41	1.81	1.44
	45-64	13.67	8.50	10.58	7.79	5.88	3.85
	>65	39.89	15.91	37.61	12.91	22.54	9.46
Nonwhite male	0-4	32.12	31.11	17.12	20.37	7.19	9.80
	5-14	17.97	21.87	9.67	9.05	1.46	3.95
	15-24	38.37	28.31	15.99	18.39	7.05	3.56
	25-44	131.29	86.16	105.33	86.97	46.00	30.99
	45-64	269.57	150.78	283.33	156.03	149.11	66.35
	>65	313.81	148.02	328.24	160.44	274.07	104.07
Nonwhite female	0-4	23.09	20.60	21.69	17.64	9.49	7.14
	5-14	18.20	20.09	10.64	11.51	2.00	3.19
	15-24	38.79	26.46	20.64	19.76	7.43	5.83
	25-44	61.14	52.39	30.16	33.97	16.92	14.30
	45-64	67.13	35.78	55.11	47.98	38.33	19.24
	>65	190.20	66.48	134.55	65.69	97.43	48.19

Impact of Migrant Population on Tuberculosis Rates

Agriculture, especially tobacco growing, is the largest industry in North Carolina, and therefore North Carolina has a large migrant population. The number of cases of tuberculosis reported in migrants from 1983 through 1986 was as follows: 1983—21 cases (2.7% of all tuberculosis reported), 1984—19 cases (2.5%), 1985—12 cases (1.8%), and 1986—12 cases (1.7%). The breakdown of the 64 cases in migrants by race and gender was as follows: white male—12 (18.7%), nonwhite male—45 (70.3%), white female—one (1.6%), nonwhite female—six (9.4%). The breakdown of the nonwhite group was black 49, Indian 0, and Hispanic 2.

Impact of HIV-1 Infection on Tuberculosis

Between 1982 and 1987, 22 patients with AIDS appeared on the tuberculosis surveillance list (Table 4). The relationship of AIDS diagnosis and tuberculosis diagnosis was as follows: in seven patients tuberculosis developed before AIDS, in four patients AIDS developed before tuberculosis, in six patients both conditions developed at approximately the same time, and five patients were dead when the diagnosis of tuberculosis was made. Stratified analysis revealed that 7.5% of 213 black non-Hispanics with AIDS had tuberculosis compared with 2.0% of 252 white non-Hispanics. Tuberculosis developed in 4.6% of male AIDS patients and 4.1% of female AIDS patients. Tuberculosis incidence varied by AIDS risk group (number of AIDS patients within risk group): homosexual/bisexual men, 2.6% (273); homosexual/bisexual men who also used intravenous drugs, 0% (20); intravenous drug abusers, 10.2% (88), hemophiliacs, 0% (22); blood transfusion recipients, 11.1% (27); parent within high-risk group, 0% (5); heterosexual contact, 4.3% (23); and unknown, 11.1% (18).

The median age of patients with AIDS and tuberculosis was 37 (range 26 to 66). The tuberculosis was pulmonary (one site) in ten, miliary in six, pulmonary (two sites) in three, lymphatic in one, pleural in one, and peritoneal in one. At the time of diagnosis, five patients (22.4%) were dead. Among the remaining 17 patients who started tuberculosis therapy, cumulative mortality was as follows: six months—29.4%, 12 months—52.9%, 24 months—64.7%, and 36 months—70.6%. Of the five patients presumably still alive as of June 1988, one began therapy in 1985 and four in 1987.

Trends in Site of Tuberculosis

Between 1975 and 1987, extrapulmonary tuberculosis was noted in 14.8% of patients. A slight trend toward an increased incidence of extrapulmonary tuberculosis has been noted. In all years between 1975 and 1983, the percentage of patients with extrapulmonary tuberculosis was less than or equal to 14.8% (minimum = 12.7%),

whereas in all years since 1983 the percentage of patients with extrapulmonary tuberculosis has been greater than 14.8% (maximum 21.1%).

Blacks were slightly more likely to have extrapulmonary disease than whites, 15.9% versus 12.4%. Female subjects were also more likely to have extrapulmonary disease than male subjects, 18.9% versus 12.8%. The likelihood of extrapulmonary disease also varied by age: 0 to 4 years, 22.3%; 5 to 14 years, 17.8%; 15 to 24 years, 18.6%; 25 to 45 years, 17.2%; 45 to 64 years, 12.3%; and more than 65 years, 14.5%.

Sites of extrapulmonary disease (1975 to 1987) were as follows: pleural 618, miliary 280, lymphatic 230, other 172, genitourinary 167, bone/joint 156, meningeal 65, and peritoneal 55.

TABLE 4. North Carolina AIDS/Tuberculosis Cases by Year of Antituberculous Therapy and AIDS Diagnosis

Year Tuberculosis Therapy Was Begun	*No. of Patients*	*Year AIDS Was Diagnosed*					
		1982	*1983*	*1984*	*1985*	*1986*	*1987*
1982	0	0	0	0	0	0	0
1983	2	0	0	1	1	0	0
1984	4	0	0	4	0	0	0
1985	4	0	0	0	3	0	1
1986	5	0	0	0	0	2	3
1987*	9	0	0	0	0	0	9
Total	22	0	0	5	4	2	11

*CDC AIDS case definition revised to include tuberculosis.

DISCUSSION

The incidence of tuberculosis has been declining in the United States since the turn of the century.[30] General improvements in the standard of living appear to have been the most important factor in this decline, although the increase in rate of decline coincided with the introduction of effective antituberculous drugs. Between 1953 and 1985 the number of cases of tuberculosis fell from 84,304 (incidence 53.0/100,000) to 22,201 (incidence 9.3/100,000) and the number of deaths attributable to tuberculosis, from 19,707 (incidence 12.4/100,000) to 1,680 (0.7/100,000).[3] Provisional data for 1987 indicate a further decline to 22,014 cases.[31] This continued decline in tuberculosis has resulted in part from ongoing surveillance, screening of high-risk subpopulations, and contact investigation coupled with prophylaxis for infected individuals and effective therapy for diseased individuals. The discovery of effective antituberculous drugs and development of effective short course regimens of treatment have also aided public health control measures.

Despite this dramatic decline tuberculosis remains a major public health problem. In 1986 tuberculosis ranked No. 6 on the list of diseases reportable to the Centers for Disease Control, exceeded only by gonorrhea, salmonellosis, syphilis, hepatitis A, and hepatitis B. Among reportable diseases, tuberculosis continues to lead the mortality list. Recent reports note the continued high incidence of tuberculosis within certain subpopulations: Hispanics,[9,10] American Indians/Alaskan Natives,[11] Asians/Pacific Islanders,[12-15,21] homeless populations,[16,17] blacks,[10,18] and persons infected with HIV-1 or who have AIDS.[19-25]

Only a minority of individuals who are infected with *M tuberculosis* (ie, those who show a positive reaction to skin testing with purified protein derivative [PPD]) will have clinical disease. The incidence of tuberculosis, as measured by surveillance, depends on three components: the risk of becoming infected, the risk of infection leading to active disease, and the risk of reactivation of latent infection. Factors influencing risk of infection appear to be quite different from those influencing risk of disease after infection has occurred. Unfortunately, only limited data are available regarding the relative significance of individual risk factors and relative contribution of all three components to overall disease incidence. Further, the complex interactions between individual risk factors make it difficult to attribute variations in disease incidence to any of these factors in isolation.

The risk of acquiring tuberculous infection is usually low per day of exposure. Past studies indicated that 48% to 68% of household contacts were infected at the time of ascertainment of the index case. In recent data from the Centers for Disease Control, 15% of close contacts and 2% of other contacts were infected.[3]

Multiple factors have been associated with the risk of acquiring tuberculous infection: age, gender, and race; level of contact; geography; and socioeconomic factors. First, nonwhite and male subjects have been more likely to be infected than white and female subjects.[7,32,33] Increasing age is associated with an increasing prevalence of tuberculous infection, although few studies provide simultaneous cross-sectional data on subjects from early childhood to late adult life. Second, level of contact with source case is associated with the risk of infection. Advanced disease, production of sputum, and large numbers of tuberculous bacteria in the sputum have been associated with an increased risk of infection in contacts.[34-38] Treatment greatly reduces the risk of transmission.[39] Third, data obtained on military recruits suggest a geographic variation in the prevalence of infection.[40,41] A higher frequency of infection was noted in recruits from large cities, Appalachia, Pennsylvania coalfields, the Southwest, and the

Southeast. Recruits who had lived abroad were at slightly greater risk than lifetime residents of the United States. Fourth, infection also appears to be related to various socioeconomic factors, being higher in urban than in farm residents, higher in households with crowding, and higher in recruits than in college men.[40,41] Other studies have noted that the risk of infection is associated with lower socioeconomic status.[8,42]

The risk of clinical tuberculosis after infection also appears to depend on multiple factors. Major risk factors include time interval since infection, gender, age, body weight, and depressed immune function. First, the risk of active tuberculosis is highest within the first few years after infection.[6,32,39,43,44] Infants are at special risk for development of active disease.[45] Second, the risk of clinical tuberculosis during late adolescence and early adult life is higher in infected female subjects than in male subjects. After age 50 men are at greater risk.[45-47] Third, the onset of active tuberculosis peaks during infancy and early childhood, early adult life, and late adult life. Fourth, among infected persons, heavier persons appear to develop tuberculosis less frequently than lighter ones.[48-50] Fifth, conditions (ie, HIV-1 infection) or medications that depress immune function may increase the risk of reactivation of tuberculosis. Gender, age, and immune function may also be related to risk of acquiring infection with *M tuberculosis*, and thereby to disease incidence. Other factors reported as being related to the development of infection include socioeconomic class, psychosocial stress,[32] and genetic factors.

Risk of reactivation of tuberculosis has also been related to multiple factors.[51] Factors reported to increase the risk of reactivation include extensive disease, younger age, and nonwhite race. Risks of reactivation decrease with time since "arrest of disease" and with adequate chemotherapy.

Stratified analysis of 21,115 cases of tuberculosis reported in North Carolina between 1966 and 1986 revealed that age, gender, and race were independently predictors of the incidence of tuberculosis. Age was the most significant predictor. The age distribution of tuberculosis revealed a small peak in childhood (0 to 4 years of age) and a much larger peak in older individuals. The peak in older individuals is in large part due to a cohort effect which reflected the higher incidence of acquisition by the elderly of infection during the childhood years.[52] In addition, waning of the immune system which leads to loss of skin test reactivity may also lead to increased reactivation.[53]

In every age group nonwhites had an incidence of tuberculosis 3.2 to 22.5 times higher than whites of the same gender group. The increased incidence of tuberculosis in nonwhites is most likely related to a higher prevalence of infection, although good data are scarce. The prevalence of a positive tuberculin skin test among military recruits tested between 1958 and 1969 was 3.8% for whites, 12.4% for blacks, and 60.2% for Asians.[32] A study of tuberculin reactivity among 50,000 employees of the New York City Board of Education tested in 1973–1974 revealed an age-adjusted rate of 30.54% for Puerto Ricans and 26.04% for blacks, compared with 8.39% for whites.[6]

Three prospective studies in the United States have analyzed the development of active tuberculosis among tuberculin reactors by race. Study populations included school children in Alabama and Georgia,[5] military recruits,[32] and Puerto Ricans.[6,45] Incidence rates for blacks and whites in the three studies were as follows: Alabamians —black 76, white 43 (follow-up 20 years), military recruits—black 91, white 78 (follow-up four years), and Puerto Ricans—black 87, white 91 (follow-up 19 years). Thus, the first two studies detected a higher incidence of tuberculosis among nonwhites than whites. However, in a careful review of these and other studies, Kushigemachi and co-workers[54] concluded that current data are insufficient to isolate race as a risk factor for the development of tuberculosis.

Review of our data revealed that the rate of tuberculosis is roughly equal in the male and female population (within the same racial group) for subjects 0 to 24 years of age, while the rate is twofold to threefold higher in men than in women more than 25 years old. These findings suggest one or more of the following: (1) older male subjects were more likely than older female subjects to acquire primary tuberculosis; (2) older men were more likely than older women to have acquired tuberculosis in their early years, and the factors that led to this exposure have not been present in North Carolina since 1941; and (3) older men are more likely to have reactivation of tuberculosis than older women.

Our data revealed that the incidence of tuberculosis had declined steadily between 1966 and 1985. During this 20-year period the number of cases of tuberculosis decreased at an annual average rate of 2.85%/year and the incidence of tuberculosis decreased at an annual average rate of 4.2%/year. This decline has occurred among all racial, age, and gender groups. Although North Carolina reported an increase in cases in 1986 compared with 1985, provisional data reported 662 cases in 1987.[37] Tuberculosis among migrant workers has remained relatively constant from

1983 through 1986, accounting for 1.7% to 2.7% of the state's cases. Nevertheless, these low numbers may reflect underascertainment. A study of migrant workers on the Delmarva peninsula (Delaware, Maryland, Virginia) revealed a prevalence of skin test reactivity of 37%.[55] Additional population-based data are desirable.

Whereas the incidence of tuberculosis in association with HIV-1 infected individuals has steadily increased, tuberculosis within this group accounts for only a small proportion of cases reported in North Carolina. Matching of tuberculosis and AIDS registries in New York City, Connecticut, and Florida revealed that 5% to 10% of patients with a diagnosis of AIDS also had tuberculosis.[19-21] Approximately 2% of tuberculosis cases occurred in patients with AIDS. Our finding of tuberculosis in about 5% of AIDS patients is similar to that in previous reports. It is of public health significance that for seven of 22 patients with AIDS and tuberculosis, the diagnosis of tuberculosis preceded the diagnosis of AIDS. Since HIV-1 infection appears to be a significant risk factor for tuberculosis the CDC recommends that HIV-1 infected persons be given a tuberculin skin test and that if it is positive, preventive therapy with isoniazid should be given after active tuberculosis has been ruled out, regardless of age.[2]

The proportion of cases of tuberculosis in extrapulmonary sites has increased slightly over the 21-year study period. Nonwhite and female subjects were somewhat more likely to have extrapulmonary disease.

Although the incidence of tuberculosis has decreased in all age groups, the decrease is least apparent for older Americans (>45 years of age). Tuberculosis in North Carolina is clearly and increasingly a geriatric disease. During the period 1966 to 1968, 55.0% of tuberculosis cases occurred in persons over age 45 and 20.2% in persons over age 65. By comparison from 1984 to 1986, 71.0% of patients with tuberculosis were over age 45 and 38.5% were over age 65. Because most disease in these age groups is presumably the result of reactivation rather than recent transmission, public health programs could focus on detection of tuberculous infection and prophylaxis in younger individuals and/or detection and treatment of disease in the elderly. However, during the interval 1984 to 1986 only 17.1% of the tuberculosis cases occurred in patients under age 35, which emphasizes the need for public health programs to be targeted at detection of tuberculosis in the geriatric population. The high prevalence of infection in residents of extended care facilities[53,56] and multiple reports of cross-transmission have led to recommendations to screen entries into extended care facilities.[57]

Although the incidence of tuberculosis among minorities declined between 1966 and 1986, the level of discrepancy between whites and nonwhites has been remarkably constant. Even in the youngest age groups where the incidence of tuberculosis reflects new infection, nonwhites continue to have a significantly higher incidence of tuberculosis than whites.

Comparing county-specific incidence rates over the 21-year study period revealed a predominance of tuberculosis in the eastern part of North Carolina. Even after standardization for race, gender, and age the marked eastern predominance persisted. This eastern predominance cannot be entirely explained by population density or socioeconomic level. There are several possible explanations for this observation. The first is an increased incidence of infection leading to an increased incidence of disease, though this would not explain why the increased incidence of disease is found only in the older age groups. Second, an environmental, social, or economic factor more prevalent in the east might lead to increased frequency of reactivation of latent infection. Third, some environmental, social, or economic factor might lead to increased transmission of *M tuberculosis*, though this would be difficult to reconcile with the view that most disease in older individuals represents reactivation and with the similar rates of disease in younger individuals. Fourth, migrant farm workers employed in the agricultural eastern region of North Carolina could account for the eastern predominance, but this is not supported by the relatively few cases found among migrant workers.

Tuberculosis continues to be a major public health problem, especially within certain subpopulations such as the homeless, Asians, and Hispanics. The gap between whites and nonwhites did not improve over the 21 years of our study and requires new public health approaches. The consistent finding that 5% to 10% of AIDS patients have tuberculosis is of concern for several reasons. First, 1.0 to 1.5 million Americans are estimated to be infected with HIV-1, which in the majority will progress to AIDS. This will have substantial impact on the incidence of tuberculosis. Second, tuberculosis in patients with AIDS is more difficult to diagnose because skin tests are often negative because of anergy, there is a higher incidence of extrapulmonary disease, chest roentgenograms are often atypical, and it is more difficult to isolate *M tuberculosis* from the sputum by

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smear or culture. Finally, since AIDS patients are frequently hospitalized there is the possibility of increased nosocomial transmission, though such transmission has not proved to be a major problem.

With the exception of HIV-1 infected persons, our data suggest that tuberculosis will increasingly become a geriatric disease, especially of elderly nonwhite men. New strategies and technologies will need to be developed to address this problem.

The predominance of tuberculosis in eastern North Carolina remains unexplained, and unraveling this observation may increase our understanding of acquisition of infection or development of disease. Because tuberculosis is concentrated in defined geographic pockets in North Carolina, intensive use of preventive measures may be most effective, particularly for persons under 35 years of age. Unfortunately, only 17.1% of cases in North Carolina from 1984 to 1986 occurred in persons under 35 years of age. Active case-finding, treatment, and extensive use of chemoprophylaxis may be necessary to eliminate the relatively high incidence of tuberculosis in eastern North Carolina.

We have used the standardized morbidity ratio for summarizing tuberculosis morbidity in differing geographic areas. The SMR eliminates the effects of age, race, and gender composition of the various regions and allows comparison of observed rates with expected rates of tuberculosis based on national data. Using this method we have shown that the geographic predominance of tuberculosis in eastern North Carolina is not due to demographic makeup of the region. Other states can use similar methods to define relative risks and excess morbidity for their state or counties, as compared with the population of the United States. Such information will allow the development of more precisely targeted programs to prevent and treat tuberculosis.

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