WORLD HEALTH ORGANIZATION

Regional Office for the Eastern Mediterranean

ORGANISATION MONDIALE DE LA SANTÉ

Bureau régional pour la Méditerranée orientale

REGIONAL SEMINAR ON RECENT TRENDS IN TUBERCULOSIS CONTROL

Karachi, 23 - 30 October 1975

EM/SEM.TB/8

19 August 1975

ENGLISH ONLY

RECENT ADVANCES IN EPIDEMIOLOGICAL RESEARCH IN TUBERCULOSIS

by

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Tuberculosis epidemiology is dealing with the natural trend of tuberculosis, i.e. with the natural relationship between the tubercle bacillus and a given population, without any man-made interference.

Naturally, the aim of any tuberculosis programme is to interfere in the natural relationship between tubercle bacilli and the people, to the benefit of the people and the disadvantage of tubercle bacilli.

Several expressions should be clarified before we discuss our topic, especially the distinction between a parameter and a variable.

A parameter is defined as a constant indicating the numerical value which links together two variables. For instance, a "contagious" parameter refers to an average number of persons infected with virulent tubercle bacilli during one year by one source of infection; or the disease ratio expresses the proportion of cases in which infection with virulent tubercle bacilli will lead to the development of a source of infection; etc. It has to be stressed, however, that the parameters are constant under natural conditions only, i.e. without man-made interference.

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For this reason, post-war routine statistics in developed countries cannot be used for exploring various parameters in tuberculosis epidemiology, as there has been an uninterrupted interference in the natural trend of tuberculosis, especially with chemotherapy, influencing one or more parameters. On the other hand, some estimates on how great this influence can be under ideal conditions can be determined from well conducted controlled trials. A very important source of data for studying various parameters are the many prevalence surveys which were carried out by WHO teams in different samples of populations in developing countries in the 1950s and the early 1960s, before intensive tuberculosis policies were introduced into those countries. In those surveys, the most important tools, namely standard tuberculin testing and reliable examination of sputum for tubercle bacilli have been used systematically in the randomly selected samples of the population.

The other expression to be clarified, is the term variable; the word indicates that the values of a variable do not remain constant but vary with time in a given population and among various population groups. Two important variables are used in connection with tuberculosis epidemiology, namely prevalence and incidence.

A prevalence is the proportion of the population which, on a given day, has a well defined attribute; i.e. a proportion of subjects of a particular age-group found to have been infected with virulent tubercle bacilli on December 31st, or a proportion of persons, aged 10 years or more found to have excreted tubercle bacilli demonstrable by microscopy, on the day of a survey, etc.

The most important examinations for establishing reliable prevalence data in tuberculosis are the standard tuberculin test and the microscopic (and culture) examinations of sputum for tubercle bacilli. As will be shown later, by far the most important sources of infection are persons discharging sputum containing so many tubercle bacilli that they can be demonstrated by direct microscopy, and therefore numbers and rates for smear-positive patients should always be reported and analysed separately.

Prevalence, being a simple proportion of the population who have, on a given day,

well defined attributes, should be referred to as a ratio, as it describes the static epidemiological situation in the population.

An incidence gives the number of persons of a given population, who, during a given period of time (usually during 1 year), will acquire a well defined attribute. The attributes in which we are interested for incidences are again the annual incidence of people infected with tubercle bacilli and the annual incidence of bacteriologically confirmed cases (separately for those positive on smear and those positive on culture only); in addition, we wish to know the annual mortality from tuberculosis.

Incidence is referred to as a rate.

As already mentioned, tuberculosis epidemiology should provide us with the values of all important parameters. Although a considerable amount of information about various parameters has been recently collected, it is necessary to undertake more fundamental research into the way in which tuberculosis is behaving and maintaining itself in the community.

In our opinion, three distinct events should be studied:

I. The transmission of tubercle bacilli

The aim of the study is to discover the average chance or risk of a person in a given community inhaling tubercle bacilli.

II. Development from infection to pulmonary disease

The overall probability of developing a "case of pulmonary tuberculosis" is different for

a) those who are non-reactors at the time of infection, and

b) those who are reactors to tuberculin at the time of (super)infection.

III. From development of a "case of pulmonary tuberculosis" to recovery or death

The aim of the study is to discover the probability of recovery (absence of tubercle bacilli of say two years) or death from tuberculosis.

I. "Contagious" parameter (average number of persons infected with tuberculosis during one year by one source of infection)

This is a parameter which links together two variables: annual tuberculosis infection rate and prevalence of the sources of infection.

A. Annual tuberculosis infection rate. This rate indicates the proportion of the population under study which will be primarily infected, or reinfected (in those who have been previously infected) with virulent tubercle bacilli in the course of one year.

The annual tuberculosis infection rate is derived from the results of tuberculin testing. A technique for converting information on prevalence of infection into a smooth series of annual rates of tuberculous infection has been developed recently by the TSRU (Tuberculosis Surveillance Research Unit) and published in a comprehensive report in 1969 (TSRU, 1969). To obtain reliable estimates of the annual tuberculosis infection rates and their changes in a particular period, several tuberculin surveys are required at intervals, each in a representative sample of non-BCG vaccinated subjects of the same age, tested by the same technique.

The approach used by the TSRU for estimating the average annual risks of tuberculous infection in the Netherlands is complicated, partly because little was previously known about the way in which the risk of infection was changing and this had to be assessed carefully, and partly because it was desirable, in the process, to make comprehensive use of the extensive prevalence data available in the Netherlands. However, for routine tuberculosis control a simple method of estimating the annual tuberculosis infection rate is described in the short section VIII of the same report. Appendix I shows an example of how the annual tuberculosis infection rates can be estimated easily.

The annual risk of tuberculous infection is usually expressed as a percentage. If, in a given community, the annual risk of infection is say 3%, 3000 persons of each 100,000 inhabitants will be infected during 12 months, with virulent tubercle bacilli from human sources of infection (in the absence of bovine infection). A proportion of the 3000 infected will acquire primary infection (mostly children and young adults),

the remaining part (mostly middle-aged, elderly and old people) will be superinfected. For the purpose of our study, we have to consider the risk of inhaling tubercle bacilli to be of the same magnitude (for the same age-group) for those not yet infected (tuberculin-negatives) and those already infected (tuberculin-positives).

B. Prevalence of sources of infection. In this context, one has to define the most important sources of infection. In our opinion, persons who have been in intimate contact with tuberculous patients represent the most suitable population group for the study of this problem. Several studies demonstrate that smear-positive patients play the greatest role in spreading infection and in doing so perpetuate the epidemic; in contrast, those patients in whom the presence of bacilli in the sputa can be demonstrated by culture only, or who are culture-negative, are relatively harmless.

Figure 1 shows the situation in Rotterdam (the Netherlands). The percentage of positive reactors, i.e. the infection prevalence, was high among intimate contacts of smear-positive index cases; 50% of such contacts aged 0-14 years were found to be infected, as compared with 1% in the same age-group among the general population. However, the prevalence of infection was low (about 6%) in child contacts of culture-positive and culture-negative index cases. (For the full report see TSRU report no.3, in press.)

An extensive study on morbidity in contacts (more than 8,000 intimate "white" and Indian contacts, and more than 11,000 casual contacts in the same two racial groups) has been recently carried out in British Columbia and Saskatchewan (TSRU report no.3, in press). Appendix Tables II and III show that tuberculosis was rare in intimate contacts of culture-negative sources, and no cases of tuberculosis were observed among casual contacts of culture-negative sources. Disease rates were also substancially lower (0.8 per cent for whites and 2.3% for Indians) among intimate contacts of culture-positive cases than among intimate contacts of smear-positive sources (5.9% and 8.2% respectively).

These observations confirm once more that the bacillary status of the patients decides the extent to which he can transmit tubercle bacilli to other hosts. The

most important transmitters are patients in whose sputa tubercle bacilli can be demonstrated by direct smear examination.

For the purpose of our study, patients with smear-positive tuberculosis will be considered as sources of infection.

C. The "contagious" parameter is computed as:

$$\frac{\text{Annual tuberculosis infection rate (\%)}}{\text{Prevalence of sources of infection (per 100,000)}} \times 1{,}000$$

Assuming no effective chemotherapy, the prevalence rate of smear-positive cases (at all ages) is twice as high as the incidence rate of smear-positive cases, and the incidence rate of smear-positive cases is twice as high as the death rate from tuberculosis.

We have recently analyzed the relationships between the annual tuberculosis infection rates and mortality and mobidity rates in the Netherlands. The data refer to the infection rates published in TSRU report no.1 (TSRU, 1969, Table 5), to the official mortality rates for the period 1921-1938 (Table 1A), and to the morbidity rates for the period 1951-1968 (Table 1B).

In order to obtain estimates for the "contagious" parameter concerning prevalence (and not mortality, or incidence), estimates related to mortality rates (column 3, Table 1A) were divided by 4, as the prevalence of smear-positive cases was assumed to be four times as high as mortality from tuberculosis; and estimates related to the incidence (column 3, Table 1B) were divided by 2, as the prevalence of smear-positive cases was assumed to be twice as high as the incidence of smear-positive cases. The estimates derived from both mortality (Table 1A) and morbidity (Table 1B) indicate that, on average, about 14 persons were infected with tuberculosis during one year by one source of infection in the Dutch community in the periods 1921-1938 and 1951-1968.

The "contagious" parameter may depend, to some extent, on various socio-economic conditions; one should therefore attempt to obtain values for different populations. Sutherland and Fayers calculated annual tuberculosis infection rates for Lesotho and Uganda (TSRU report no.3, in press); their rates can be related to the estimates of smear-positive tuberculosis cases aged 10 years and over from the original WHO surveys

carried out in the late 1950s. The "contagious" parameter for these two countries is about 10, as there was a prevalence of about 100 smear-positive cases per 100,000 population for each one per cent of infection.

II. Development of tuberculosis following infection

It is evident that the risk resulting from tuberculous infection is greater for persons not yet infected than for those who have been already infected with virulent tubercle bacilli. The disease following primary infection is usually called "primary" tuberculosis. The disease which occurs in those previously infected with virulent tubercle bacilli should be called "secondary" tuberculosis. For the purpose of epidemiological studies, it is necessary to adopt a precise (working) distinction between "primary" and "secondary" pulmonary tuberculosis. Dr Holm suggested the following definitions:

A. Any pulmonary tuberculosis developing (and being diagnosed) during the first five years following primary infection is classified as "primary" tuberculosis.

B. Any pulmonary tuberculosis diagnosed more than five years after primary infection is classified as "secondary" tuberculosis.

A. Primary tuberculosis

If the risk of tuberculous infection is high, as it was in developed countries before World War II and still is in many developing countries at present, primary tuberculosis occurs mostly among children. If the risk of infection is low, primary tuberculosis occurs (at a low rate), in addition, among young persons.

Extensive information on the bacteriological status in children suffering from primary tuberculosis is available in many developed countries where BCG vaccination has not been practised. All the statistics show that few children with primary tuberculosis develop bacillary tuberculosis (in Norway 2.6%; in Denmark 4.9%; in the Netherlands 0.9% - based on reported cases during the period 1951-1968); and very few children develop smear-positive tuberculosis which is considered to be the most important source of infection.

However, much less is known about the development of the disease, and especially its bacteriological status, if the primary infection occurs during the adolescence or adult age.

Extensive information on this subject is available from the MRC Vaccines Trial in which 13,000 children aged 14 3/4 years, chosen at random, were left unvaccinated, and were followed by means of tuberculin tests and x-rays of the chest for a period of about 10 years. Out of 1261 persons with indurations 10 mm or more, 7.5% developed clinical tuberculosis during the 10 years following primary infection. Unfortunately, there is no complete information on bacteriological status in persons who developed clinical tuberculosis.

We have studied this problem among the general population of the province of Saskatchewan (Canada), where extensive tuberculin and MMR surveys of the entire population have been carried out since 1955. During the period 1960-1973, a total of 529 smear-positive cases of pulmonary tuberculosis were reported in the Province (just below 1 million inhabitants). Seven cases occurred among children aged 0-14 years, 113 cases among those aged 15-29 years and the remaining 409 patients were older than 20 years at the time of the diagnosis of their disease. About one-third of smear-positive pulmonary tuberculosis in the age-group 15-29 years originated from the "previously tuberculin-negative" group. If all cases (smear-positive and smear-negative) from the latter group aged 15-29 years are considered (97 cases), smear-positive pulmonary tuberculosis form nearly 25% of all primary tuberculosis cases.

In my opinion, "primary" tuberculosis has a limited impact on the transmission of tuberculous infection: (a) Sources of infection among children are infrequent both in low and high prevalence countries; (b) sources of infection following primary infection acquired during the adolescence or adult age are relatively frequent if the risk of tuberculous infection is low (about 25% of all cases in the age-group 15-29 years) but their contribution to all smear-positive cases discovered in the entire adult population is numerically small; (c) sources of infection among middle-aged, elderly and old people are uncommon both in low and high prevalence countries.

B. Secondary tuberculosis

As we are unable to detect superinfection by means of tuberculin testing among those who have been previously infected with virulent tubercle bacilli, we cannot directly discover whether or not exogenous superinfection is important in the development of secondary tuberculosis.

The problem of the endogenous or exogenous origin of secondary tuberculosis has long been at the centre of the arguments about phtisiogenesis, and opposing opinions have been put forward on this subject.

The proponents of the endogenous theory maintain that the tubercle bacilli resulting from primary infection can remain alive within their human host for his life-time, and that they can at any time, for reasons mostly unknown, start multiplying and produce such pathology in the lungs that a discharge of tubercle bacilli through the respiratory tract will result. They also maintain that such endogenous flare-up of an old infection is the most common cause of secondary pulmonary tuberculosis, or in other words, that exogenous infection (inhalation of tubercle bacilli by already infected persons) plays an unimportant role. The basis for this theory must be that primary tuberculosis infection induces a high degree of immunity and that this protection lasts for a very long period and usually for life.

The proponents of the exogenous theory maintain that exogenous re-infection plays an important role in the development of secondary pulmonary tuberculosis. In other words, the inhalation of tubercle bacilli by persons who had a tuberculosis infection more than five years ago represents a considerable risk of development of pulmonary tuberculosis relatively shortly after this re-infection.

The controversy between the two theories is not only interesting from the academic point of view but is of vital importance in the planning of rational tuberculosis control programmes in high prevalence countries. If the unitary concept of tuberculosis in man is the answer to the problem, efforts should be primarily directed towards the prevention of primary infection. If exogenous infection in high prevalence countries often leads to secondary tuberculosis, the programme should be primarily

focused on the decrease in sources of infection.

The TSRU has been dealing with this problem for a number of years. Sutherland and Svandova presented their mathematical model (limited to the age-group 40-59 years) to the International Tuberculosis Conference in Moscow in 1971. Two years later, the proponents of the endogenous theory had an opportunity to explain their arguments at the International Tuberculosis Conference in Tokyo. A more comprehensive model of the TSRU covering a larger proportion of the population than that referred to in Moscow will be presented, by the same authors, at the coming Conference in Mexico. Reference is made to the first two series of the reports published in the Proceedings of the Conference in Moscow and Tokyo.

At this occasion, I would like to refer to two observations showing the impact of the high levels of tuberculosis infection rates on the magnitude of the tuberculosis problem in the respective populations, and the close relationship between these two variables.

The first observation concerns Eskimo in Alaska, Greenland and North-west Territories of Canada. The annual incidence rates of tuberculosis among the native population were extremely high in all three circumpolar areas in the early 1950s, in the order of 2.5% of new (mostly bacteriologically confirmed) cases of tuberculosis each year (Fig.2). The annual tuberculosis infection rate in Alaska estimated by Comstock and Philip was, at that time, as high as 25% (!) In 20 years tuberculosis incidence rates decreased dramatically, in Greenland from about 2500 per 100,000 in 1950-1954 to about 60 per 100,000 in the early 1970s, and in Alaska from a similar rate in the early 1950s to less than 200 in 1967, or by more than 90% in about 15 years.

Naturally, decrease in the tuberculosis problem can also be seen in mortality rates (Fig.3). They fell from about 750 per 100,000 in 1950 to less than 5 per 100,000 during the last few years - a reduction of some 40% each year.

The dramatic decreases in mortality and morbidity rates have been preceded, naturally, by a sharp decrease in the tuberculous infection rates. Whereas more than

95% of Eskimo children were reported to have been infected with tubercle bacilli at the age of 6-7 years in 1950, the tuberculin surveys from 1970 discovered practically no infections at that age (Fig.4).

The further two graphs (Fig.5 and 6) illustrate the decreases in the incidence rates not only among children and young adults but at all ages, i.e. also in persons previously infected. Thus the same number of infected subjects aged say 35 years or more in the N.W.T. of Canada produced 0.9% bacillary cases each year during 1967-1969, whereas the incidence was "only" 0.3% each year in 1973-1975 (Fig.5). In Greenland, the rates in the same age-group fell from nearly 3.0% in 1955-1957 to less than 1.0% in 1963-1965 (Fig.6).

The second observation refers to the relationship between tuberculosis infection rates, and mortality and morbidity rates. The data for the Netherlands have been already presented in Tables 1A and 1B; this time, we shall study the above-mentioned relationship. The results are presented below:

a. Relationship between the mortality from tuberculosis (all forms) and the tuberculosis infection rates, The Netherlands, 1921-1938

Year	Death rate from tuberculosis (per 100,000)	Risk of tuberculous infection (%)	Ratio of death to risk x)
1922	115.1	6.02	19
1925	100.3	5.13	20
1928	87.9	4.37	20
1931	70.5	3.72	19
1934	55.5	3.16	18
1937	47.7	2.69	18
1921-1938	-	-	19

b. Relationship between the incidence of smear-positive tuberculosis and the risk of tuberculous infection, The Netherlands, 1951-1968

Year	Incidence rate of smear-posit. tuberculosis (per 100,000)	Risk of tuberculous infection (%)	Ratio of incidence to risk x)
1952	13.9	0.400	35
1955	7.8	0.265	29
1958	5.7	0.176	32
1961	4.6	0.116	40
1964	3.2	0.077	42
1967	2.4	0.051	47
1951-1968	-	-	38

x) Expressed as mortality from tuberculosis and incidence of smear-positive cases respectively per 100,000 general population for each 1 per cent of the tuberculosis infection rate.

The above table under a. shows the relationship between the estimated risk of tuberculosis infection for the years 1921-1938, and observed death rates from tuberculosis. Assuming no effective chemotherapy, death rates correspond, as already mentioned, to one-half of the incidence rates of smear-positive cases of tuberculosis. The same table shows that in the Netherlands the ratio between the estimated risk of tuberculous infection and observed death rates during the period under study, was 1% risk of infection for 19 deaths from tuberculosis per 100,000 general population.

The above table under b. shows the relationship between the estimated risk of tuberculous infection for the years 1951-1968, and observed incidence rates of smear-positive cases of pulmonary tuberculosis during the same period. The ratio for the whole period is 1% risk of infection for 38 smear-positive cases per 100,000 general population.

The relationship between the incidence of smear-positive tuberculosis and the risk of tuberculous infection has also been studied for Lesotho and Uganda. For these countries there are estimates of the prevalence of smear-positive tuberculosis at ages 10 years and over (and for Uganda an estimate of all bacillary tuberculosis)

in the late 1950s from the original WHO surveys, and these may be compared with estimated risk of infection in the same year derived from tuberculin surveys made at the same time and later (calculated from the figures given by Sutherland and Fayers, TSRU report no.3, in press); see Appendix IV.

Considering smear-positive tuberculosis only, the ratios of prevalence to risk agree closely in the two countries (Appendix IV); the all-ages prevalence of smear-positive tuberculosis per 100,000 population is about 100 for every 1 per cent in the risk of infection in the same calender year. Assuming that the prevalence of smear-positive cases in a general population is twice the incidence of smear-positive cases, the incidence may be taken as 50 cases per 100,000 general population for each 1% in the risk of infection.

In my opinion, there is reliable evidence that exogenous superinfection plays a predominant role in the pathogenesis of pulmonary tuberculosis in the adults, if the risk of tuberculous infection is high. And there is ample evidence that the risk of tuberculous infection is high, at present, in most developing countries.

(Note: For the evidence that exogenous superinfection is important in the development of secondary tuberculosis based on various anatomical and bacteriological studies see Dr Canetti's report "Endogenous reactivation and exogenous reinfection. Their relative importance with regard to the development of non-primary tuberculosis" read at the International Tuberculosis Conference in Moscow; Bull.int.Un.Tub., 1972, 47, 116.)

III. From development of smear-positive tuberculosis to recovery or death

I know of two sources of information concerning this problem. The first refers to extensive Holm's studies based on the Danish material for the period between the two World Wars (Fig.7). His estimates of recovery and death from smear-positive tuberculosis, assuming no interference by effective treatment (the upper part of Fig.7), are compared with those where interference by chemotherapy did occur (the lower part of Fig.7). This material is taken from Dr Holm's contributions to various meetings

of the TSRU.

The upper part of Fig.7 indicates what the situation will be for one hundred persons, diagnosed as smear-positive pulmonary tuberculosis at a year "0", and followed yearly for 8 years without interference by effective treatment. After 8 years half of them will have died from their disease and the other half will have recovered in the sense that they have stopped discharging tubercle bacilli. After two years about half of those who are to die, will have died, and half of those who are to recover, will have recovered. The dotted area represents the prevalence of known sources of infection, and it has been found that this area is about double the area corresponding to one year. The area to the left of year "0" respresents the undiagnosed sources of infection; it consists mainly of sources of infection before they are diagnosed. If this area corresponds to the area of one year, one-third of the real prevalance of sources of infection is represented by undiagnosed cases.

The lower part of Fig.7 indicates theoretically what may be obtained by adequate chemotherapy given immediately after diagnosis to all the 100 persons with smear-positive tuberculosis. The sputum can be converted in about 95% of all of them within a short time, and with very little chance of relapse. The 5% treated but not converted will live longer than if they were not treated, and act as sources of infection, but a certain proportion of them will recover spontaneously as if no treatment had been given. The prevalence of smear-positive cases after diagnosis may be cut down to less than 1/4 but, by the treatment, we have of course not influenced the prevalence of undiagnosed cases. The end result of such an almost ideal treatment measure would be that we would cut the total prevalence of sources of infection to about half of what it would be without interference with treatment. With such a treatment measure we would expect to cut the annual infection rate to half of what it would be without treatment. It should, however, be noted that even with a 100% effective treatment giving immediate sputum conversion, we could by treatment only cut down the prevalence of sources of infection to one-third.

The second source of information from the late 1970s is the longitudinal study which was carried out by the Indian Health Authorities in co-operation with WHO in Bangalore. We are eager to study the results of this extremely important experience, after its publication.

Table 1A

RELATIONSHIP BETWEEN THE ANNUAL TUBERCULOSIS INFECTION RATES AND THE MORTALITY FROM TUBERCULOSIS (all forms)

The Netherlands, 1921-1938

Year	The annual tuberculosis infection rate (%) (1)	Death rate from TB (all forms) per 100,000 x) (2)	$\frac{(1)}{(2)}$ x 1000 (3)	$\frac{(3)}{4}$ xx)
1922	6.02	115.1	52.3	13.1
1925	5.13	100.3	51.1	12.8
1928	4.37	87.9	49.7	12.4
1931	3.72	70.5	52.8	13.2
1934	3.16	55.5	56.9	14.2
1937	2.69	47.7	56.4	14.1
1921-1938	--	--	53.2	13.3

x) Averages for 1921-1923, 1924-1926, ... 1936-1938

xx) Ratio Mortality: Prevalence = 1 : 4 (see text)

Table 1B

RELATIONSHIP BETWEEN THE ANNUAL TUBERCULOSIS INFECTION RATES AND THE INCIDENCE OF SMEAR-POSITIVE TUBERCULOSIS

The Netherlands, 1951-1968

Year	The annual tuberculosis infection rate (%) (1)	Incidence rate of smear-positive tuberculosis (per 100,000 x) (2)	$\frac{(1)}{(2)}$ x 1000 (3)	$\frac{(3)}{2}$ xx)
1952	0.400	13.9	28.8	14.4
1955	0.265	7.8	34.0	17.0
1958	0.176	5.7	30.9	15.4
1961	0.116	4.6	25.2	12.6
1964	0.077	3.2	24.1	12.0
1967	0.051	2.4	21.2	10.6
1951-1968	--	--	27.4	13.7

x) Averages for 1951-1953, 1954-1956, ... 1966-1968

xx) Ratio Incidence: Prevalence = 1 : 2 (see text)

Figure 1

PERCENTAGE OF POSITIVE REACTORS AMONG CONTACTS AGED 0-14 YEARS, Rotterdam, 1967-69

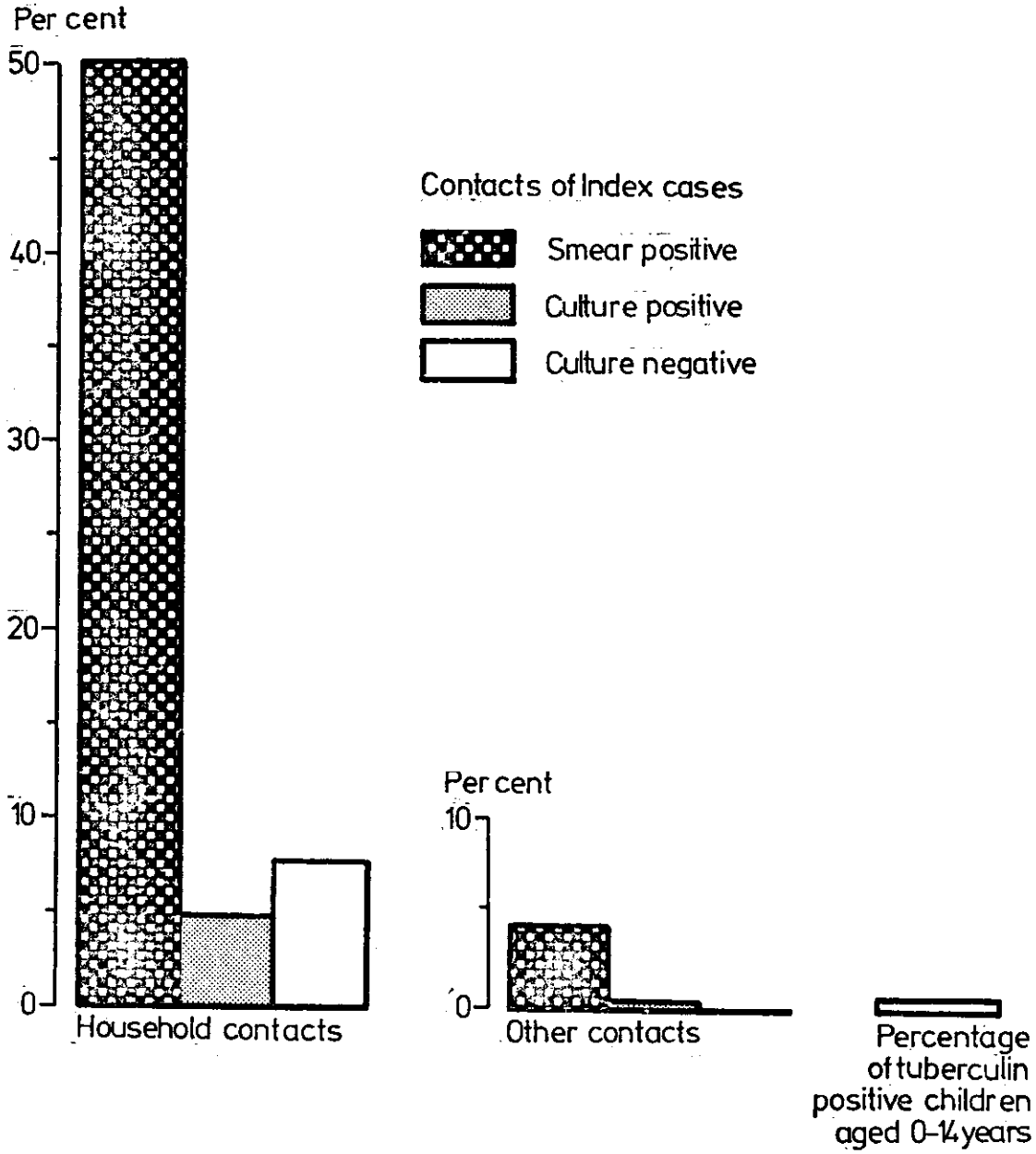

FIG. 2

TUBERCULOSIS INCIDENCE RATES IN GREENLAND, ALASKA, NWT OF CANADA, AND CANADA AS A WHOLE (NATIVE POPULATION), 1950-1972

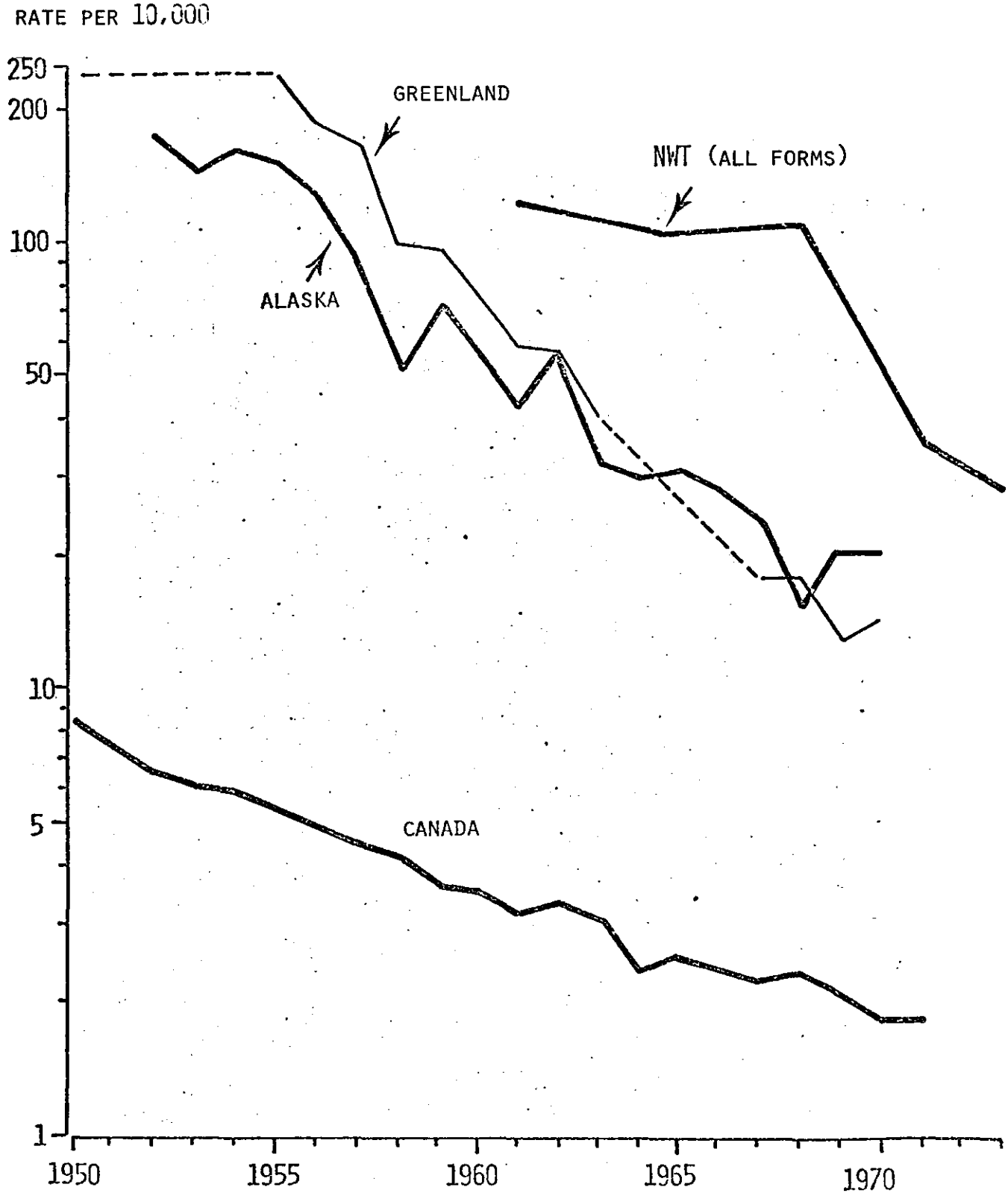

FIG. 3

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Figure 3

TUBERCULOSIS DEATH RATES IN THE NATIVES OF ARCTIC
1950 - 1972

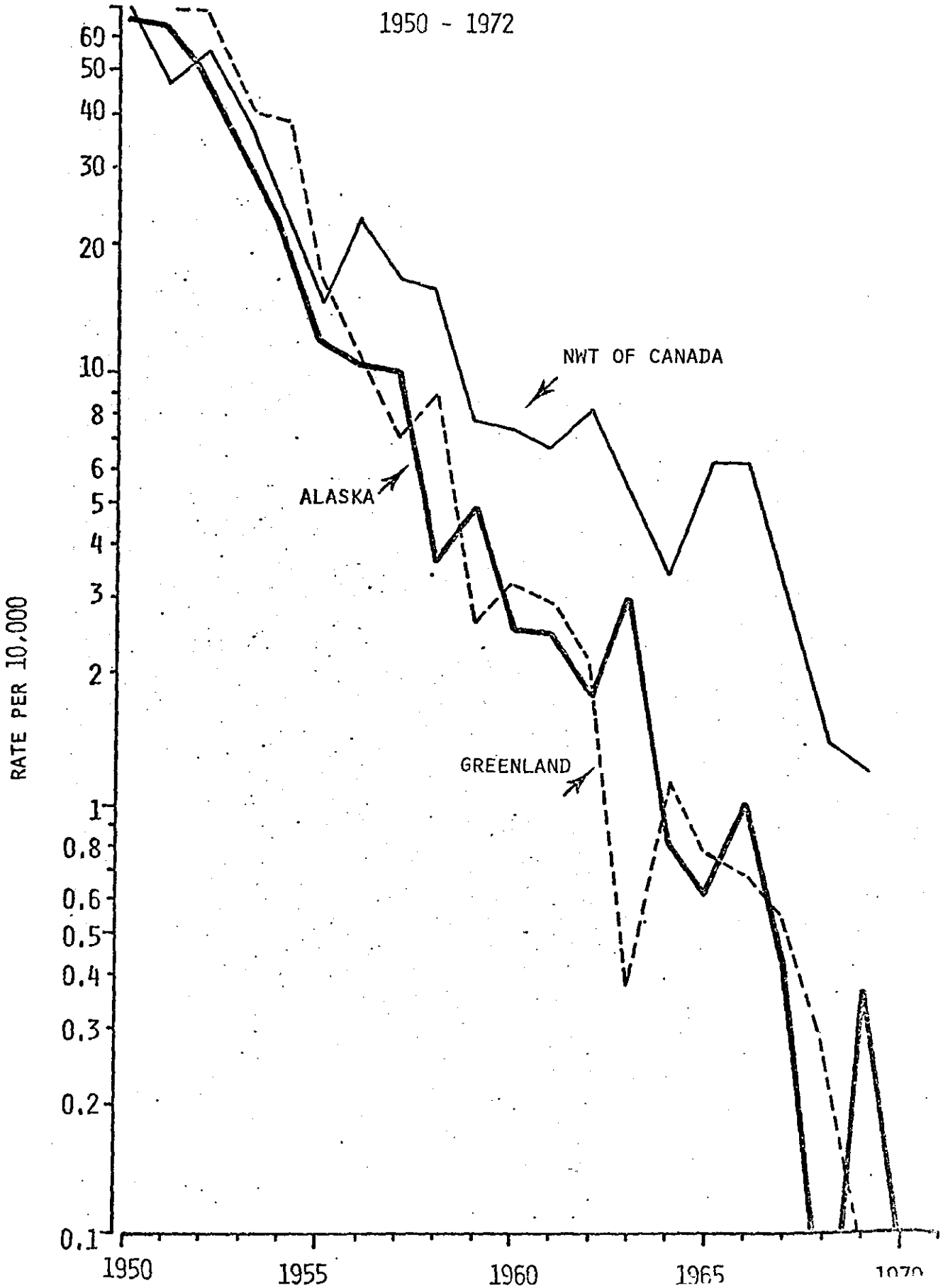


FIGURE 4

PREVALENCE OF TUBERCULIN SENSITIVITY AMONG ESKIMO CHILDREN TESTED IN FIVE SUCCESSIVE SURVEYS, BY AGE

YUKON, KUSKOKWIM DELTA, ALASKA

1949-51 TO 1969-70

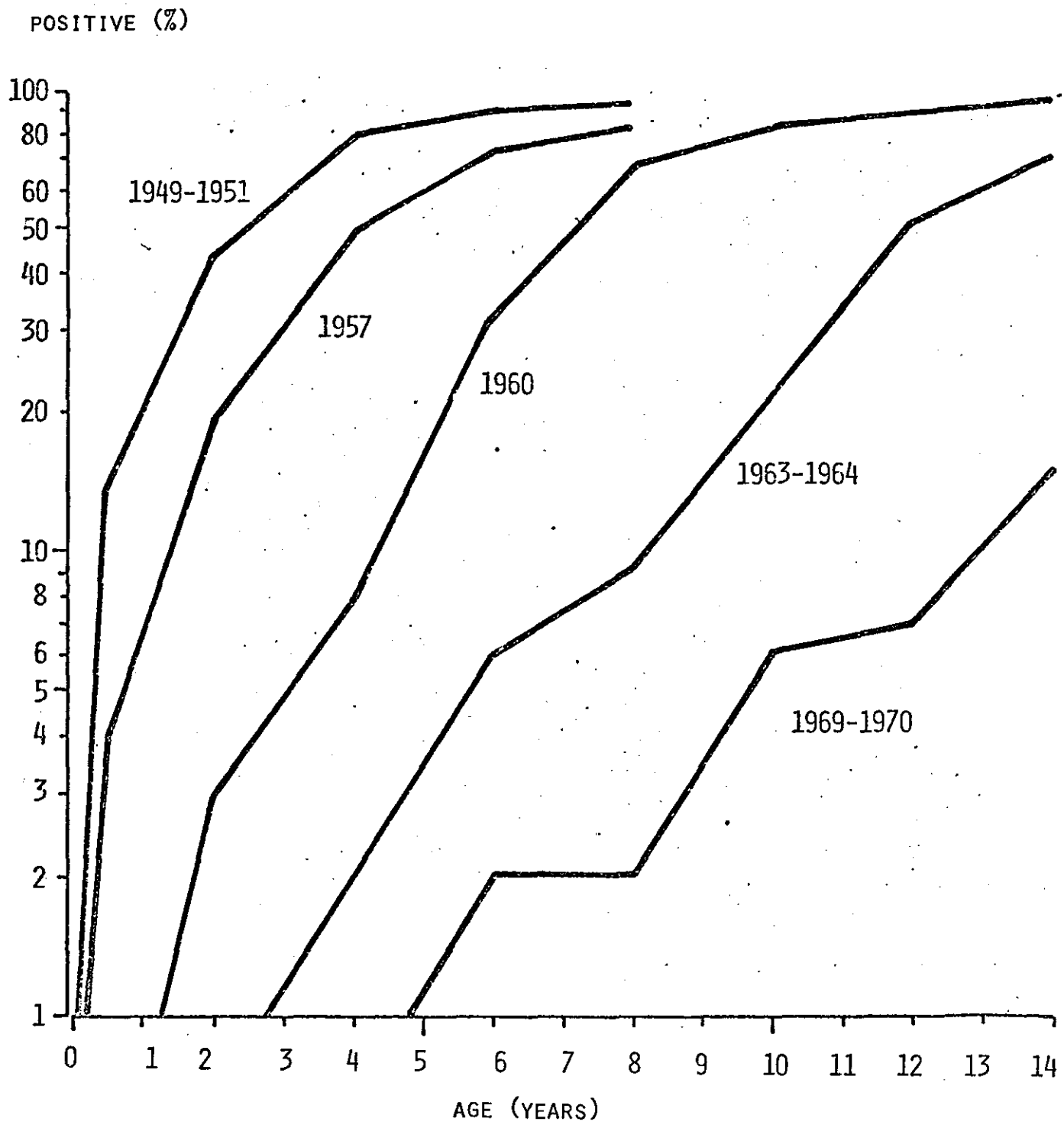


Figure 5

THE AVERAGE ANNUAL RATES (per 10,000) BY SEX AND AGE, N.W.T.

1967-1969, 1970-1972 and 1973-1974

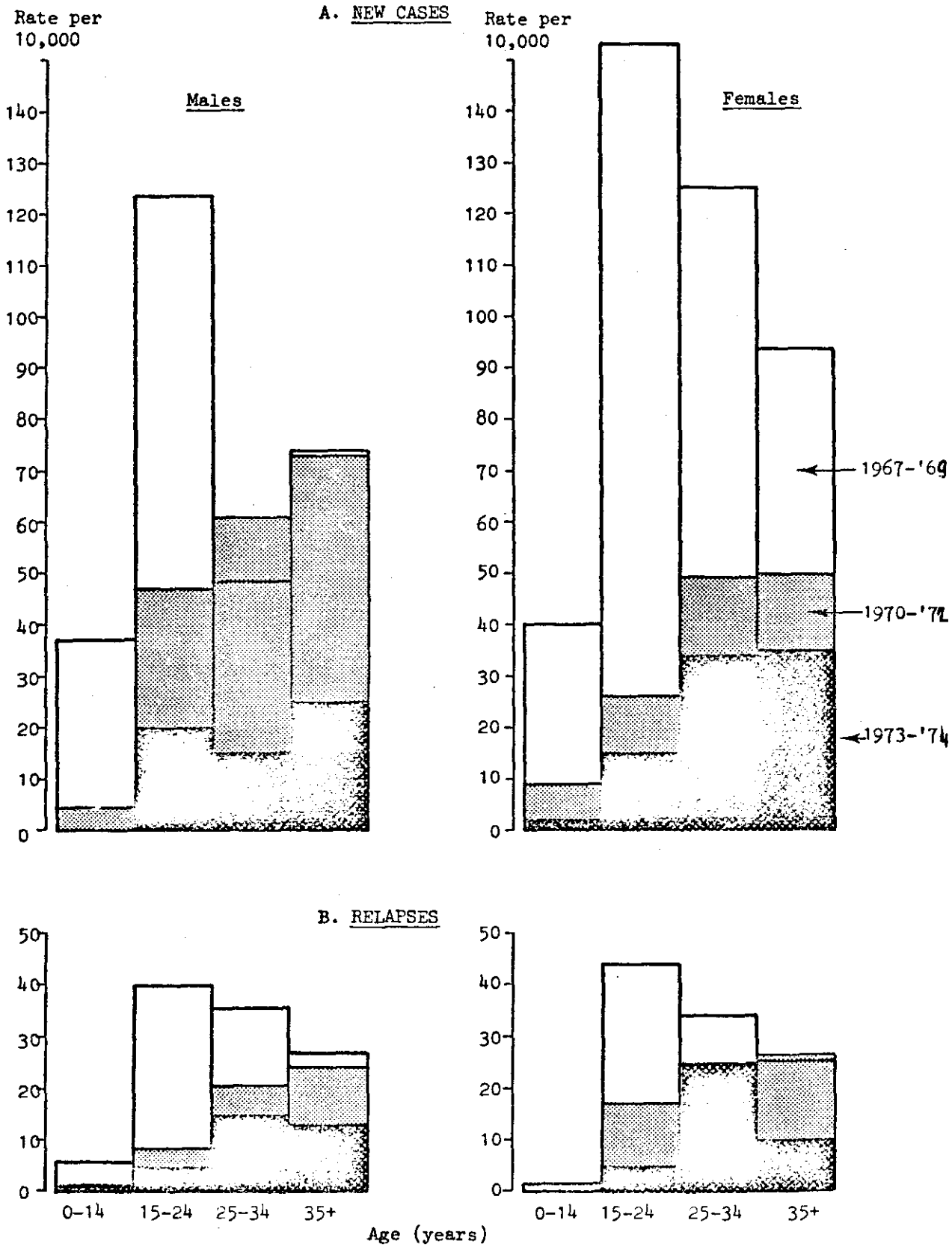
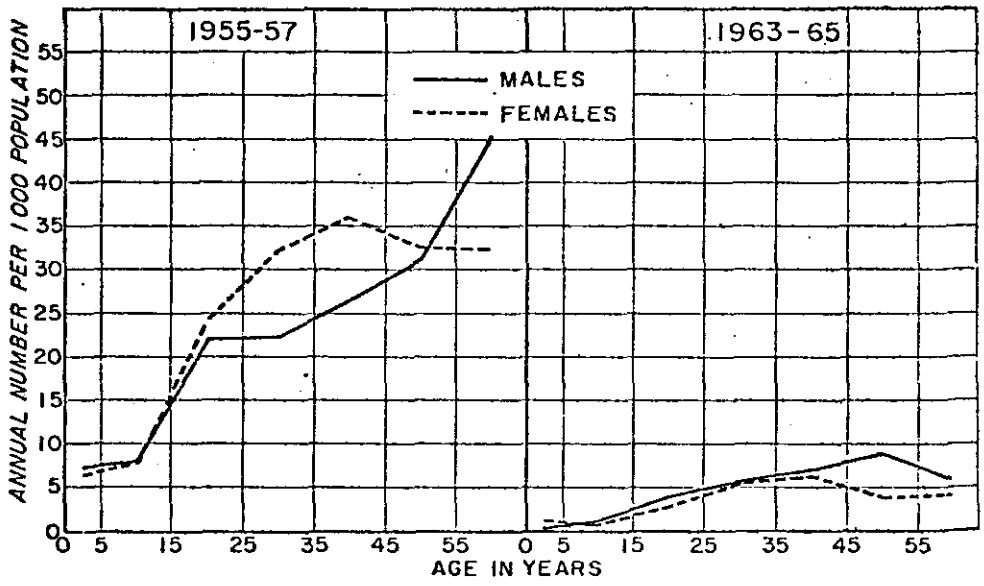


Figure 6

INCIDENCE OF RESPIRATORY TUBERCULOSIS BY SEX AND AGE

Greenland, 1955-1957 and 1963-1965

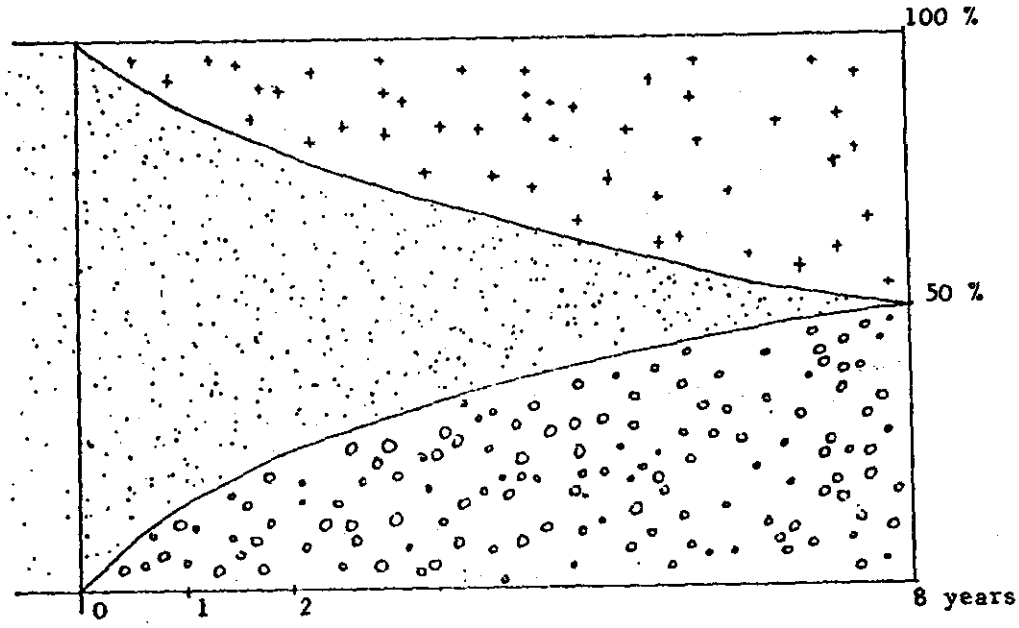


Stein et al., *Arch Environ Health—Vol 17, Oct 1968*

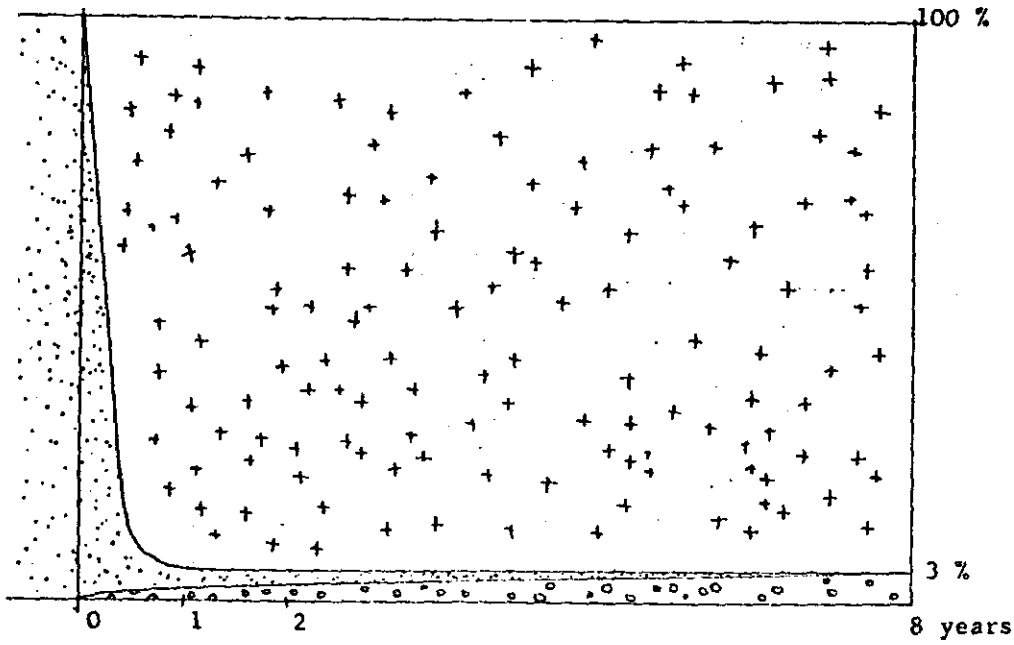
Figure 7

ESTIMATES OF RECOVERY AND DEATH FROM SMEAR-POSITIVE PULMONARY TB

a. assuming no interference by effective treatment



b. assuming interference by effective treatment



Source of information: Dr.Holm, internal report to the TSRU, 1971

Appendix I

HOW TO ESTIMATE THE ANNUAL TUBERCULOSIS INFECTION RATES?

There are:

Two steps in assessing the annual tuberculosis infection rates

a) Estimation of the percentage decrease in the annual risk of infection using Appendix Table C of TSRU report no.1.

Table 1 shows a part of this table. The percentage decrease in the annual tuberculosis infection rates can be estimated if two or more prevalence figures are available for subjects of the same age. If the prevalence of infection in children aged, say 10 years was, for instance 5.5% in 1966, and 2.5% in 1972, entry 80 in the table is divided by 6 years (from 1966 to 1972) to give the approximate annual percentage decrease, which is about 13%. The approximate annual percentage decrease is needed for use in Appendix Table B.

Table 1
DECREASES IN INFECTION RISK CORRESPONDING TO VARIOUS PERCENTAGES INFECTED BY THE SAME AGE AT TWO DIFFERENT SURVEYS (TSRU)

PERCENTAGE ALREADY INFECTED AT THE TIME OF	THE LATER SURVEY													
	0.2	0.4	0.6	0.8	1.0	1.5	2.0	2.5	3.0	3.5	4.0	.....		
0.4	69													
0.6	110	41												
0.8	139	70	29											
1.0	161	92	51	22										
1.5	202	133	92	63	41									
2.0	231	162	121	92	70	29								
2.5	254	184	144	115	92	52	23							
3.0	272	203	162	133	111	70	41	18						
3.5	288	218	178	149	127	86	57	34	16					
4.0	302	232	191	163	140	99	70	48	29	14				
4.5	314	244	203	175	152	111	82	60	41	26	12			
5.0	324	255	214	185	163	122	93	71	52	36	23	11		
5.5	334	265	224	195	173	132	103	80	62	46	33	21	10	
etc.														

THE EARLIER SURVEY

Divide the entry in the table by the interval in years between the surveys to obtain the approximate annual percentage decrease for use in Appendix Table B.

b) Using the estimate of the percentage decrease, Appendix Table B of the same report provides direct assessments of the risk of tuberculous infection in two calendar years, namely the year in which the prevalence of tuberculous infection was determined, and a few years earlier (Table 2). In the above mentioned case one consults Appendix Table B for children aged 10 years, last column (13% annual

decrease in risk of infection each year). The table indicates the following annual tuberculosis infection rates:

1966 : 0.25% (and in 1956 : 0.92%)

1972 : 0.11% (and in 1962 : 0.41%)

Table 2

ANNUAL PERCENTAGE RISKS OF TUBERCULOUS INFECTION CORRESPONDING TO THE PERCENTAGE ALREADY INFECTED BY THE AGE OF 10 YEARS (TSRU)

PERCENTAGE ALREADY INFECTED	APPROXIMATE PERCENTAGE DECREASE IN RISK OF INFECTION EACH YEAR						
	1		3		5....11	13	
	Risk this year	Risk 10 yrs ago	Risk this year	Risk 10 yrs ago	etc.	Risk this year	Risk 10 yrs ago
1.0	0.09	0.10	0.08	0.11	etc.	0.04	0.16
1.5	0.14	0.15	0.12	0.16		0.07	0.25
2.0	0.18	0.20	0.16	0.22		0.09	0.33
2.5	etc.		etc.			0.11	0.41
3.0						0.14	0.50
3.5						0.16	0.58
4.0						0.18	0.67
4.5						0.20	0.75
5.0						0.23	0.84
5.5						0.25	0.92
etc.							

Source of information: Bleiker, M.A.: Epidemiological trends in low prevalence countries, Bull.int.Un.Tub., 49, 128, 1974

Appendix II

Table 5

ACTIVE TUBERCULOSIS AMONG INTIMATE CONTACTS ACCORDING TO BACTERIOLOGICAL STATUS OF SOURCES

British Columbia and Saskatchewan, 1966 - 1971

Table 5A - Whites

Age-group (years)	a. No. of contacts b. No.of active cases c. % with active tb	Bacteriological status of source				% active tuberculosis in general population in 1966-1971
		Smear positive	Culture positive	Culture negative	Total	
0 - 14	a. b. c.	1088 123(36)** 11.3(3.3)	578 10(5) 1.7(0.9)	464 3(-) 0.6(-)	2130 136(41) 6.4(1.9)	883,800* 476(174) 0.009(0.003)
15 - 29	a. b. c.	721 31(13) 4.3(1.8)	394 1(-) 0.3(-)	290 0 -	1405 32(13) 2.3(0.9)	692,400 673(428) 0.016(0.010)
30+	a. b. c.	1276 27(22) 2.1(1.7)	721 2(1) 0.3(0.1)	428 0 -	2425 29(23) 1.2(0.9)	1,397,200 2,752(2030) 0.033(0.024)
Total	a. b. c.	3085 181(71) 5.9(2.3)	1693 13(6) 0.8(0.4)	1182 3(-) 0.3(-)	5960 197(77) 3.3(1.3)	2,973,400 3,901(2632) 0.022(0.015)

*Population figures do not include Registered Indians in Saskatchewan
**Figures in brackets represent bacteriologically confirmed cases

Table 5B - Indians

0 - 14	a. b. c.	707 85(35)* 12.0(5.0)	396 11(6) 2.8(1.5)	192 4(2) 2.1(1.0)	1295 100(43) 7.7(3.3)
15 - 29	a. b. c.	262 13(6) 5.0(2.3)	154 4(3) 2.6(1.9)	57 1(-) 1.8(-)	473 18(9) 3.8(1.9)
30+	a. b. c.	301 6(5) 2.0(1.7)	157 1(1) 0.6(0.6)	67 0 -	525 7(6) 1.3(1.1)
Total	a. b. c.	1270 104(46) 8.2(3.6)	707 16(10) 2.3(1.4)	316 5(2) 1.6(0.6)	2293 125(58) 5.5(2.5)

* Figures in brackets represent bacteriologically confirmed cases

Appendix III
Table 6

ACTIVE TUBERCULOSIS AMONG CASUAL CONTACTS ACCORDING TO BACTERIOLOGICAL STATUS OF SOURCES
British Columbia and Saskatchewan, 1966 - 1971

Table 6A - Whites

Age-group (years)	a. No.of contacts b. No.of active cases c. % with active tb	Bacteriological status of source				% active tuberculosis in general population in 1966-1971
		Smear positive	Culture positive	Culture negative	Total	
0 - 14	a. b. c.	1927 44(12)** 2.3(0.6)	870 4(-) 0.5(-)	424 0 -	3221 48(12) 1.5(0.4)	883,800* 476(174) 0.009(0.003)
15 - 29	a. b. c.	1871 28(18) 1.5(1.0)	607 3(1) 0.5(0.2)	415 0 -	2893 31(19) 1.1(0.7)	692,400 673(428) 0.016(0.010)
30+	a. b. c.	2408 19(13) 0.8(0.5)	1011 7(5) 0.7(0.5)	603 0 -	4022 26(18) 0.6(0.4)	1,397,200 2,752(2030) 0.033(0.024)
Total	a. b. c.	6206 91(43) 1.5(0.7)	2488 14(6) 0.6(0.2)	1442 0 -	10136 105(49) 1.0(0.5)	2,973,400 3,901(2632) 0.022(0.015)

* Population figures do not include Registered Indians in Saskatchewan
**Figures in brackets represent bacteriologically confirmed cases

Table 6B - Indians

0 - 14	a. b. c.	453 35(11)* 7.7(2.4)	239 5(1) 2.1(0.4)	81 0 -	773 40(12) 5.2(1.6)
15 - 29	a. b. c.	197 7(1) 3.6(0.5)	150 0 -	24 0 -	371 7(1) 1.9(0.3)
30+	a. b. c.	224 3(2) 1.3(0.9)	155 0 -	48 0 -	427 3(2) 0.7(0.5)
Total	a. b. c.	874 45(14) 5.1(1.6)	544 5(1) 0.9(0.2)	153 0 -	1571 50(15) 3.2(1.0)

* Figures in brackets represent bacteriologically confirmed cases

Appendix IV

RELATIONSHIP BETWEEN THE PREVALENCE OF SMEAR-POSITIVE TUBERCULOSIS AND THE RISK OF TUBERCULOUS INFECTION

Lesotho (1957) and Uganda (1958)

Country	Year	Bact. positivity	Prevalence (excreting acid-fast bacilli) per 1000 aged 10+ (with 95% Poisson range)	Percent of population aged 10+	Prevalence at all ages per 1000[x]	Estimated risk of infection at age 10 per cent	Ratio of prevalence to risk[xx]
			(a)	(b)	(a) x (b)	(c)	(a)x(b):(c)
Lesotho (Basutoland)	1957	Direct	5 (3-9)	70.8	3.54	3.89	91
Uganda	1958	(Direct ((Direct + (Culture	3.2(1.7-5.5) 7.5(2.5-19.7))	69.3	(2.22) ( ) ( ) (5.20)	2.24	(99 (((232

x Assuming there is no bacteriologically positive tuberculosis under age 10

xx Expressed as a prevalence per 100,000 population for each 1 per cent in the risk of infection.