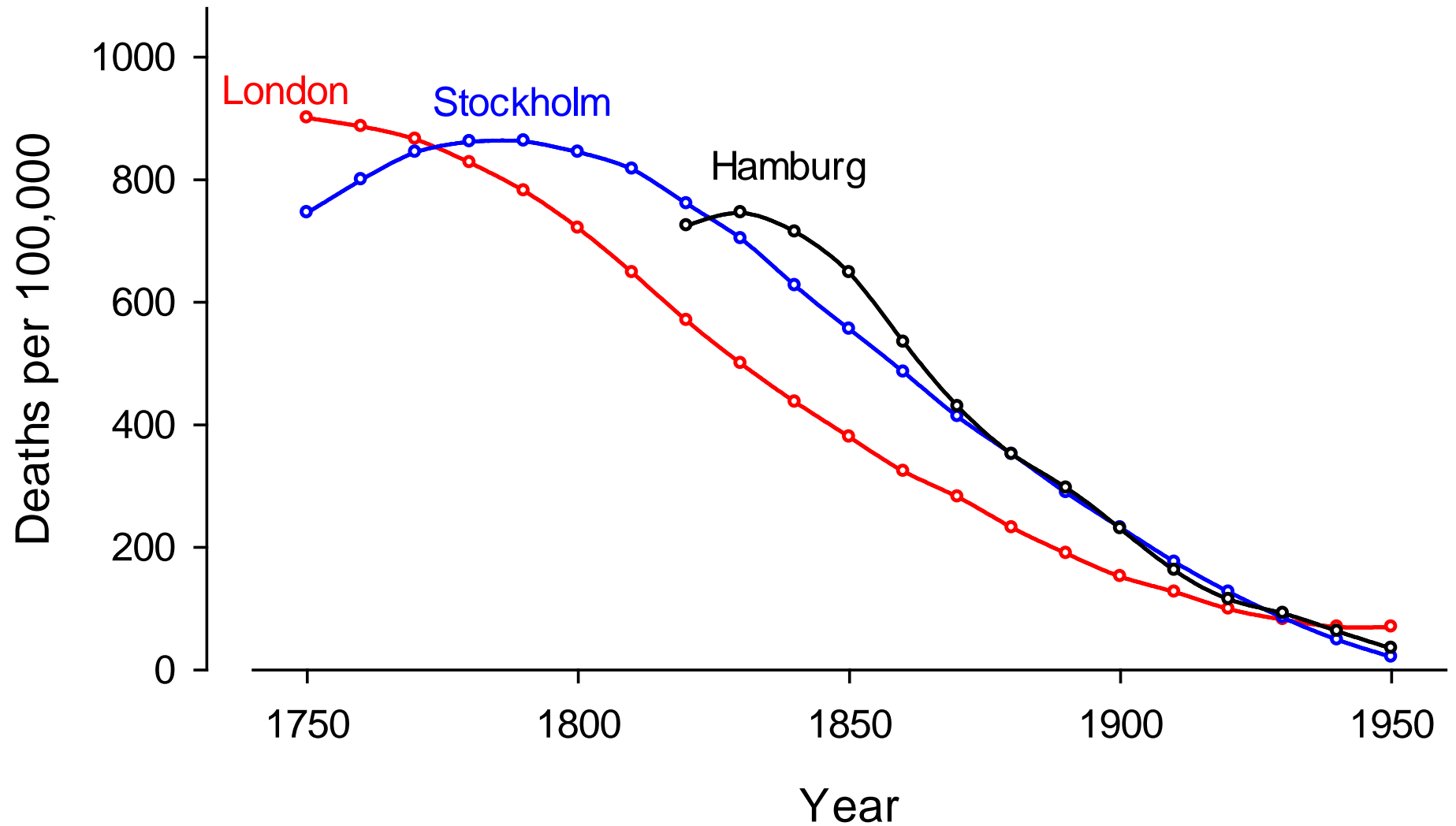


Which factors influence the decrease of TB?

Hans L Rieder

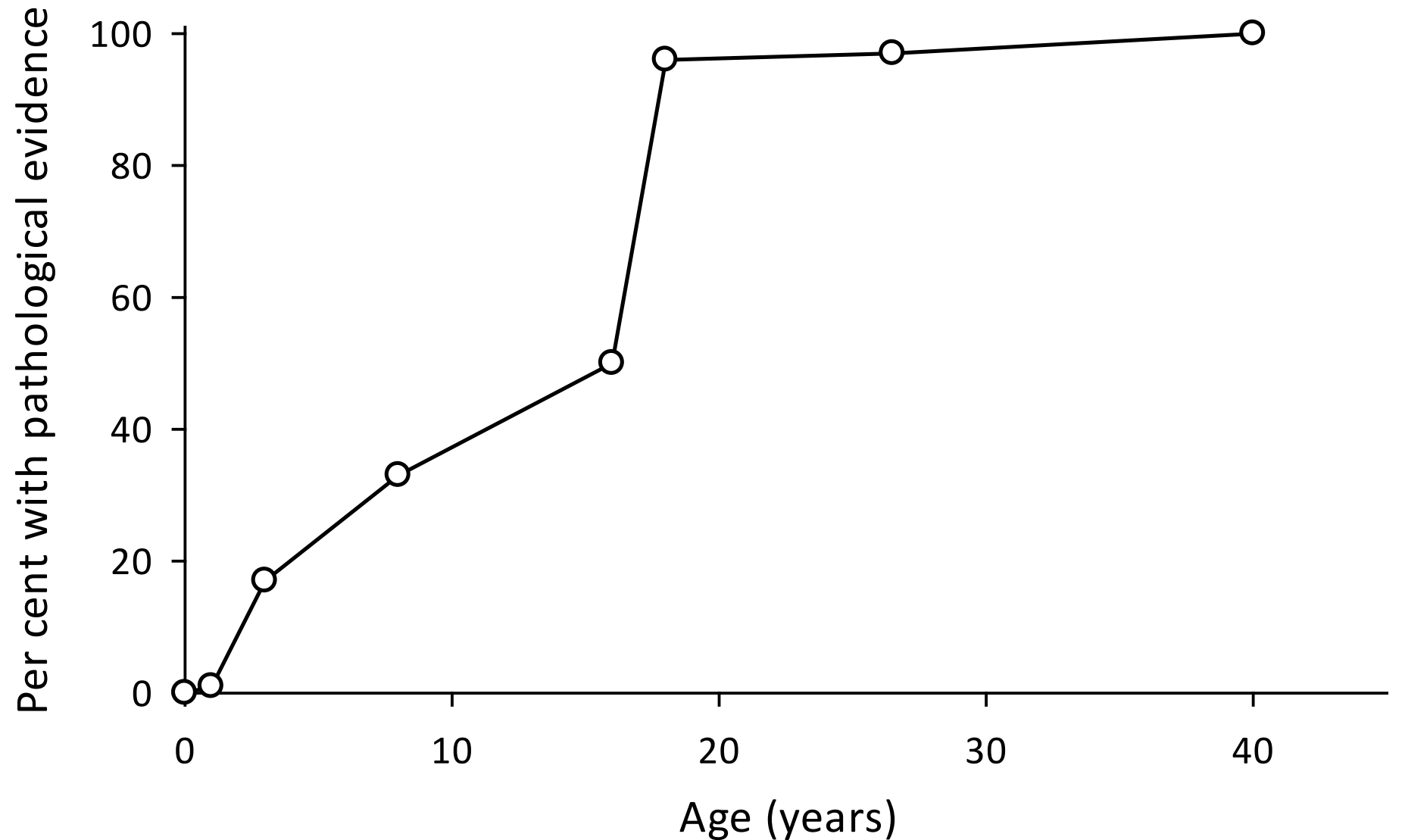
Münchenwiler, 20 March 2014

Tuberculosis Mortality in Three European Cities, Modeled From Available Data, 1750 - 1950



Grigg ERN. Am Rev Tuberc Pulm Dis 1958;78:151-72

Evidence of current or past tuberculosis in an unselected series of 500 autopsies, Zürich, Switzerland, 1895-1900

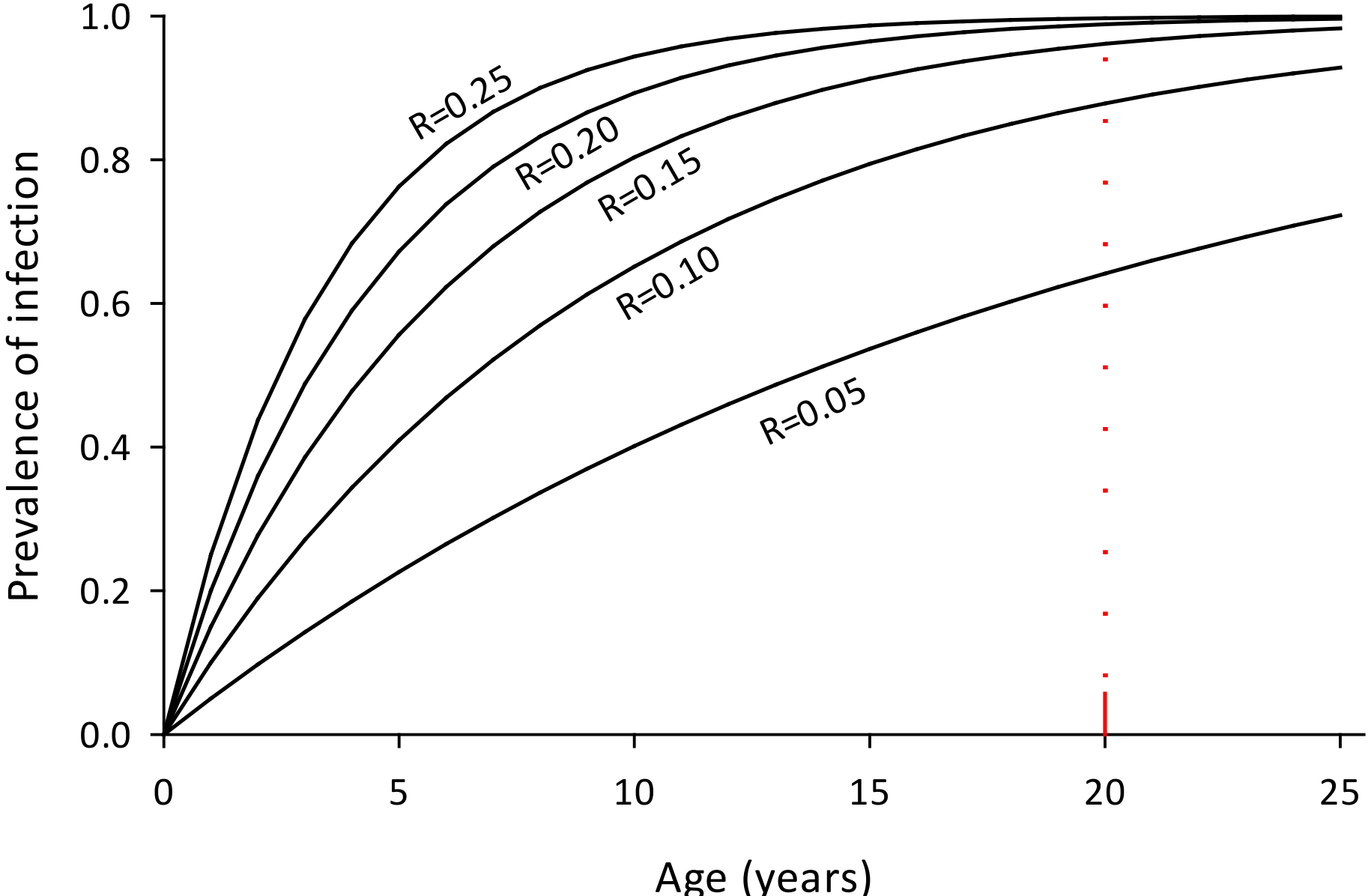


Naegeli O. Virchow's Arch 1900;160:426-72

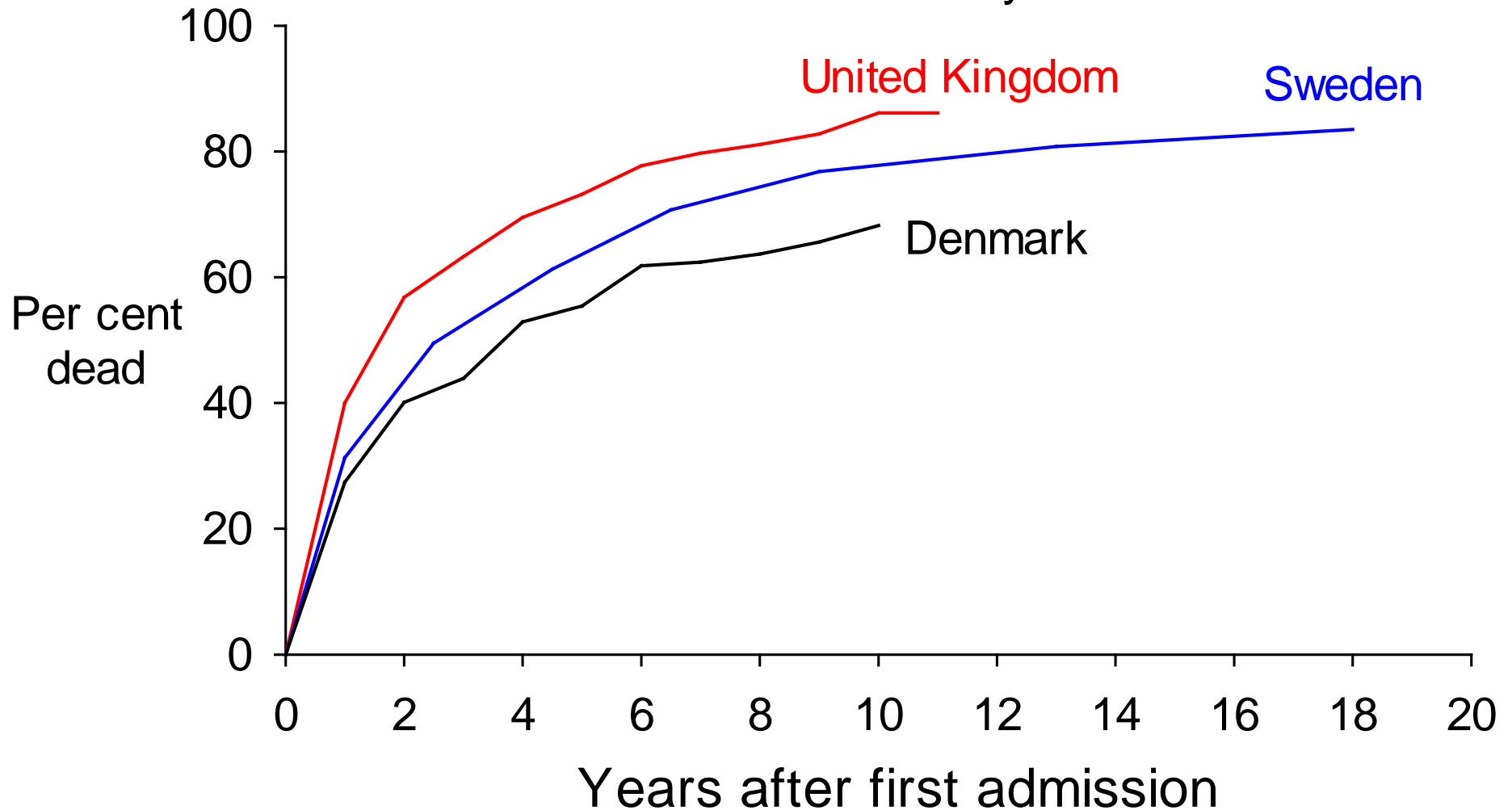
How does one reconcile an antecedent massive decline in tuberculosis mortality and still finding that virtually everybody has histo-pathological evidence of a primary complex by age 20?

Repeat assault, i.e. re-infection diminishing, thus decline possible, but not translating (yet) into lower age-specific prevalence of infection?

Age-specific prevalence of infection with *M tuberculosis*, given varying (secular constant) incidence of infection



Cumulative Case Fatality from Untreated Sputum Smear-Positive Pulmonary Tuberculosis

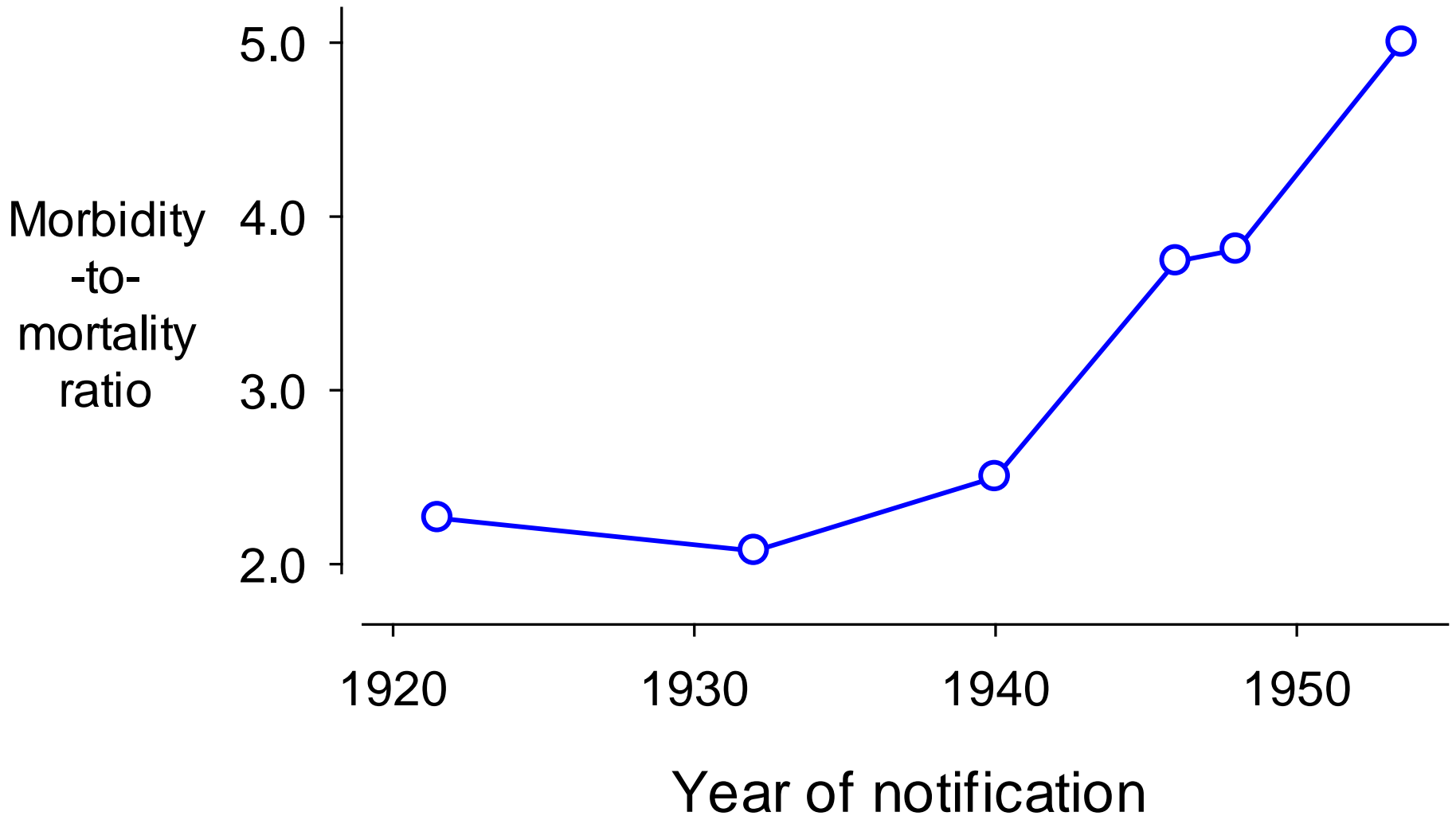


Thompson BC. Br Med J 1943;2:721

Berg G. Acta Tuberc Scand 1939;(suppl):1-207

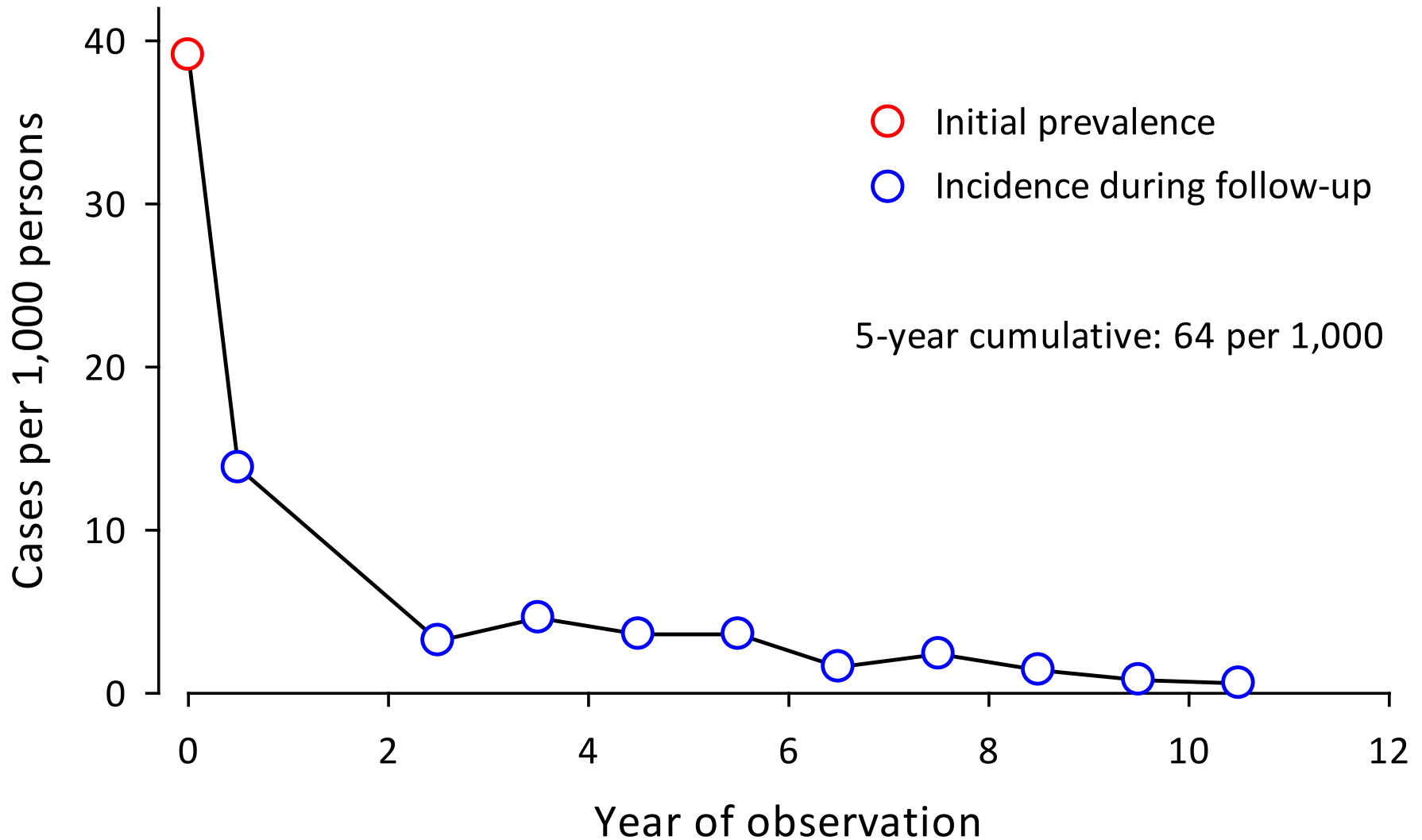
Buhl K, et al. Bull World Health Organ 1967;37:907-25

Ratio of Incident Pulmonary Tuberculosis to Pulmonary Tuberculosis Death, Denmark, 1922-1953



Horwitz O, et al. Dan Med J 1955;2:173-80

Tuberculosis prevalence and incidence among tuberculin reactor household contacts, US Public Health Service, intake 1957-1958



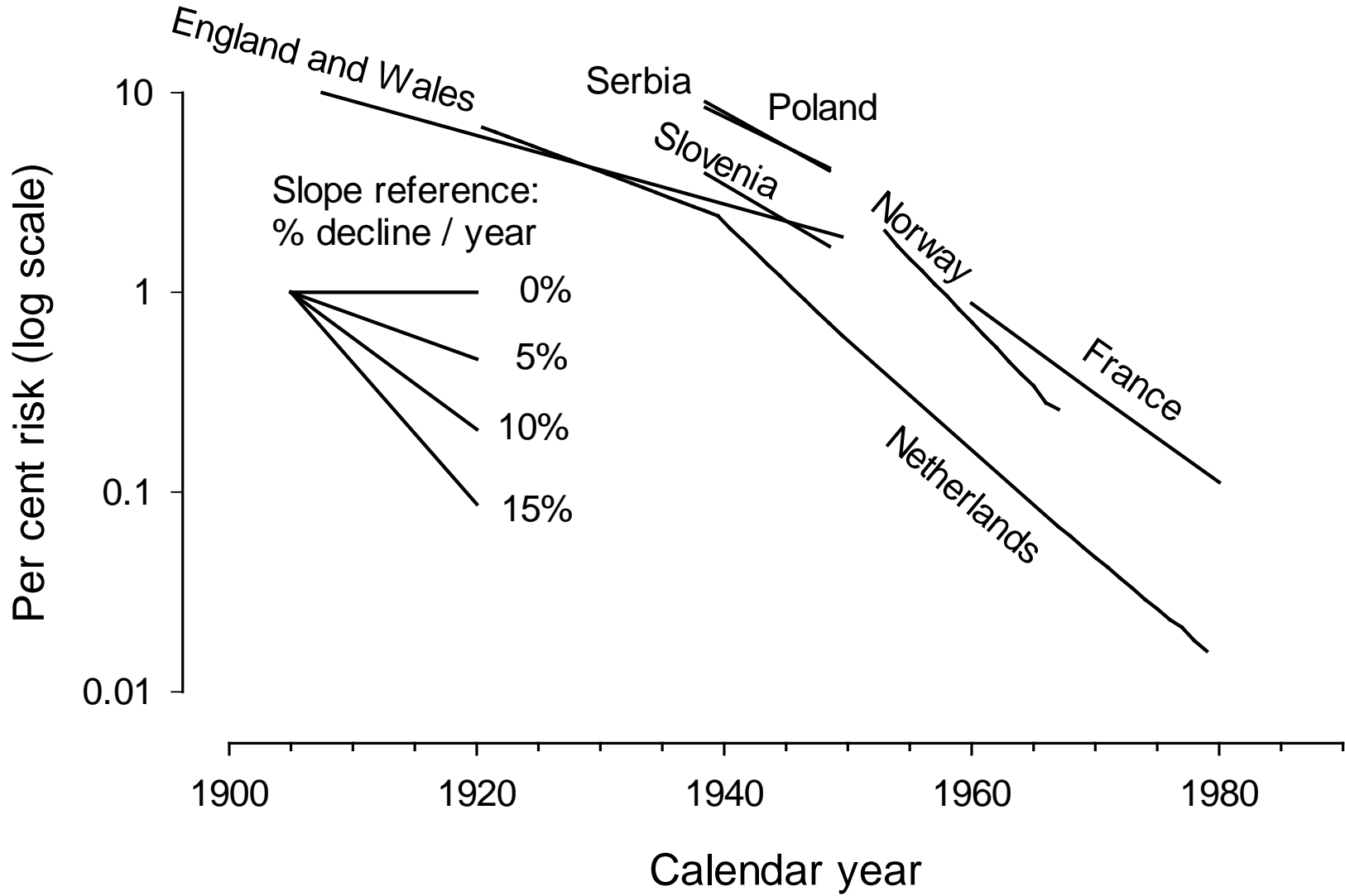
Ferebee S H, Mount F W. Am Rev Respir Dis 1962;85:490-521

Ferebee S H. Adv Tuberc Res 1970;17:28-106

Age structure of Swiss population, 1900-2009



Secular Trend in Annual Risk of Infection, Selected European Countries



Waalder H, et al. *Bull Int Union Tuberc* 1975;50:5-61

Sutherland I, et al. *Bull Int Union Tuberc* 1971;45:75-114

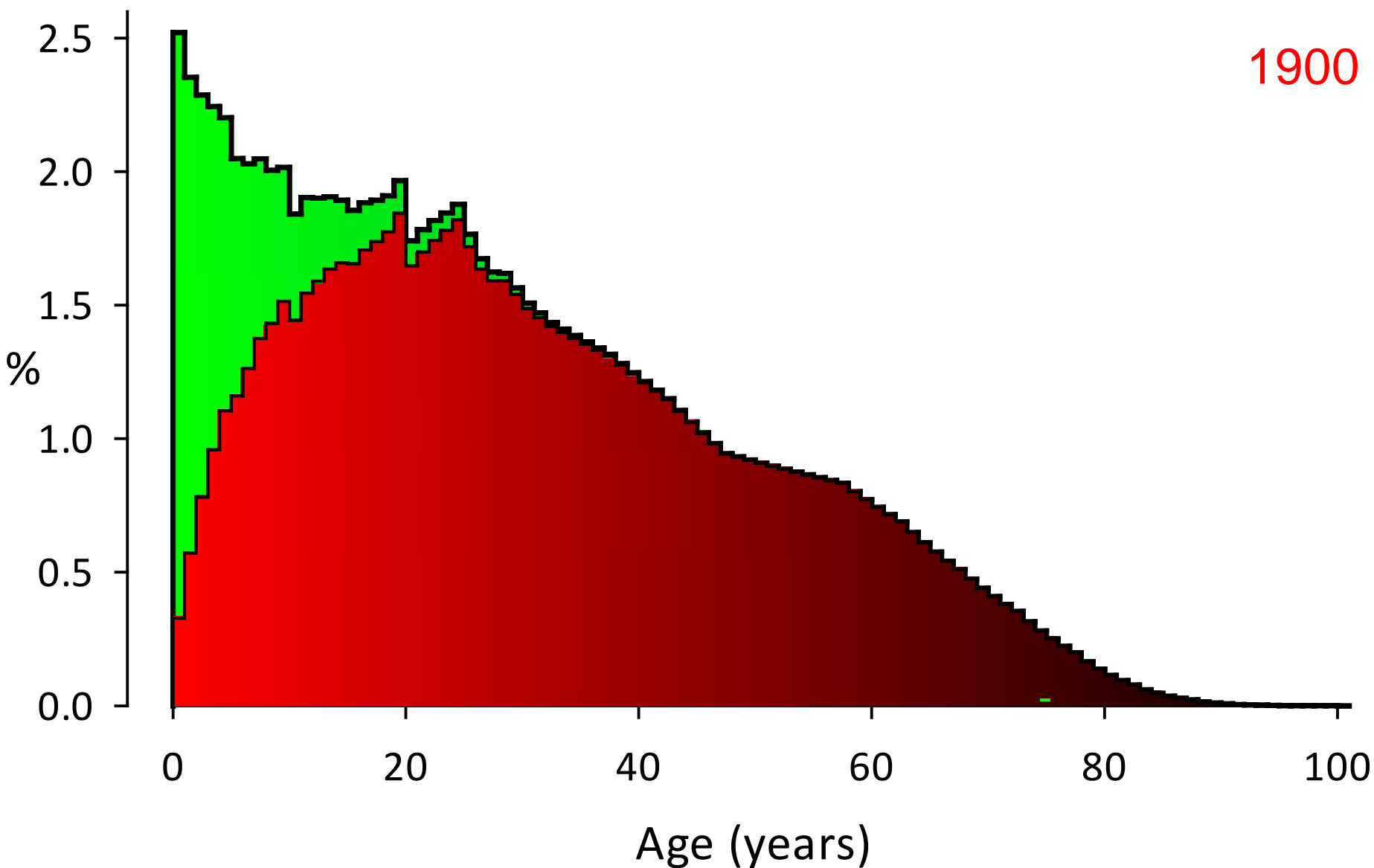
Lotte A, et al. *Int J Epidemiol* 1973;2:265-82

Sutherland I, et al. *Tubercle* 1983;64:241-253

Styblo K, et al. *Bull Int Union Tuberc* 1969;42:5-104

Vynnycky E, et al. *Int J Tuber Lung Dis* 1997;1:389-96

Age-specific tuberculous infection, Switzerland, 1900-2009



An epidemiologic view of and approach to tuberculosis interventions

Reduction of the **incidence** of tuberculous infection

Essence of the **tuberculosis control strategy**: identification and curative chemotherapy for cases transmitting *M. tuberculosis*

Reduction of the **prevalence** of tuberculous infection

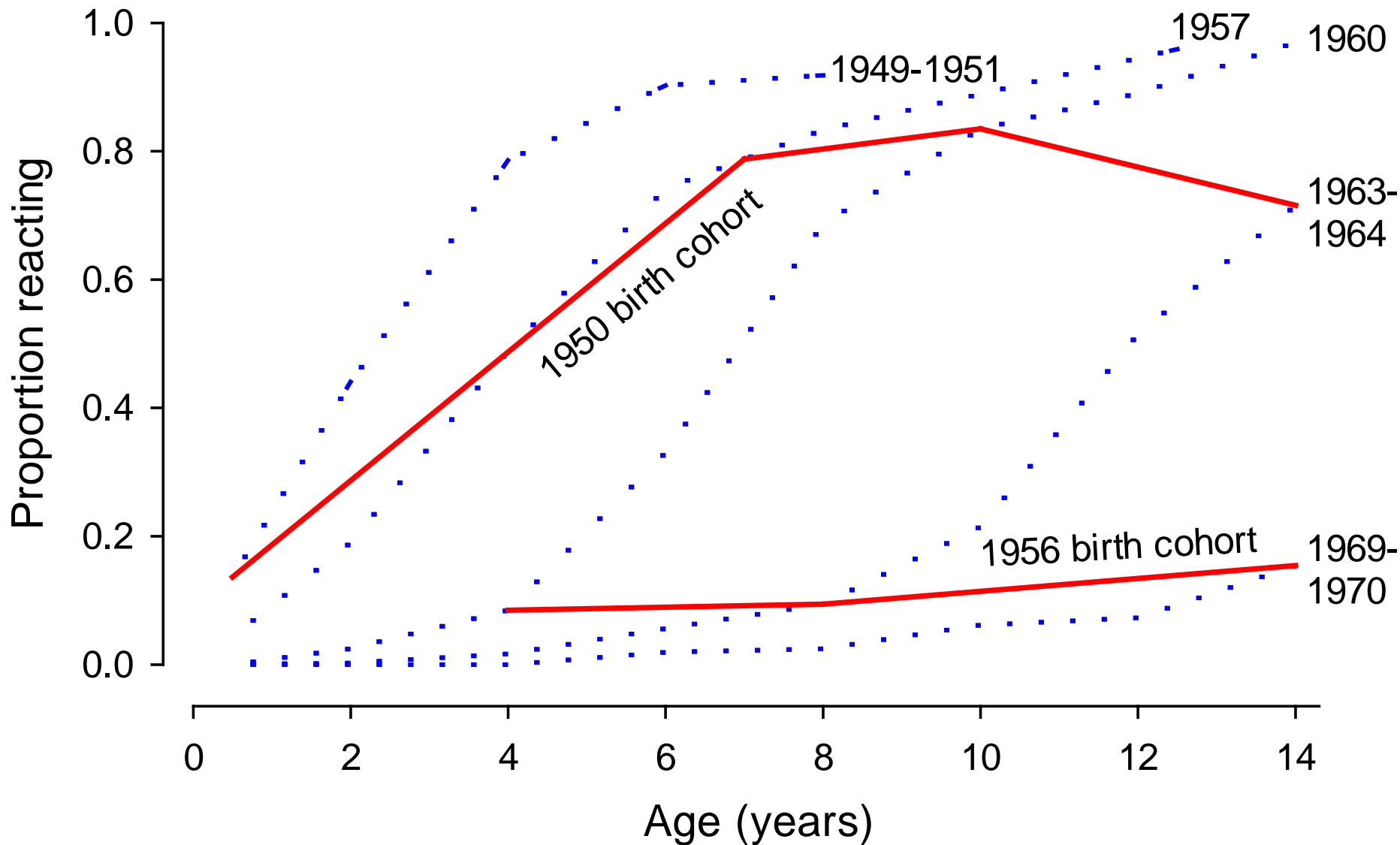
Component of the **tuberculosis elimination strategy**: identification and preventive chemotherapy for persons already infected

Quite a few promises...

“... Mass preventive treatment was used to control epidemic tuberculosis successfully in Alaska in the 1960s, and is the only strategy that can reduce tuberculosis transmission, incidence, and latency rates ...”

Corbett EL, et al. Lancet 2002;359:2177-87

Prevalence of Tuberculin Sensitivity Among Eskimo Children by Age, Yukon-Kukoskwim Delta, Alaska



Comstock GW, Porter ME. Public Health Rep 1959;74:621-34
Kaplan GJ, Fraser RJ, Comstock GW. Am Rev Respir Dis 1972;105:920-6

Epidemiology and Interventions in Alaska

Epidemiology: infection with *M. tuberculosis*

Largest effect on cohorts born between 1950 and 1956

Interventions: BCG, chemotherapy, and preventive therapy

1949-1951 BCG mass campaign, then used sporadically only and entirely stopped around 1955-1956

1953 Alaska Native Medical Center opens

1955 Chemotherapy program initiated

1957 Preventive therapy trials begin

1964 Preventive therapy becomes routinely used in IHS

A Trial of Mass Isoniazid Preventive Therapy for Tuberculosis Control

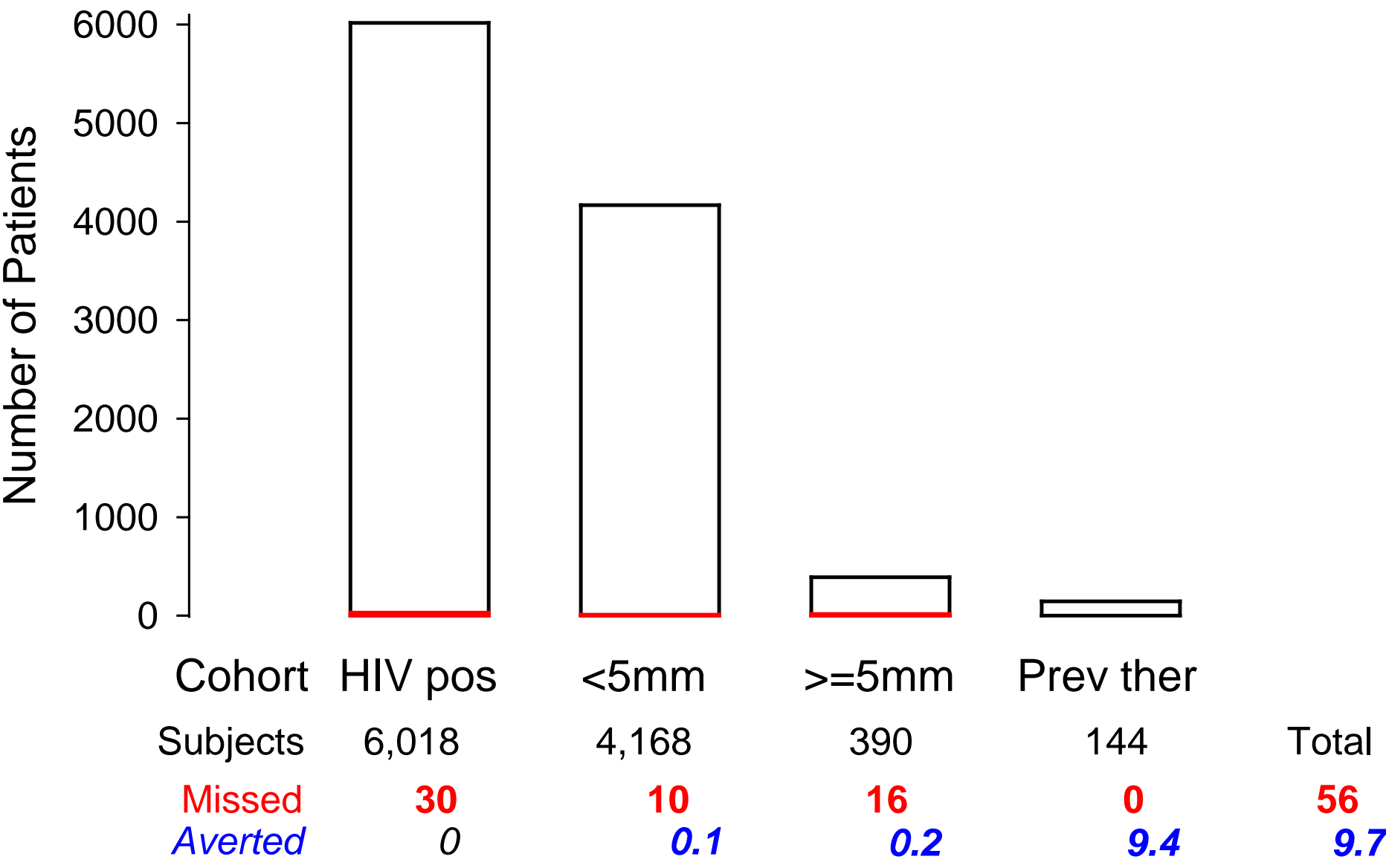
Gavin J. Churchyard, M.B., B.Ch., Ph.D., Katherine L. Fielding, Ph.D., James J. Lewis, Ph.D., Leonie Coetzee, D.Soc.Sc., Elizabeth L. Corbett, M.B., B.Chir., Ph.D., Peter Godfrey-Faussett, F.R.C.P., Richard J. Hayes, D.Sc., Richard E. Chaisson, M.D., and Alison D. Grant, M.B., B.S., Ph.D., for the Thibela TB Study Team

CONCLUSIONS

Mass screening and treatment for latent tuberculosis had no significant effect on tuberculosis control in South African gold mines, despite the successful use of isoniazid in preventing tuberculosis during treatment.

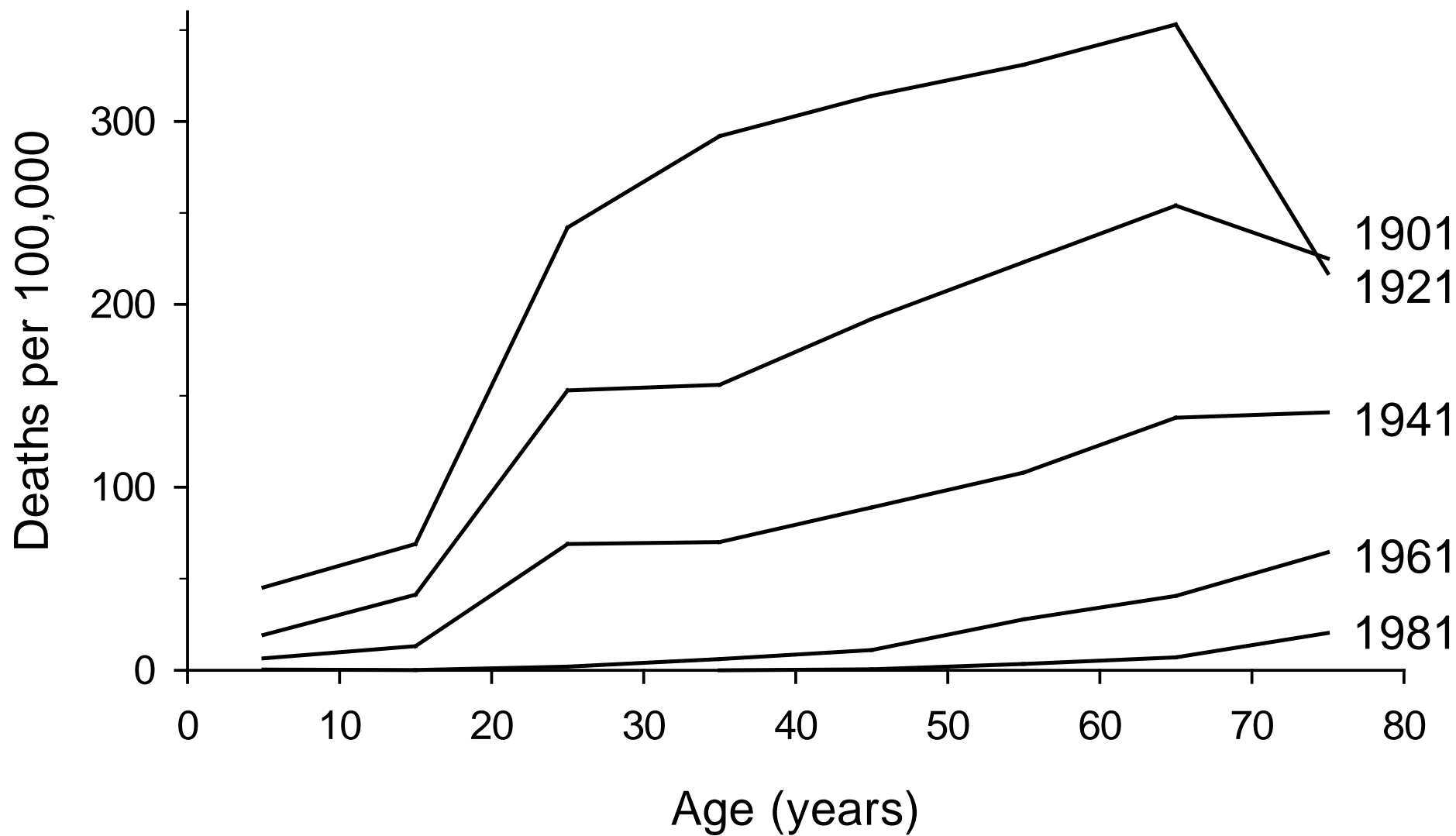
Churchyard GJ, et al. N Engl J Med 2014;370:301-10

Tuberculosis Incidence in an HIV-Infected Cohort of Patients on Anti-Retroviral Therapy, Switzerland, 1996-2005

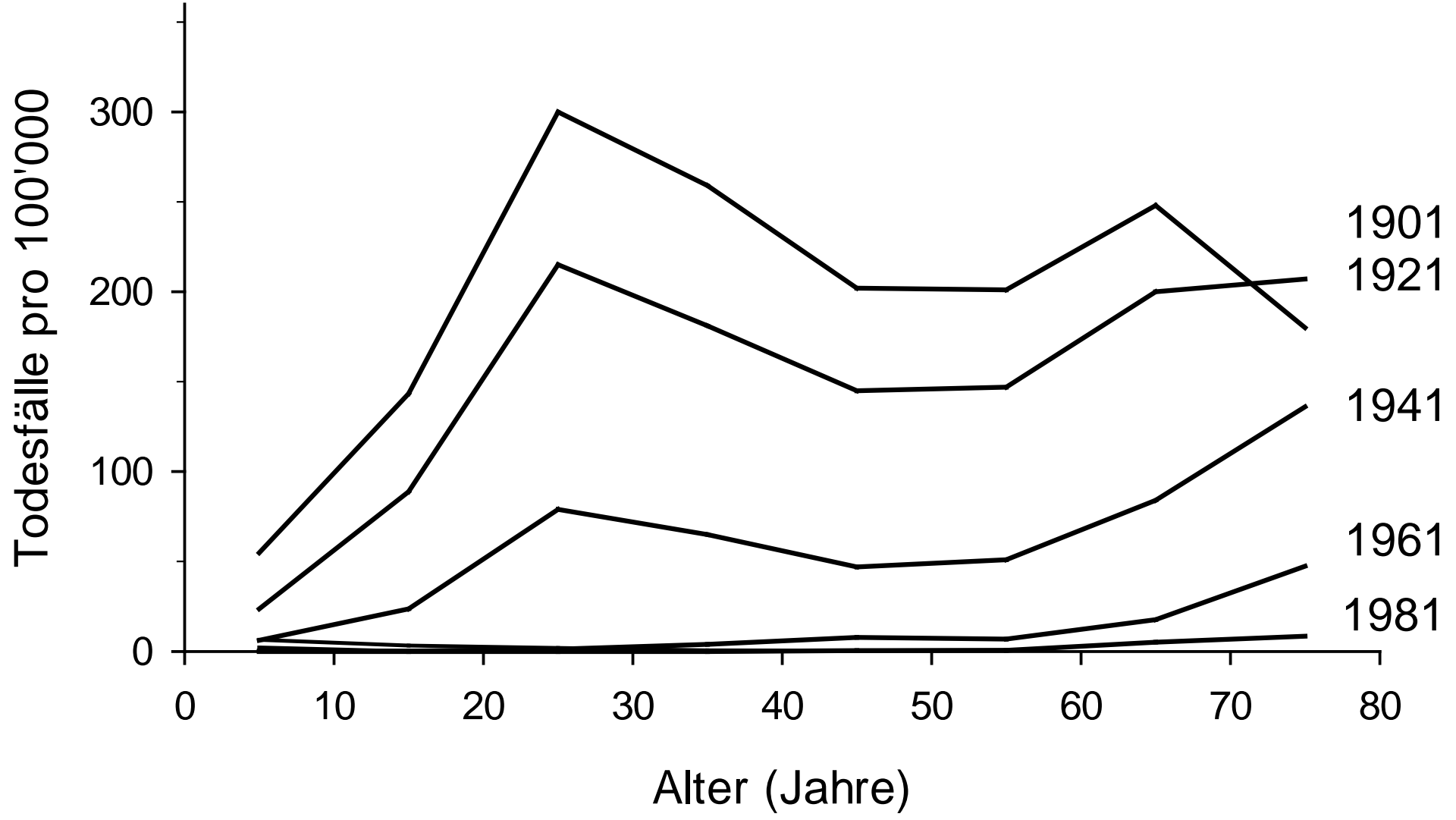


Elzi L, et al. Clin Infect Dis 2007;44:94-102

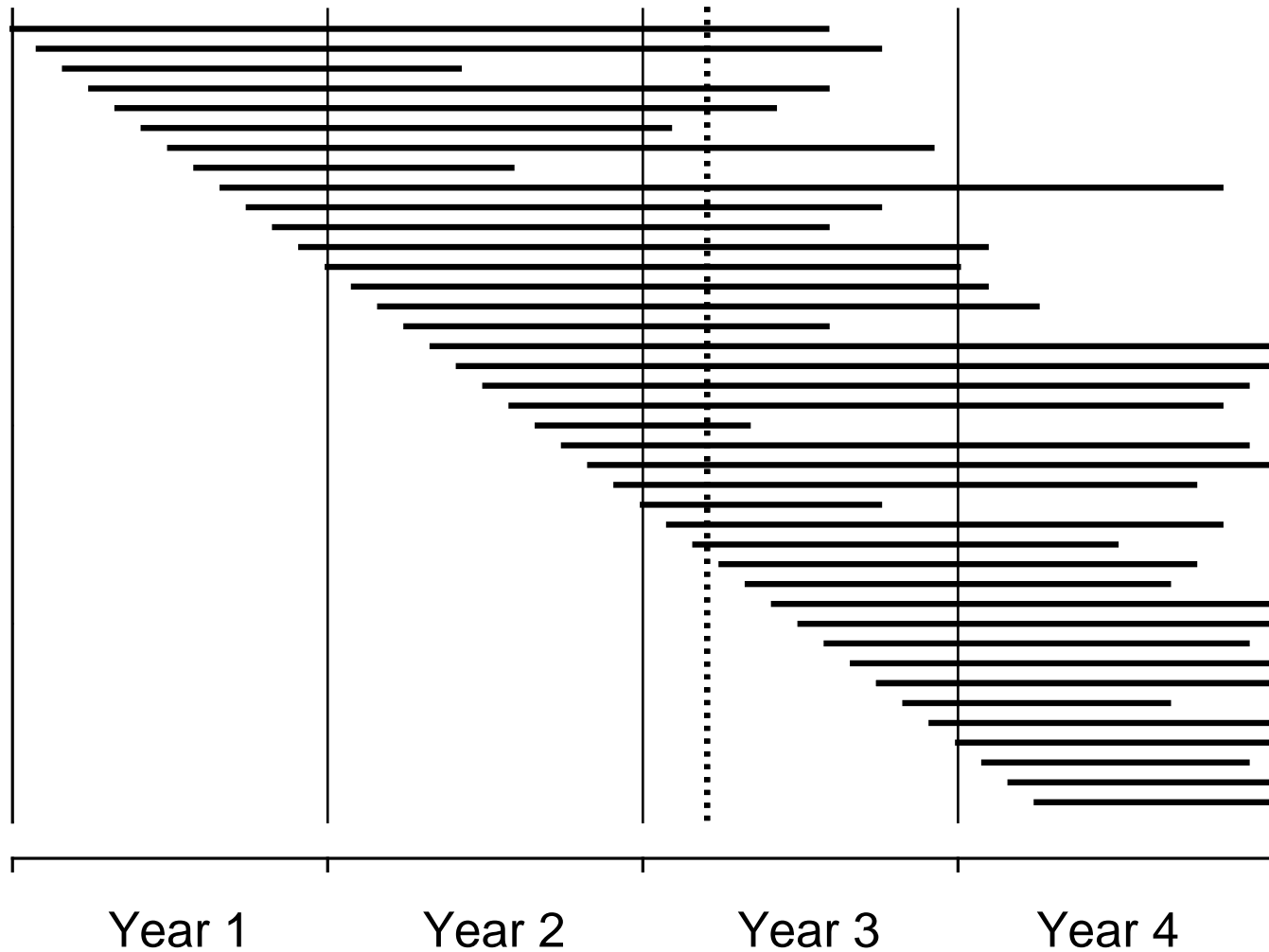
Mortality from Respiratory Tuberculosis Among Males, Cross-Sectionally, Switzerland



Mortality From Respiratory Tuberculosis Among Females Cross-Sectionally, Switzerland



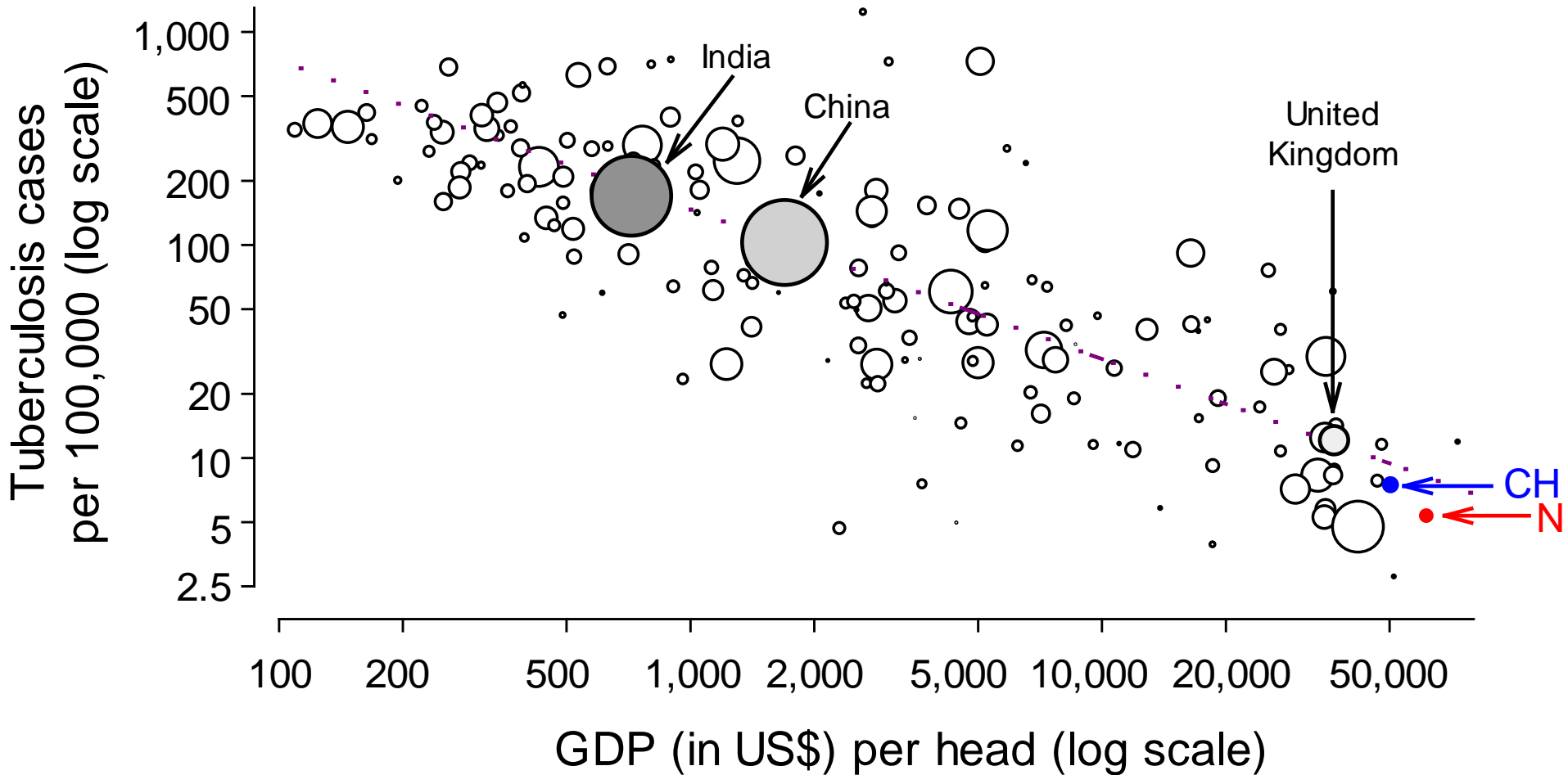
Incidence, Point Prevalence, and Period Prevalence



In year 3:

Incidence:	12 cases
Point prevalence, March 15:	24 cases
Period prevalence year 3:	288 person-months

Relationship between estimated tuberculosis incidence rates 2004 and per capita gross domestic product 2005



Epidemiological “room for manoeuver” to explain secular decline in 19th century (and earlier)

Measure

Implication

Epidemiology

Infection	Virtually everybody infected by end of adolescence => it cannot get much worse, but repeat reinfection after overcoming primary infection?
Morbidity	Lifetime risk 10% => A lot of room for worse: change could have occurred here, i.e. a reduction of risk of disease given infection over time, host factors, organism factors?
Fatality	Cumulatively 80% => not much room to have been worse earlier

Social improvements

Worker protection	Factory acts: UK: 1833 (labor of children); CH federal level: 1877 protecting children <14 yrs
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Medical interventions

Sanatoria	Removal of sources of infection (Wilson L), too small-scale and does not explain decline before the sanatorium movement
Chemotherapy	Substantial reduction in incidence of infection => secular trend Massive reduction of case fatality (80% => 5%) => period effect

Conclusion: many uncertainties, few certainties

- o It remains quite unclear why tuberculosis declines since 150 to 250 years (varying by industrialization)
- o Individually, chemotherapy massively reduced case fatality
- o Epidemiologically, timely diagnosis coupled with effective chemotherapy of sources of infection dramatically accelerated the decline in the risk of infection with *M tuberculosis*