Eur Respir J 1998; 11: 816–820
DOI: 10.1183/09031936.98.11040816

European Respiratory Journal
ISSN 0903 - 1936

Mortality among tuberculosis patients in the Netherlands in the period 1993–1995

M.W. Borgdorff*, J. Veen*, N.A. Kalisvaart*, N. Nagelkerke+

Mortality among tuberculosis patients in the Netherlands in the period 1993–1995. M.W. Borgdorff, J. Veen, N.A. Kalisvaart, N. Nagelkerke. ©ERS Journals Ltd. 1998.

ABSTRACT: This study aimed to estimate excess mortality among tuberculosis patients in the Netherlands and identify risk factors for tuberculosis-associated mortality.

The national tuberculosis register provided data on patients diagnosed in the period 1993–1995. Excess mortality in tuberculosis cases, according to age and sex, was determined by comparison with national mortality rates. Risk factors were identified and adjustment for confounders was carried out using Cox's proportional hazard analysis.

Of 4,340 patients alive at diagnosis, 258 died within 1 yr while on treatment. The Kaplan-Meier survival probability after 1 yr was 93%. Tuberculosis patients had a standardized mortality ratio of 8.3. Independent risk factors for mortality were: gender; age; presence of a malignancy or human immunodeficiency virus (HIV) infection; addiction to alcohol or drugs; localization of tuberculosis; and the type of medical officer having made the diagnosis. Of all deaths, 83% occurred in two risk groups comprising 21% of tuberculosis patients: those aged Š65 yrs and those having HIV infection or a malignancy.

Tuberculosis patients in the Netherlands are at a considerably increased risk of death. However, the prognosis is very good for those aged less than 65 yrs and without human immunodeficiency virus infection or a malignancy.

Eur Respir J 1998; 11: 816–820.

*Royal Netherlands Tuberculosis Association, The Hague, The Netherlands. +Erasmus University, Dept of Public Health, Rotterdam, The Netherlands.

Correspondence: M.W. Borgdorff
Royal Netherlands Tuberculosis Association
PO Box 146
2501 CC The Hague
The Netherlands
Fax 31 70 3584004

Keywords: Age
cohort analysis
human immunodeficiency virus
mortality
risk factors
tuberculosis

Received: July 30 1997
Accepted after revision January 5 1998

Worldwide, tuberculosis is the main infectious cause of death among adults, with most of these deaths occurring in developing countries [1–3]. Many tuberculosis-associated deaths may be preventable by adequate chemotherapy. In developed countries, despite a decline in the overall tuberculosis-associated mortality, the risk of death of patients with tuberculosis has increased, with an upward shift in the age distribution of tuberculosis cases [4–6].

In the Netherlands, the risk of tuberculosis infection has strongly decreased since the Second World War, leading to a low prevalence of infection among the young, although the prevalence of infection among the older cohorts is still high [7]. Consequently, as the incidence among the young age groups has decreased more strongly than that among the older ones, this cohort effect has shifted the age distribution of tuberculosis cases in the Netherlands as well.

Recently, the total incidence of tuberculosis in the Netherlands has increased due to immigration from high-prevalence countries [8–10]. Among the Dutch, tuberculosis in the younger age groups is increasingly concentrated in risk groups such as homeless and alcohol or drug addicts [7, 8]. It is conceivable that high-risk groups for tuberculosis are increasingly difficult to reach by the health services with an adverse effect on treatment outcome. In addition, prognosis may be influenced by human immunodeficiency virus (HIV) infection [11, 12].

The mainstay of tuberculosis control is treatment, in order to remove infectious sources from the population [2, 7, 13]. Treatment outcome is, therefore, extremely important in assessing performance of a tuberculosis control programme [14]. For the individual patients and their physicians there is also a more immediate interest in treatment outcome, in particular in the probability of surviving the disease.

In the present paper we estimate the size of excess mortality among tuberculosis patients and identify risk factors for tuberculosis-associated mortality for patients diagnosed in the Netherlands in the period 1993–1995, using survival analysis.

Methods

The national tuberculosis register provided data on tuberculosis patients diagnosed in the period 1993–1995. New and relapsed cases of tuberculosis were notified (by name) to the Ministry of Health. Since 1993, in addition, patient data at diagnosis were reported anonymously to the national tuberculosis register on a precoded report form. These include: demographic data; localization of diseases; earlier treatment for tuberculosis; case finding method; bacteriological confirmation; and risk groups. After completion of treatment, death or loss to follow-up, the outcome was also reported to the national tuberculosis register, on a separate precoded form. Patients were identified by identification numbers assigned by the tuberculosis control section of the public health services, who completed the report forms. If necessary, data from (private) physicians treating the patients were collected by the public health services.

Data analysis

The outcome of treatment was classified as follows: cured (with microbiological evidence of cure); completed treatment (and assumed cured); defaulted (*i.e.*, lost to follow-up); died (cause of death tuberculosis); died (cause of death other than tuberculosis); and continuing treatment elsewhere.

If patients were referred within the Netherlands the public health service in the new area of residence should report treatment outcome. Therefore, the latter outcome category was combined in the analysis with those reported lost to follow-up. In the national register, treatment failure was not recorded as an outcome; the final outcome is reported after completion of treatment (or death or loss to follow-up).

In the present analysis, follow-up was censored at 1 yr after diagnosis. The outcome death within 1 yr after diagnosis was studied. Excess mortality in tuberculosis patients according to age and sex, was determined by comparison with published national mortality rates from the Netherlands' Central Bureau of Statistics in 1994 [15]. Survival from those alive at diagnosis up to 1 yr after the start of treatment was determined using the Kaplan-Meier method.

The risk of death (case fatality ratio) was compared between subgroups to identify risk factors. Adjustment for confounders was carried out using Cox's proportional hazard analysis for all variables except HIV infection. As the risk of HIV infection was not proportional over time, we used logistic regression to adjust for confounders in estimating the risk of death associated with HIV infection. In the multivariate proportional hazards model, analysis was restricted to those without HIV infection.

The multivariate model was built starting with the variables with basic characteristics likely to be associated with mortality: sex; age; presence of malignancy; and localization of tuberculosis. Next, we examined variables associated with case finding; method of case detection (active or passive); nationality (country which issued the passport); patients being asylum-seekers; and the type of physician making the diagnosis. Finally, it was established whether addiction to alcohol or drugs was associated with increased mortality. Variables were selected based on either *a priori* knowledge, or if there was a univariate association with mortality. Survival curves were constructed for three risk groups identified on the basis of this analysis.

Results

In the period 1993–1995, of 4,981 registered tuberculosis patients, 105 (2%) had died at the time of diagnosis. Treatment outcome and duration were reported for 4,340 (89%) of those alive at diagnosis. Reporting of treatment outcome was not associated with sex or age of the patient, but was somewhat less complete for recent immigrants from Somalia (82%) and the former Yugoslavia (82%) than for other nationalities. Reporting was less complete for those diagnosed in 1995 (80%) than for those diagnosed in 1993 (92%) and 1994 (94%), suggesting some reporting delay.

Of the 4,340 patients alive at the start of treatment and with reported treatment outcome, 539 (12%) were treated for more than 1 yr. Of these 539, 12 (2%) died after more than 1 yr, reportedly due to causes other than tuberculosis. Of the remaining 3,801, 3,099 (82%) were reported cured or had completed treatment, 444 (12%) were reported lost to follow-up or transferred out and 258 (7%) had died. Loss to follow-up occurred evenly over the treatment period at a rate of 14.3 per 100 person-years (95% confidence interval (CI) 13.0–15.7). Deaths occurred relatively frequently soon after diagnosis: Kaplan-Meier survival probabilities were 97.5% after the first month of treatment, 96% after the 3 months, 95% after 6 months and 93% (95% CI 92–94%) after 1 yr.

Excess mortality among tuberculosis patients on treatment, compared with the general population, is presented in table 1. Tuberculosis patients had a standardized

Table 1. – Excess mortality among tuberculosis patients diagnosed in the Netherlands, 1993–1995 by sex and age

	New cases of tuberculosis n	Observation person-years	Observed deaths n	Population mortality rate $n \cdot 1000^{-1}$	Expected deaths n	SMR (95% CI)
Males						
<25 yrs	638	468	5	0.61	0.29	17 (5.6–40)
25–34 yrs	784	572	9	0.78	0.45	20 (9.2–38)
35–44 yrs	404	291	14	1.50	0.44	32 (17–53)
45–54 yrs	242	168	14	3.82	0.64	22 (12–37)
55–64 yrs	173	118	25	11.68	1.38	18 (12–27)
65–74 yrs	194	129	41	33.74	4.35	9.4 (6.8–13)
75+ yrs	168	91	62	115.14	10.48	5.9 (4.5–7.6)
All	2603	1837	170		18.02	9.4 (8.1–11)
Females						
<25 yrs	487	354	2	0.39	0.14	14 (1.7–52)
25–34 yrs	422	320	4	0.43	0.14	29 (7.8–73)
35–44 yrs	232	174	4	1.06	0.19	22 (5.9–55)
45–54 yrs	150	114	3	2.61	0.30	10 (2.1–29)
55–64 yrs	114	86	4	6.26	0.54	7.4 (2.0–19)
65–74 yrs	132	90	19	16.19	1.46	13 (7.8–20)
75+ yrs	200	124	52	82.44	10.22	5.1 (3.8–6.7)
All	1737	1262	88		12.98	6.8 (5.4–8.4)
Total	4340	3099	258		31.00	8.3 (7.3–9.4)

SMR: standardized mortality ratio; 95% CI: 95% confidence interval.

Table 2. – Risk factors for death within 12 months after diagnosis among 4,340 tuberculosis patients who were alive at diagnosis

	Deaths/registered		Hazard ratio (95% CI)	
	n	(%)	Crude	Adjusted*
Sex				
Male	170/2603	(7)	1	1
Female	88/1737	(6)	0.8	0.8 (0.6–1.0)
Age yrs				
<25	7/1125	(1)	1	1
25–44	31/1842	(2)	1.9	1.6 (0.5–5.1)
45–64	46/679	(7)	16	10 (3.5–28)
65+	174/694	(25)	78	45 (17–124)
Localization of disease				
Pulmonary	175/2762	(6)	1	1
Extrapulmonary	52/1250	(4)	0.6	0.5 (0.3–0.7)
Pulmonary and extrapulmonary	31/328	(9)	1.4	1.4 (0.9–2.2)
Diagnosis made by				
Tuberculosis MO	4/1304	(0.3)	1	1
Chest physician	188/2170	(9)	28	7.4 (2.7–20)
Specialist internal medicine	44/452	(10)	31	10 (3.6–30)
Surgeon	8/117	(7)	21	13 (3.8–46)
Other specialist	11/224	(5)	15	8.9 (2.6–30)
Others	3/73	(4)	13	7.0 (1.5–32)
Addiction to alcohol	7/47	(15)	2.8	2.4 (1.1–5.3)
Addiction to drugs	12/135	(9)	1.5	3.5 (1.1–11.5)
Malignancy (HR none=1)	42/94	(45)	10	3.1 (2.2–4.4)
HIV infection** (OR none/not reported=1)	30/168	(18)	(OR 3.8)	(AOR 9.9 (5.4–18))
Nationality				
Dutch	213/1943	(11)	1	1
Moroccan	8/496	(2)	0.1	0.7 (0.3–1.6)
Somalian	2/460	(0.4)	0.04	0.5 (0.1–2.4)
Surinamese	2/100	(2)	0.2	0.5 (0.1–2.0)
Turkish	4/251	(2)	0.1	0.9 (0.3–2.4)
Former Yugoslavian	1/121	(1)	0.1	0.8 (0.1–5.9)
Other Africa	4/312	(1)	0.1	0.9 (0.2–3.7)
Other Asia	14/435	(3)	0.3	1.5 (0.8–2.6)
Others	28/969	(3)	0.3	0.7 (0.2–2.7)
Risk groups				
Asylum-seeker				
- at entry	1/293	(0.3)	0.1	0.8 (0.1–6.1)
- later	4/510	(1)	0.1	0.6 (0.2–1.8)
Illegal immigrant	4/126	(3)	0.5	3.7 (1.1–12.5)
Homeless	4/55	(7)	1.3	1.4 (0.4–4.8)
Known with prior tuberculosis disease or infection				
Yes	55/470	(12)	2.5	1.1 (0.8–1.5)
No	166/3465	(5)	1	1
Unknown	37/405	(9)		
Detected through				
Complaints	210/2907	(7)	1	1
Contact tracing	4/424	(1)	0.1	1.2 (0.5–3.5)
Screening of risk group	6/691	(1)	0.1	1.2 (0.4–2.8)
Other or unknown	38/318	(12)		
Bacteriological confirmation				
Yes	194/2883	(7)	1.5	0.8 (0.6–1.1)
No	64/1457	(4)	1	1

*: adjusted for sex, age, localization of tuberculosis, malignancy, diagnosis made by, and addiction to alcohol or drugs, limited to the group without human immunodeficiency virus (HIV) infection; **: for HIV infection odds ratios (ORs) were calculated, as the risk was not proportional over time. HR: hazard ratio; 95% CI: 95% confidence interval; MO: medical officer; AOR: adjusted odds ratio.

mortality ratio (SMR) of 8.3. The SMR was higher in those aged <65 yrs compared to those aged Š65 yrs (ratio of SMRs 2.9; 95% CI 2.2–3.7).

Risk factors associated with death are presented in table 2. The risk of death was somewhat lower in females than in males (adjusted hazard ratio (AHR) 0.8) and strongly increased with age. Compared with patients having pulmonary tuberculosis, the risk of death was lower in patients with extrapulmonary disease (AHR 0.5) and increased in those with combined pulmonary and extrapulmonary disease (AHR 1.4). The case fatality ratio was much higher among those diagnosed by clinical specialists than those

diagnosed by a medical officer for tuberculosis control. The risk of death was strongly increased in tuberculosis patients addicted to alcohol (AHR 2.4) or drugs (AHR 3.5).

Increased mortality was observed in those having a malignancy (AHR 3.1) and those having HIV infection (age and sex adjusted odds ratio 19; 95% CI 11–34). After adjustment for other confounders, HIV infected patients were found to have a tenfold increased risk of death (odds ratio 9.9; 95% CI 5.4–18). The additional risk of death in HIV infected people appeared to be more pronounced in the second 6 months after diagnosis.

Mortality was lower among the non-Dutch compared with the Dutch ($p<0.05$), in particular among asylum seekers. Most of these were diagnosed by tuberculosis officers. After taking into account the medical officer who made the diagnosis, country of origin did not provide additional explanatory power and was removed from the model. Illegal immigrants had an increased mortality (AHR 3.7) although numbers were small. No tuberculosis-associated deaths were observed among 59 prisoners, 97 health workers and 71 travellers to endemic countries.

The apparently increased risk of death for those known to have had prior tuberculosis disappeared after adjusting for age. Those detected by screening or contact tracing had a smaller risk of death in univariate analysis compared with patients self-reporting with complaints. As noted above, this effect was captured by taking into account who made the diagnosis. The risk of death was not associated with bacteriological confirmation of the diagnosis after adjustment for age and sex. Antimicrobial resistance at the start of treatment was observed among 329 patients and was associated with a nonsignificantly increased risk of death (AHR 1.6).

Results of a multivariate analysis in those without reported HIV infection are also presented in table 2. Mortality was found to be independently increased in: males; older age groups; those having a malignancy; and in alcohol or drug addicts. Mortality was also independently associated with the localization of tuberculosis and the type of medical officer who made the diagnosis. Addition of other variables did not significantly improve the model.

The effect of HIV decreased when taking addiction to drugs into account, and vice versa, as there was considerable overlap between the two groups: 45 out of 135 drug users (33%) were reported to have HIV infection, compared with 123 out of 4,205 people (3%) not reported to be drug users.

In order to predict the outcome of tuberculosis patients who were alive at diagnosis a simple classification was used (fig. 1). Kaplan-Meier probabilities of surviving 1 yr after diagnosis were: 72% (95% CI 68–76%) for those aged Š65 yrs (risk group I), 72% (95% CI 62–80%) for those aged <65 yrs and having either HIV infection or a malignancy (risk group II); and 99% for the remainder (95% CI 98–99%). Risk groups I and II comprised 21% of the tuberculosis patients and accounted for 83% of tuberculosis-associated deaths. Mortality differed in time between risk groups I and II, although survival was similar after 1 yr. Survival after 3 months was 82% (95% CI 79–84%) in risk group I (aged >65) and 91% (95% CI 86–94%) in risk group II. Thus, mortality in those aged Š65 yrs occurred relatively early, and in those with HIV infection or a malignancy relatively late. Losses to follow-up per 100 person-years were: 9.7 (95% CI 7.0–13.1) in risk group I; 19.4 (95% CI 12.8–28.3) in risk group II; and 14.9 (95% CI 13.4–16.4) in the remainder.

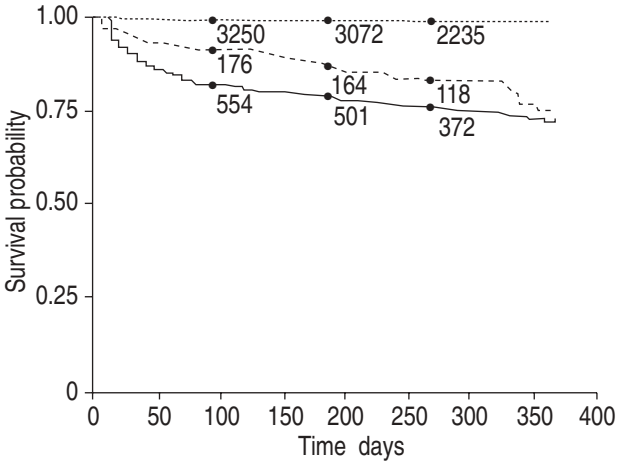

Fig. 1. – Survival curves of three risk groups among tuberculosis patients diagnosed in 1993–1995 in the Netherlands. —— : subjects aged Š65 yrs; - - - : subjects aged <65 yrs and having either human immunodeficiency virus (HIV) or a malignancy; ····· : all other subjects. Denominator data (number of surviving subjects) at day 0 were 694 in subjects aged Š65 yrs, 204 in those with HIV/malignancy, and 3,442 in other subjects. Values presented on the figure represent denominator data at that time.

Overall, 35 out of 258 tuberculosis-associated deaths (14%) were attributed to tuberculosis. These proportions were smaller in the above-mentioned risk groups: 18 out of 174 (10%) in the age group Š65 yrs, two out of 30 (7%) in those with HIV infection, and one out of 42 (2%) in those with a malignancy.

Discussion

This study has shown that in the Netherlands, patients with tuberculosis are at a considerably increased risk of death compared with the general population. Over 80% of tuberculosis-associated deaths occurred in those aged Š65 yrs and those with HIV infection or with a malignancy. These risk groups comprised 21% of all tuberculosis patients. The subdivision in risk groups may be helpful for counselling patients regarding their prognosis, which is very good for those aged <65 yrs and without HIV infection or a malignancy.

In reports from the Netherlands and the UK, increases in the crude case fatality ratio of tuberculosis were attributed to ageing of the patient population [4, 5]. Though, as in the UK, the standardized mortality ratio was lower in the older age groups [16], the excess number of tuberculosis-associated deaths was much larger than in the younger age groups. Difficulty in diagnosing tuberculosis in the elderly leading to diagnostic delay and a reduced immune response in this group have been suggested as explanations for their increased case fatality [4, 5]. Underdiagnosis is suggested in the current study by the relatively large number who were diagnosed after death [17, 18]. Therefore, a high level of clinical suspicion among physicians treating elderly patients remains necessary [19].

Tuberculosis patients with HIV infection were approximately 10 times more likely to die than tuberculosis patients without HIV. The prevalence of HIV among tuberculosis patients was low, at 4%. As reported elsewhere,

excess mortality generally occurred relatively late in the course of treatment and was attributed to causes other than tuberculosis [11, 12, 20]. As offering HIV testing to tuberculosis patients is not a national policy, the reported number of HIV-infected patients should be regarded as a minimum estimate. If HIV testing was more likely in those with serious disease or responding poorly to treatment, the additional risk of HIV infection may be overestimated by the present study.

Patients from high prevalence countries were less likely to die than Dutch patients, even after adjusting for differences in age. If migrants represent a relatively healthy group of the population of origin, this might be interpreted as a "healthy migrant effect". Alternatively, as a large proportion of cases among immigrants were detected through a screening programme, patients may have been detected relatively early in the course of disease leading to a better prognosis. Possibly, the screening programme has not only reduced transmission through early case detection, but also benefited the patients being detected.

A very strong association was found between the type of physician diagnosing tuberculosis and case fatality. This is partly explained by the better prognosis of patients detected through screening, as these were all diagnosed by tuberculosis medical officers. An additional reason lies in the referral system. In the Netherlands, the first point of contact of a patient with the healthcare system is with the general practitioner. The general practitioner may refer patients either to a clinical specialist such as a chest physician, or to a tuberculosis medical officer in the public health service. Patients who are seriously ill are more likely to be referred to hospital, be attended to by a clinical specialist, and also to die. Differences in case management are unlikely to explain the observed differences in case fatality.

Overall, the rate of loss to follow-up was 14.3 per 100 person-years. Losses to follow-up were slightly lower in the elderly and slightly higher among those with HIV infection or a malignancy. If losses to follow-up were associated with decreased or increased mortality, tuberculosis-associated mortality may have been somewhat over- or underestimated. Ideally, mortality among those lost to follow-up would be traced in the mortality registration. However, the national tuberculosis register is anonymous, making this linkage very difficult. As losses to follow-up were not strongly associated with the identified risk factors, major bias in the risk factor analysis seems unlikely.

In many tuberculosis patients, multiple causes of death may act simultaneously, so the cause of death may not be determined with accuracy [21, 22]. Recently, in Norway, this misclassification was shown to be considerable [23]. In the present study, most of the analyses included all deaths, irrespective of the cause of death, so misclassification of the cause of death cannot have had a major influence on the results obtained.

In conclusion, tuberculosis is still a serious disease, even in developed countries. Mortality occurs mainly in risk groups that can be identified at the start of treatment.

Acknowledgements: The authors would like to thank the dedicated staff of the public health services in the Netherlands, without whose support this study would not have been possible.

References

1. Dolin PJ, Raviglione MC, Kochi A. Global tuberculosis incidence and mortality during 1990–2000. *Bull WHO* 1994; 72: 213–220.
2. Murray C, Styblo K, Rouillon A. Tuberculosis. *In:* Jamison DT, Mosley WH, Measham AR, Bobadilla JL, eds. Disease Control Priorities in Developing Countries. New York, Oxford University Press, 1993; pp. 233–259.
3. Raviglione MC, Snider DE, Kochi A. Global epidemiology of tuberculosis - mortality and morbidity of a worldwide epidemic. *JAMA* 1995; 273: 220–226.
4. de Meer G, van Geuns HA. Rising case fatality of bacteriologically proven pulmonary tuberculosis in The Netherlands. *Tubercle Lung Dis* 1992; 73: 83–86.
5. Doherty MJ, Spence DPS, Davies PDO. Trends in mortality from tuberculosis in England and Wales: effect of age on deaths from non-respiratory disease. *Thorax* 1995; 50: 976–979.
6. Raviglione MC, Sudre P, Rieder HL, Spinaci S, Kochi A. Secular trends of tuberculosis in Western Europe. *Bull WHO* 1993; 71: 297–306.
7. Styblo K. Epidemiology of tuberculosis. Selected papers 24, The Hague, KNCV, 1991.
8. Veen J. Kalisvaart NA. Index tuberculosis 1996. The Hague, KNCV, 1997.
9. Rieder HL, Zellweger JP, Raviglione MC, Keizer ST, Migliori GB. Tuberculosis control in Europe and international migration. *Eur Respir J* 1994; 7: 1545–1553.
10. Rieder HL. Epidemiology of tuberculosis in Europe. *Eur Respir J* 1995; 8: Suppl. 20, 620s–632s.
11. Small PM, Schecter GF, Goodman PC, Sande MA, Chaisson RE, Hopewell PC. Treatment of tuberculosis in patients with advanced human immunodeficiency virus infection. *New Engl J Med* 1991; 324: 289–294.
12. Chaisson RE, Schecter GF, Theuer CP, Rutherford GW, Echenberg DF, Hopewell PC. Tuberculosis in patients with the acquired immunodeficiency syndrome. *Am Rev Respir Dis* 1987; 136: 570–574.
13. Blower SM, Small PM, Hopewell PC. Control strategies for tuberculosis epidemics: new models for old problems. *Science* 1996; 273: 497–500.
14. Maher D, Chaulet P, Spinaci S, Harries A. Treatment of tuberculosis: guidelines for national programmes. Geneva, World Health Organization, 1997.
15. Centraal Bureau voor de Statistiek Statitisch Jaarboek 1997. Voorburg/Heerlen: Centraal Bureau voor de Statistiek, 1997.
16. Cullinan P, Meredith SK. Deaths in adults with notified pulmonary tuberculosis 1983–5. *Thorax* 1991; 46: 347–350.
17. Xie HJ, Enarson DA, Chao CW, Allen EA, Grzybowski S. Deaths in tuberculosis patients in British Columbia, 1980–1984. *Tubercle Lung Dis* 1992; 73: 77–82.
18. Selby C, Thomson D, Leitch AG. Deaths in notified cases of tuberculosis in Edinburgh: 1983–1992. *Respir Med* 1995; 89: 369–371.
19. Rieder HL, Kelly GD, Bloch AB, Cauthen GM, Snider DE. Tuberculosis diagnosed at death in the United States. *Chest* 1991; 100: 678–681.
20. Nunn P, Brindle R, Carpenter L, *et al.* Cohort study of human immunodeficiency virus infection in patients with tuberculosis in Nairobi, Kenya - Analysis of early (6-month) mortality. *Am Rev Respir Dis* 1991; 144: 750–755.
21. Buhl K, Nyboe J. Epidemiological basis of tuberculosis eradication - 9. Changes in the mortality of Danish tuberculosis patients since 1925. *Bull WHO* 1967; 37: 907–925.
22. White MC, Portillo CJ. Tuberculosis mortality associated with AIDS and drug or alcohol abuse: analysis of multiple cause-of-death data. *Publ Health* 1996; 110: 185–189.
23. Heldal E, Naalsund A, Kongerud J, Tverdal A, Boe J. Deaths from active tuberculosis: can we rely on notification and mortality figures? *Tubercle Lung Dis* 1996; 77: 215–219.