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Trends in mortality from tuberculosis in England and Wales: effect of age on deaths from non-respiratory disease

M J Doherty, D P S Spence, P D O Davies

Abstract

Background **– Although mortality from tuberculosis has continued to fall in recent years, there has been little change in the case fatality rate for tuberculosis over the same period. This has previously been shown to be due to the increasing proportion of cases of tuberculosis occurring in the elderly. Tuberculosis mortality and case fatality were therefore analysed to determine if this disappointing trend in case fatality rate has occurred from disease in all or only certain sites.**

Methods **– A retrospective analysis of the tuberculosis mortality and case fatality rates in England and Wales for the period 1972–92 was carried out. The average annual percentage change in tuberculosis was calculated for each disease site and by age group and the results were compared.**

Results **– The analysis showed that, although the mortality rate fell steadily by 5·6% per annum, the case fatality rate decreased by only 0·9% (95% CI −1·7 to −0·1) per annum. The case fatality rate for respiratory and central nervous system disease declined, but no decline in tuberculosis at "other" sites was observed (1·01% (+2·2 to −0·2) for all age groups combined). In the group aged 75 and over, however, the proportion of deaths due to disease at other sites increased by 3·2% (2·2 to 4·3) per annum whilst in the other age groups the mortality rate declined.**

Conclusions **– This analysis suggests that clinicians may be becoming less able to recognise non-respiratory presentations of tuberculosis, particularly in the elderly, and underlines the need to consider tuberculosis as a diagnosis to avoid delay in treatment.**

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Aintree Chest Centre, Fazakerley Hospital, Liverpool L9 7AL, UK
M J Doherty

Royal Liverpool University Hospital, Liverpool L7 8XP, UK
D P S Spence

Tuberculosis Research Unit, Cardiothoracic Centre, Liverpool L14 3RE, UK
P D O Davies

Reprint requests to:
Dr M J Doherty.

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With the exception of the war years, mortality from tuberculosis has been falling in England and Wales since records were first kept.[1,2] This has probably been the result of improvements in living conditions[3,4] and the introduction of chemotherapy in the early 1950s. In recent years mortality from tuberculosis has continued to fall, but at a slower rate. However, case fatality rate (the ratio of deaths from tuberculosis to the total number of disease notifications) is a better measure of how successfully the disease is being managed than mortality, as the mortality rate depends on the notification rate and these vary as a result of factors such as rising poverty and immigration which are outside the control of those which treat tuberculosis.[5,6] The case fatality rate for tuberculosis has declined only very slowly, by 0·13% annually in England and Wales for the period 1974–87.[7] The lack of a more substantial decline is due to the increasing proportion of cases of tuberculosis occurring in the elderly, as this group has the highest rate of mortality from the disease. The study by Nisar and Davies in 1991 analysed tuberculosis mortality for all sites combined; however the mortality and morbidity data published by the Office of Population Censuses and Surveys (OPCS) also categorises disease by site.[8] The sites are defined as respiratory, central nervous system (CNS), and "other", and the number of notifications and case fatalities are recorded for each site. Other sites used by the OPCS include miliary tuberculosis, tuberculosis of the bones and joints, and tuberculosis of the urogenital and gastrointestinal tracts.

In this study we have measured changes in both the mortality rate and the case fatality rate for tuberculosis, and have determined whether changes in these indicators reflect changes in all or only some of the disease sites.

Methods

Data on the notifications of, and deaths from, tuberculosis for England and Wales, excluding deaths due to the late effects of tuberculosis, were extracted from the relevant OPCS monitors for the years 1972–92.[8,9] Reported deaths for the years 1972–83 were corrected for the change in coding which became effective in 1984, using the bridge coding exercise of the OPCS,[10] so that death rates before and after that year could be better compared. Data were extracted for all forms of tuberculosis combined, and for respiratory, CNS, and other forms separately. Data on deaths from tuberculosis are provided by death certificates supplied to the Registrar General. The estimated mid year population of England and Wales was extracted from the OPCS for the years 1972–92[11] and used to calculate the mortality rate (per one million persons) and the case fatality rate (per 100 notifications) by each disease site for each year. Case fatality rates for respiratory tuberculosis and tuberculosis at other sites for various age groups were also calculated for the years 1973–92, data being

Table 1 Deaths and case fatality rate (per 100 cases) for tuberculosis of the respiratory and central nervous system (CNS), "other" sites, and all sites combined for the years 1972–92 (corrected by the relevant conversion factor for the years before 1984)

	Respiratory tuberculosis deaths	*Respiratory case fatality*	*CNS tuberculosis deaths*	*CNS case fatality*	*"Other" tuberculosis deaths*	*"Other" case fatality*	*All tuberculosis deaths*	*All case fatality*
1972	1066	12·27	32	32·8	144	6·28	1242	11·2
1973	947	10·87	32	33·4	140	5·98	1119	10·03
1974	852	10·52	31	28·3	158	6·4	1041	9·75
1975	795	9·68	34	33	127	5·06	956	8·84
1976	688	8·92	33	37·3	118	5·15	839	8·81
1977	576	8·08	25	30·4	110	4·76	711	7·47
1978	548	7·74	25	23·9	104	4·15	677	6·99
1979	540	7·94	20	22·6	116	4·88	676	7·29
1980	522	7·84	40	37·8	116	4·89	678	7·42
1981	511	8·26	31	30·5	106	5·39	648	7·97
1982	499	8·58	24	23·6	97	5·91	620	8·37
1983	413	7·77	16	19·8	85	5·65	514	7·56
1984	376	7·72	30	48·4	84	6·69	490	7·98
1985	408	8·76	18	33·9	97	8·13	523	8·93
1986	376	7·9	15	18·3	80	6·63	471	7·86
1987	329	8·2	20	37	81	7·63	430	8·46
1988	384	9·55	13	17·8	81	7·21	478	9·26
1989	333	8·03	22	42·3	88	6·9	443	8·15
1990	313	7·94	13	16	64	5·21	390	7·49
1991	334	8·45	8	8·2	80	5·48	422	7·76
1992	308	7·33	15	16·8	94	5·98	418	7·21

only available by age group from 1973. The age groups were 0–14 years, 15–44 years, 45–74 years, and 75 years and over. They were chosen to represent children, young adults (the group in which any changes due to HIV related tuberculosis would be expected to be seen), the middle aged, and the elderly. Tuberculosis of the CNS was not studied by age as this group contained so few cases that further subgrouping would be meaningless. These data were then used to calculate the percentage annual change (with 95% confidence interval (CI)) of the mortality rate and case fatality rate for each group using regression equations on the $\log_e$ of each rate. The annual percentage change of each disease site group was compared with the change for all sites combined to determine whether the changes in total mortality from tuberculosis were due to changes in all or in only one site. The annual average percentage change of each age group for respiratory disease and disease at other sites was compared to determine whether changes in case fatality rate were the same throughout the whole age range. The proportion of all deaths occurring in those aged over 75 years of age was calculated for each site and the annual percentage change in this proportion determined. The analysis also determined whether the proportion of all deaths by site had changed over the 21 years of the study.

Results

The corrected number of deaths and case fatality rate for each disease site and for all sites combined are shown in table 1. This shows that the case fatality rate for tuberculosis of the CNS is much higher (by a factor of three) than the rate for respiratory disease which, in turn, has a higher case fatality rate than disease at "other" sites.

The mean annual percentage change in both mortality and case fatality rates for each disease site is shown in table 2. This shows that the mortality rate for all disease decreased over the time period by 5·6% (95% CI 6·3% to 4·9%) per annum. In 1992 mortality from tuberculosis was almost one third of its 1972 level. Mortality from tuberculosis significantly decreased at all sites, but this decrease was smallest in subjects with tuberculosis at "other" sites, a decrease of 3·5% (4·3% to 2·7%). The death to notification ratio (case fatality rate) for all sites decreased much less during this period, by 0·9% (1·7% to 0·1%) per annum. When the case fatality rate was analysed by disease site, both respiratory and CNS disease also decreased significantly. However, disease at "other" sites showed a non-statistically significant increase in the case fatality rate, the change being 1·01% (+2·2% to −0·2%).

Table 3 shows the mean annual percentage change in the proportion of the total number of notifications and deaths occurring in those aged over 75 years at each disease site. The proportion of deaths occurring in the elderly increased in both respiratory tuberculosis and tuberculosis at "other" sites by 3·2% (2·2% to 4·2%) and 3·2% (2·2% to 4·3%) respectively.

The proportion of all deaths due to disease at respiratory sites decreased slightly by 0·4% (0·6% to 0·2%) per annum, whilst the pro-

Table 2 Mean annual percentage change (with 95% confidence intervals) in mortality rate, case fatality rate, and proportion of total deaths due to tuberculosis at each disease site for the years 1972–92

	Mean % annual change in tuberculosis mortality rate	*Mean % annual change in tuberculosis case fatality rate*	*Mean % annual change in proportion of all tuberculosis deaths*
All tuberculosis	−5·6 (−6·3 to −4·9)	−0·9 (−1·7 to −0·1)	
Respiratory tuberculosis	−6·1 (−6·8 to −5·3)	−1·3 (−2·1 to −0·5)	−0·4 (−0·6 to −0·2)
CNS tuberculosis	−5·4 (−7·4 to −2·7)	−3·3 (−6·1 to −0·2)	+0·2 (−1·9 to +2·3)
Other tuberculosis	−3·5 (−4·3 to −2·7)	+1·01 (+2·2 to −0·2)	+2·15 (+1·5 to +2·7)

All statistically significant results are underlined.

Table 3 Mean annual percentage change (with 95% confidence intervals) in the proportion of notifications of, and deaths from, tuberculosis in subjects aged over 75 years for the years 1973–92

	Respiratory tuberculosis	*CNS tuberculosis*	*Other tuberculosis*
Annual % change in proportion of total deaths in patients aged over 75 years	+3·2 (+2·2 to +4·2)	+9·1 (−3·1 to +21)	+3·2 (+2·2 to +4·3)
Annual % change in proportion of total notifications in patients aged over 75 years	−0·03 (−0·3 to 0·2)	+2·6 (1·5 to 3·8)	+0·25 (−0·5 to 1)

All statistically significant results are underlined.

Table 4 Mean annual percentage change in case fatality rate due to respiratory tuberculosis and tuberculosis at "other" sites according to age group during the years 1973–92

	"Other" case fatality	*Respiratory case fatality*
0–14 years	−31·6 (−52 to −8·7)	−2·7 (−5 to −3·3)
15–44 years	−2·1 (−4·4 to +0·2)	−2·4 (−4·6 to −0·3)
45–74 years	−1·8 (−3·3 to −0·4)	−2·3 (−3·2 to −1·4)
>74 years	+1·3 (+2·8 to −0·2)	−2·9 (−3·8 to −2)
All age groups combined	+1·01 (+2·2 to −0·2)	−1·3 (−2·1 to −0·5)

All statistically significant results are underlined.

portion of deaths at all sites due to CNS disease did not change, +0·2% (−1·9% to +2·3%) per annum. Deaths due to disease at other sites therefore made up an increasing proportion of total deaths, increasing by 2·15% (1·5% to 2·7%) per annum (table 2).

Table 4 shows the mean annual percentage change in the case fatality rate at respiratory and "other" sites for the different age groups. The case fatality rate decreased significantly in all age groups for respiratory disease, but for disease at "other" sites it decreased in the groups aged 0–14 years and 45–74 years, was unchanged in the group aged 15–44 years, and in the group aged over 75 years it showed an upward trend of 1·3% (+2·8% to −0·2%) per annum.

For 1992, the most recent year for which published data are available, the overall mortality for tuberculosis was 8·15 per one million population and the case fatality rate was 7·21%.

Discussion

Data compiled by the OPCS have several shortcomings that could affect the accuracy of mortality and morbidity data – for example, undernotification[12] and false notifications which are not later denotified. Although these problems exist, we have no evidence that they have varied nationally over the period of the study. OPCS data, with all their imperfections, are the best national morbidity and mortality data that cover the time period under study. The OPCS defines a death from tuberculosis when the patient is "thought" to have died from tuberculosis by the doctor completing the death certificate.

As 90% of patients who die from tuberculosis do so within six months of the start of their treatment,[13] patients who die from tuberculosis will usually have been notified as having the disease within a relatively short period of the time of death.

Conversion factors were published by the OPCS in 1984 to correct previous data. The conversion factors were introduced after it was realised that many deaths were being misclassified, the terminal event being given rather than the real cause of death. The use of these conversion factors, all of which were produced on data collected in a single year (1984), may produce inaccuracies but are the recommended method for comparing quantitatively death rates before and after 1984.

The mortality rate for tuberculosis has continued to decrease but this has mainly been due to a decrease in the number of cases as seen by the decline in notifications. However, the increase in tuberculosis notifications in England and Wales since 1987[14] has not been matched by a rise in mortality,[15] and has occurred mainly in young peple and at "other" sites and is therefore probably due to non-respiratory tuberculosis in immigrants which (excluding meningitis) has a low mortality rate.

Although the mortality rate has fallen by 5·6% per annum, the case fatality rate has decreased less. There are a number of possible reasons for this. Firstly, there has been an increase in the proportion of tuberculosis in the elderly and, as people in this age group are more likely to die from their disease, the relative increase in notifications is likely to result in an increase in the case fatality rate. Secondly, as 50% of people who die from tuberculosis do so either before or within two weeks of starting their treatment,[13] improvements in medical care and chemotherapy are unlikely to have much effect on the case fatality rate. Education leading to earlier recognition and prompt treatment are likely to be more helpful. Thirdly, the proportion of deaths due to disease at "other" sites has increased, as shown in this study. These include tuberculosis of the bones, joints, gastrointestinal tract, kidneys and, most importantly, miliary tuberculosis, and account for 20–28% of all notifications. That case fatality and the proportion of total deaths is rising only in this group could be due to the disease not presenting in a characteristic and easily recognisable pattern. Therefore, as the level of expertise in tuberculosis falls with the decrease in notifications,[16,17] the ability to recognise dis-

ease at non-respiratory sites diminishes, leading to delay in treatment and increased mortality. The increase in the case fatality rate and in the age at presentation of miliary tuberculosis seen in Edinburgh over the last 40 years supports this.[18] It has been suggested that, as an epidemic of tuberculosis in a population wanes due to the increased development of immunity, a greater proportion of disease is likely to occur in the elderly and to be non-respiratory.[19] Our findings support this hypothesis.

Although HIV related tuberculosis is more likely to occur at other sites, it does not seem to play a large part in the level of tuberculosis in England and Wales[20] and is unlikely to be the cause of the increase in the proportion of deaths due to tuberculosis at other sites as this occurred only in the group aged over 75 years.

Non-respiratory tuberculosis is more common in the non-white immigrant population.[21] However, tuberculosis in immigrants tends to occur at a younger age and has a lower case fatality rate than in the white population. Thus, although immigration may be responsible for the increase in tuberculosis morbidity,[14] it is unlikely to be the cause of the increase in the proportion of deaths due to disease at "other" sites. Non-respiratory disease in the white population is likely to include cases of miliary and disseminated or "crytogenic" disease which have a high fatality.

The increase in the number of cases in the elderly may add to the difficulties in diagnosis, as older patients often present with non-specific symptoms and so come under the care of physicians who may have no specialist respiratory background, and who may overlook the diagnosis.[22,23] There were 194 deaths due to tuberculosis in this age group in 1992; of these, 42 were at "other" sites, similar to that seen 20 years earlier despite a dramatic fall in the number of notifications and deaths from respiratory tuberculosis over the same period. Miliary and bone and joint tuberculosis accounted for most of these 42 deaths.

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