

Motor neuron disease and multiple sclerosis mortality in Australia, New Zealand and South Africa compared with England and Wales

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Abstract

There has been a marked increase in the reported mortality from motor neuron disease (MND) but not multiple sclerosis (MS) in England and Wales and in a number of other countries. A comparison has been made of the mortality from MND and from MS for two time periods in Australia, New Zealand and South Africa. An increase in MND mortality occurred in Australia and New Zealand between 1968-77 and 1978-87, greater than that which occurred in England and Wales, but there was no increase in MS mortality. Among the white population of South Africa, the MND mortality was half of that in England and Wales, Australia and New Zealand in both time periods. Both MND and MS mortality is higher in the English-speaking than in the Afrikaans-speaking white South African-born. The marked increase in MND mortality which has now been reported from many countries, is good evidence that an environmental factor is important in causing this disease. The large differences in MND mortality in different populations may be important clues to the environment factors causing the disease.

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The mortality from motor neuron disease (MND) has increased in England and Wales and in many other countries,¹⁻⁴ but there has been no similar increase in multiple sclerosis (MS) mortality.^{5,6} The major differences in the prevalence of MS in Australia,⁷ New Zealand,^{8,9} and particularly in South Africa,¹⁰ compared with England and Wales, prompted a similar study of the mortality from MND, and from MS as a control disease, during two periods in Australia, New Zealand and South Africa.

Method

The Office of Population Censuses and Surveys (OPCS), London, provided the reported mortality from MND and MS in England and Wales by sex and five-year age groups. These mortality statistics were then studied in two ten-year periods, 1968-77 and 1978-87. The populations at risk were obtained from the OPCS based on the 1971 and 1981 censuses. We obtained similar

information from the Australian Bureau of Statistics, Belconnen, the New Zealand National Health Statistics Centre, Wellington, and from the South African Bureau of Censuses and Statistics, Pretoria. Populations at risk were obtained from the same sources, based on the official censuses.

Birthplace was included on the death certificates in all three countries. In South Africa, however, birthplace had not been coded by the Central Statistics Office since 1978, and language group, whether English or Afrikaans-speaking, appeared on the death certificate, but was not coded. We therefore obtained copies from the Registrar of Deaths, Pretoria, of the death certificates of those who were coded as having died from MND and MS during the second ten-year period of our study, 1978-87 and also for the two subsequent years, 1988-89. A total of 94.4% of the MND and 89% of the MS death certificates were traced. Previous studies on MS prevalence had shown that MS was more common among the English-speaking than among the Afrikaans-speaking white South African-born and perhaps this also occurred in MND.¹⁰

To find out how frequently MND was noted on the death certificate, after it had been diagnosed during life, we obtained lists of patients diagnosed as having MND from the teaching hospitals of Groote Schuur and Belville, at the Cape, and at the General Hospital, Johannesburg. We ascertained from the Population Registrar which of these patients had died and how the death had been reported on the death certificate. The death certificates of 126 white patients diagnosed as having MND at three teaching hospitals in South Africa were traced. Among them, MND was reported as the primary cause of death in 81 or 64.3%, and as a contributory cause of death in 16 or 12.7%, compared with 68.3% and 11.3% in England and Wales.¹¹ Previous studies have shown that MS is reported on the death certificate as frequently, when diagnosed during life, in South Africa¹⁰ as in England and Wales.¹¹

Results were expressed as standardised mortality ratios (SMR) with rates from England and Wales taken as the standard. Confidence limits for SMRs were based on the exact method using the Poisson distribution. Statistical significance of an SMR was inferred if the relevant confidence interval (95% for $p < 0.05$; 99% for $p < 0.01$) did not include the null value of 100. Confidence intervals for the ratio of two SMRs in different groups was made using the binomial dis-

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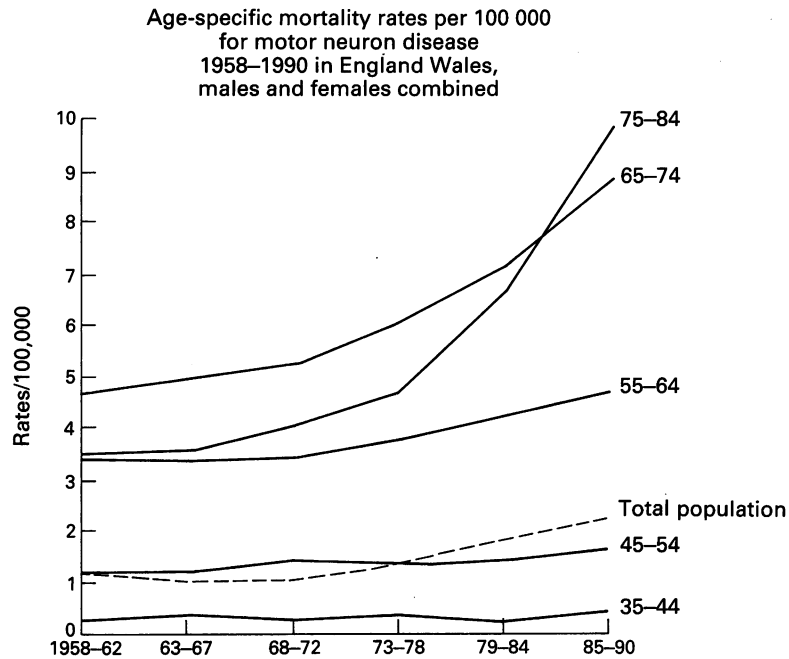


Figure 1.

tribution with significance inferred if the confidence interval did not overlap 1.0.¹²

Results

MOTOR NEURON DISEASE

Between 1958-62 and 1985-90, there was a 97.6% increase in MND mortality in England and Wales, an 83% increase in men and 116.5% in women. The greatest increase was in the older age groups, 65-74 and 75-84, (fig 1). In Australia, New Zealand and South Africa, there was also an increase in MND mortality (fig 2, male and female). England and Wales had an older population than Australia, New Zealand and South Africa, so that standardised mortality ratios (SMR) were calculated, with England and Wales rates by sex and age as the standard, for 1968-77 and 1978-87 for Australia and New Zealand and 1968-77 and 1978-79 for South Africa.

In Australia there was an increase in MND deaths from 1355 (779 male, 576 female) to

2313 (1,278 male, 1035 female) between the two time-periods (table 1). Deaths from MND were significantly lower in 1968-77 ($p < 0.01$) and significantly higher in 1978-87 ($p < 0.01$) than expected at England and Wales rates for native-born Australians, immigrants from the United Kingdom and for all Australians.

Also, in New Zealand there was an increase in MND mortality, from 345 (200 male, 145 female) to 579 (312 male, 267 female), between the two time-periods. There was no significant difference in the MND mortality between New Zealand and England and Wales in 1968-77, but in the second ten-year period, 1978-87, the MND mortality was significantly higher than in England and Wales ($p < 0.01$) for both the native-born and the immigrants from the United Kingdom. The MND mortality in both New Zealand and Australia increased therefore more rapidly than the increase in England and Wales^{4,5} between the two time-periods.

During the twenty years studied, there were thirteen deaths reported from MND among the Maori population and 25.1 was the expected number at England and Wales rates. The Maoris had about half the mortality from MND reported in the New Zealand non-Maori population and in England and Wales.

There were 175 deaths reported as due to MND in South Africa in 1968-77 (88 males and 87 females) and 255 deaths during the 12-year period, 1978-89, (150 males and 105 females). The SMR in 1968-77 compared with England and Wales was 50.2 and, for 1978-89, 41 when based on the 94.4% of the MND death certificates traced. In both periods therefore the MND mortality was approximately half of that occurring in England and Wales.

Motor neuron disease is no more common among the white immigrants than among the white South African-born. Among the 209 white South African-born MND deaths in 1978-89, 112 were English-speaking and 97 Afrikaans-speaking. The English-speaking white South African-born had a higher MND mortality (SMR compared with England and

Figure 2 England and Wales —; Australia ---; New Zealand ·····; South Africa - - - -.

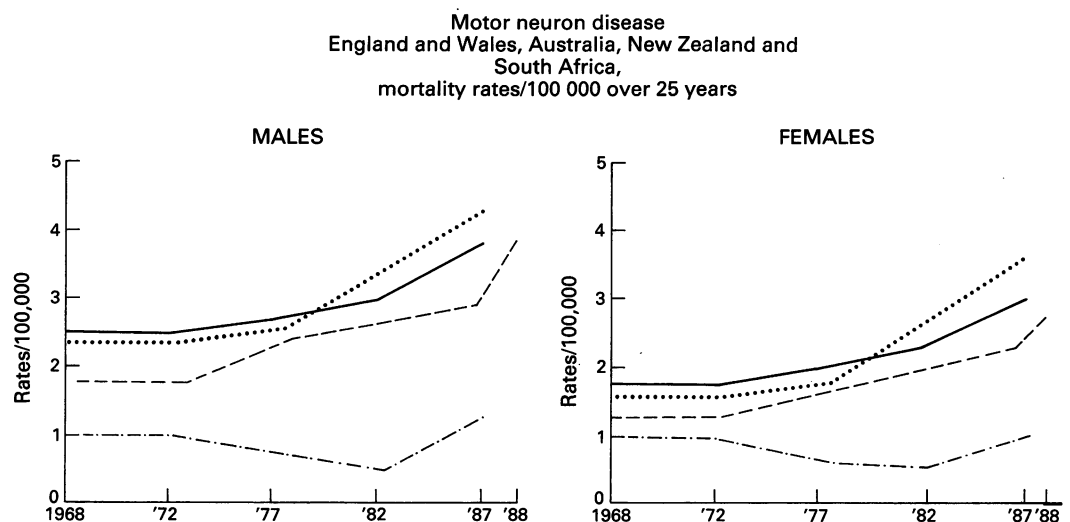


Table 1 Deaths in Australia, New Zealand and South Africa (White), standardised mortality ratios (SMR), based on the age and sex standardised expected mortality in England and Wales.

	Motor neuron disease											
	Australia				1968-77 New Zealand				South Africa			
	95% Confidence limits				95% Confidence limits				95% Confidence limits			
	Obs	SMR	Lower	Upper	Obs	SMR	Lower	Upper	Obs	SMR	Lower	Upper
Native Born	1021	93.9	(88.2	99.8*)	257	106.5	(93.9	120.4)	148	53.0	(44.8	62.2**)
UK Immigrants	181	101.2	(87.0	117.0)	66	113.4	(87.7	144.3)	12	39.5	(20.4	69.0**)
Other Immigrants	153	81.3	(69.0	95.3**)	22	78.9	(49.4	119.4)	15	45.7	(25.6	75.4**)
Total	1355	93.1	(88.3	98.2**)	345	105.4	(94.5	117.1)	175	50.2	(43.1	58.2**)
				1978-87								1978-89
Native Born	1728	114.3	(109.0**	119.8)	451	135.4	(123.1**	148.4)	209	40.0	(34.7	45.8**)
UK Immigrants	292	113.9	(101.2**	127.7)	96	137.1	(111.1**	167.5)	76	46.8	(34.3	62.4**)
Other Immigrants	293	98.5	(87.5	110.4)	32	104.9	(71.8	148.1)				
Total	2313	112.0	(107.4**	116.6)	579	133.5	(122.8**	144.8)	255	41.0	(36.2	46.4**)

* p < 0.05
** p < 0.01

Wales, 53.4; 99% CL 41.3-67.9) than the Afrikaans-speaking population (SMR 31.0; 99% CL 23.5-40.0), (p < 0.01).

MULTIPLE SCLEROSIS

Between 1958-62 and 1985-90, there was no significant change in the mortality rates from MS in England and Wales, nor in Australia, New Zealand or South Africa (fig 3, male and female).

The MS mortality in Australia, New Zealand and South Africa was significantly lower than in England and Wales (table 2, p < 0.01). It was higher in New Zealand than in Australia and low, as previously reported,¹⁰ in the South African white population. There were 728 MS patients in Australia (246 males, 482 females) in the first ten-year period and 711 (247 males, 464 females) in the second ten-year period. In New Zealand there were 264 deaths during 1968-77 (88 males, 176 females) and 255 during the second ten-year period (81 males, 174 females). The SMR for Australia compared with England and Wales was 43 in 1968-77 and 36.2 in 1978-87 and for New Zealand it was 71 in 1968-77 and 62.9 in 1978-87.

Among the Maoris of New Zealand, only two deaths were reported from MS during the twenty years studied and 35.9 was the expected number at England and Wales rates. The hospital records of one of the two Maori MS patients revealed that her mother was a Maori and her father was of European ethnic origin.

The previously reported very low mortality¹⁰ among white South Africans persisted.

The SMR for 1968-77 was 19 and for 1978-89 17.2, when based on the 89% of the MS death certificates traced. The SMR was 1.9 times as high (95% CL 1.3-2.8) among the immigrants from the United Kingdom than among the white South African-born over the 22 years studied (p < 0.05).

Among the 84 white South African-born MS deaths, in 1978-89, 44 were English-speaking and 40 were Afrikaans-speaking. The English-speaking white South African-born had a higher MS mortality (SMR, compared with England and Wales, 20.6; 95% CL 15.0-27.6) than the Afrikaans-speaking (SMR 11.8; 95% CL 8.5-16.1). The difference was just short of being significant at the 5% level.

During the 12 years studied, 1978-89, 33 MND and 8 MS deaths were reported among the 2.7 million (1980) Coloured people of South Africa. The Coloured, living mostly in Cape Province, are a younger population than the White and are the descendants of early white settlers and their slaves, who were mostly from Malaya and the East Indies. Twenty three MND and two MS deaths were reported among the 800 000 (1980) Asian population, mostly of Indian origin and living in Natal. Health care and death certification are not yet as good among the Coloured and Asian South Africans as among the white population but the reported MND and MS mortality confirmed previous studies that MS is relatively uncommon among these populations¹⁰ and that MND occurs more commonly than MS. Twenty seven MND and two MS deaths were reported in the 17 mil-

Figure 3 England and Wales —; Australia ---; New Zealand ·····; South Africa - - - - -.

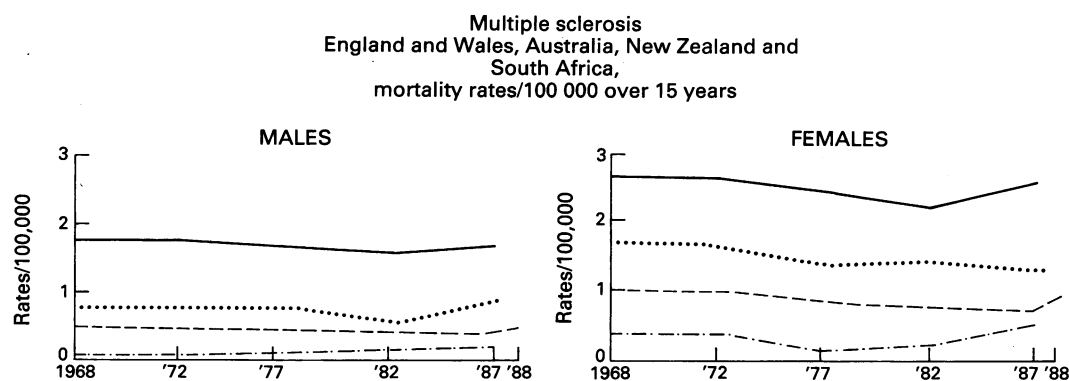


Table 2 Deaths in Australia, New Zealand and South Africa (White), Standardised Mortality Ratios (SMR), based on the age and sex Standardised Expected Mortality in England and Wales.

	Multiple Sclerosis													
	Australia				1968-77 New Zealand				South Africa					
	95% Confidence limits				95% Confidence limits				95% Confidence limits					
	Obs	SMR	Lower	Upper	Obs	SMR	Lower	Upper	Obs	SMR	Lower	Upper		
Native Born	575	45.9	(42.2	49.8)	216	76.8	(66.9	87.8)	60	16.8	(12.8	21.7)		
UK Immigrants	80	43.6	(34.6	54.3)	38	66.7	(47.2	91.5)	10	32.6	(15.6	59.9)		
Other Immigrants	73	28.6	(22.4	35.9)	10	29.9	(14.3	54.9)	11	28.2	(14.1	50.5)		
Total	728	43.0	(40.0	46.3)	264	71.0	(62.7	80.2)	81	19.0	(15.1	23.6)		
			1978-87											
Native Born	545	38.3	(35.1	41.6)	212	66.8	(58.1	76.4)	84	15.2	(12.2	18.9)		
UK Immigrants	84	37.9	(30.2	46.9)	31	54.7	(37.1	77.6)	25	29.0	(18.8	42.9)		
Other Immigrants	82	25.7	(20.5	31.9)	12	38.1	(19.7	66.5)	3	20.0	(4.1	58.4)		
Total	711	36.2	(33.6	38.9)	255	62.9	(55.4	71.1)	112	17.2	(14.1	20.7)		

All significant at $p < 0.01$.

lion (1980) Black population, excluding the Republics of Transkei, Bophuthatswana, Venda and Ciskei. Death certification in the black South Africans is incomplete.

Discussion

MND was used as a control disease in a previous study on the epidemiology of MS,¹³ because it was thought that the prevalence of MND was much the same in all parts of the world except for Guam and the Kii Peninsula.¹⁴ This is not correct¹⁵ because MND has been reported to be less common in Mexico than in North America¹⁶ and differences in MND mortality have been found within England and Wales¹⁷ and within the United States.¹⁸ The present report shows that there has been an increase in MND mortality in Australia and New Zealand, greater than occurred in England and Wales. However, in white South Africans the mortality was half of that which occurred in England and Wales and recently less than half of that in Australia and New Zealand. White South Africans have a high level of medical care and a similar proportion of those diagnosed during their life as having MND have the diagnosis on the death certificate in South Africa, as in England and Wales.

Among white South Africans MND mortality is not more common among immigrants from the United Kingdom and Europe than among the South African-born, but it is significantly higher among the English-speaking than among the Afrikaans-speaking white South African-born. There has been a fall in the male to female predominance of MND mortality in England and Wales and to a lesser extent in Australia and New Zealand, largely due to the increasing proportion of older women at risk. In South Africa in the first ten years studied, there was no difference between the male and female mortality, although recently there has been an increase in the reported MND mortality among men. This is perhaps due to the change in the environment that took place as more white South Africans moved to an industrial environment and became exposed to the environmental factor or factors.

The mortality from multiple sclerosis is higher in New Zealand than in Australia and

the lowest mortality is among the white South Africans, confirming previous prevalence studies.⁷⁻¹⁰ Among white South Africans MS is most common among immigrants from the United Kingdom and Europe and among the white South African-born it is more common among the English-speaking than it is among the Afrikaans-speaking. These mortality findings confirm previous prevalence studies, based on the 1961 Census,¹⁰ but the differences are not as marked. MS does occur among the Coloured and Asian people of South Africa but, until now, only one African has been reliably reported to have probable MS¹⁹ and among black Africans, MS appears to be very uncommon.

MND, therefore, like MS, is much less commonly reported as a cause of death in white South Africans than in England and Wales, or in Australia and New Zealand, and both diseases are less common among the Afrikaans-speaking than among the English-speaking white South Africans. There was in the past a considerable difference in the lifestyle of the English-speaking and the Afrikaans-speaking white South Africans, which might account for the difference in their MND and MS mortality. Until relatively recently, the English-speaking lived mostly in the cities and the Afrikaners, descendants of the Boers, lived more frequently in small towns or in rural areas.

There are limitations on the deductions which may be drawn from international mortality statistics and for controlling for differences in medical care.²⁰ It would appear unlikely that the low MND and very low MS mortality in South Africa could be due to poor diagnosis. Benatar *et al* showed that the level of medical care among the English and Afrikaans-speaking white population, the majority of whom are covered by health insurance, was high.²¹ When a diagnosis of MND was made in South Africa, it was as likely to be reported on the death certificate as in England and Wales. In spite of a big increase in the number of neurologists and specialist medical centres in South Africa, the reported mortality from MS has not increased over the years, evidence that the low reported prevalence and mortality in the past was not due to a failure to diagnose the disease. If MS was not overlooked in the past, at least before

death, it is unlikely that MND would be. The difference in MS mortality between the immigrants and the white South African-born has, however, lessened. Deaths reported from MND are much more common than from MS among the Coloured and Asian populations, but not as frequent as among the White population. Lower levels of medical care could account for a lower reported MND mortality among the Coloured and Asian, compared with the White population, or, the mortality among these groups could be genuinely lower. Among Asian immigrants to England—Indian and Pakistani—the MND mortality is less than half of that occurring in the general population of England and Wales.²²

The epidemiology of MS in South Africa mirrored that of poliomyelitis in adults before the advent of the Salk and Sabin vaccines.²³ Poliomyelitis was also more common among white immigrants than in the white South African-born and very uncommon among the non-white adult South Africans.²⁴ Martyn *et al* have suggested that MND may sometimes be a late consequence of a sub-clinical poliomyelitis virus infection.¹⁷ Virus infection could explain, at least partly, the lower MS and MND mortality in South Africa, an infancy infection from early contact with non-white servants leaving a life-long immunity as occurred with poliomyelitis in the past.

There appears to be a factor in the South African environment that protected against both MS and MND. There are a number of other epidemiological clues to the environmental factor, or factors, that may be responsible for MND. The disease is generally more common in males than females. Mortality rates from the disease have increased throughout the world. In England and Wales it is more common among skilled non-manual workers than among the professional or other social classes.^{25,26}

While MND occurs occasionally in two or more members of a family, this study is further evidence that an environmental factor or factors is of major importance in causing this distressing disease. The differences that occur in mortality from MND among the various communities of South Africa and elsewhere, should be important clues to the environmental factors responsible for the disease.

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