Mortality rates from multiple sclerosis: geographical and temporal variations revisited

Edward S Williams, David R Jones, Ronald O McKeran

Abstract
A review of the United Kingdom (UK) multiple sclerosis (MS) literature suggests that over the last three decades prevalence and estimated incidence rates have increased, while mortality rates have been declining. UK mortality data over a 30 year period have been studied to examine temporal and geographical variations, to estimate changes in survival, and to examine the relationship between mortality and morbidity trends. The study has shown an overall decline in mortality throughout the UK of approximately 25% over the 30 year period ending in 1983, and a reduction in the mortality differential between Scotland, and England and Wales, but no positive correlation has been found between mortality and morbidity. The overall decline in death rate in females was 23% and in males 30% over the 30 years of the survey. The total number of deaths declined by 39% between the five year periods 1954-58 and 1979-83 in Scotland compared with a 10% decline for England and Wales. Estimated median age of death increased from 52 to 59 years and the improvement in survival over the period of study was similar for both countries and is unlikely to have contributed to the reduction in mortality differential. Within England and Wales regional mortality rates did not show a clear north-south gradient. The decline in the mortality differential between Scotland and England (if not artefactual) may provide an important aetiological clue in the search for the cause of multiple sclerosis, and the rate of decline suggests an environmental rather than a genetic aetiology.

Since Limburg hypothesised almost 40 years ago that the frequency of multiple sclerosis (MS) is related to the distance of the surveyed area from the equator,1 epidemiological research seeking clues to the aetiology of the disease has been dominated by consideration of the geographic distribution of the disease. In the early 1950s, for example, McAlpine and Compston's study of United Kingdom (UK) mortality rates supported the idea of a north-south gradient,2 and several subsequent prevalence surveys have also given support to the idea that Limburg's theory holds for the UK (table 1).3-13 Recently Swingler and Compston have suggested that the gradient in prevalence in the UK correlates with regional differences in the frequency distribution of HLA-DR2 antigens in normal individuals.14

An examination of temporal trends in multiple sclerosis may, however, be important in the search for aetiological factors. An analysis of UK prevalence surveys show two interesting trends. Firstly, surveys done in the 1980s record prevalence rates which are substantially higher than rates recorded in the 1950s. For example, an early survey in North West Scotland (1954) recorded a prevalence of 67 per 100 000 where as a recent survey in south London (1986) recorded a rate of 115.13 Secondly, prevalence has increased in each area in the UK which has been studied more than once. Three surveys of North East Scotland carried out in the 1970s produced rates of 127, 144 and 178 per 100 000 respectively.9-11 An examination of indirectly estimated incidence rates shows a clear temporal trend with the more modern surveys producing higher incidence rates than earlier surveys. In North East Scotland estimates of the incidence rates have increased from 3.0 per 100 000 per annum in 1953, to 5.3 in early 1970, to 7.5 in the late 1970s.9,11

A recent review of UK mortality data, on the other hand, has shown a significant decline in mortality throughout the UK between 1921-80.16 While an increase in survival will lead to an increase in prevalence with a corresponding decrease in mortality over the short term, it is not clear to what extent changes in survival account for the changes in prevalence described above.

The epidemiological picture of multiple sclerosis in the UK is therefore somewhat unclear with morbidity and mortality data showing temporal disease trends going in apparently different directions. To describe temporal and geographical trends in mortality we have studied UK mortality data over a 30 year period. The objectives of the survey were: 1) to examine temporal and geographical variations in mortality; 2) to estimate changes in survival as far as is possible from the available data, and 3) to examine the relationship between mortality and morbidity trends.

Methods
Annual numbers of deaths attributed to multiple sclerosis (as underlying cause)15-16 and estimates of population in England and Wales, Scotland and Northern Ireland were taken from published sources for the period 1954–83,
Mortality rates from multiple sclerosis: geographical and temporal variations revisited

<table>
<thead>
<tr>
<th>Area</th>
<th>Year of survey</th>
<th>Surveyed population</th>
<th>Cases</th>
<th>Crude prevalence</th>
<th>Standardised prevalence ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northern Ireland</td>
<td>1951</td>
<td>1 370 709</td>
<td>700</td>
<td>51 (47-55)</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>1961</td>
<td>1 425 042</td>
<td>1158</td>
<td>81 (77-86)</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>1954</td>
<td>231 316</td>
<td>154</td>
<td>67 (56-77)</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>1958</td>
<td>338 770</td>
<td>214</td>
<td>63 (54-72)</td>
<td>68</td>
</tr>
<tr>
<td>Durham and Northumberland</td>
<td>1959</td>
<td>2 308 000</td>
<td>1156</td>
<td>90 (87-93)</td>
<td>56</td>
</tr>
<tr>
<td>Orkney11</td>
<td>1954</td>
<td>20 746</td>
<td>23</td>
<td>14 (12-15)</td>
<td>124</td>
</tr>
<tr>
<td></td>
<td>1962</td>
<td>18 531</td>
<td>33</td>
<td>178 (117-239)</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>1970</td>
<td>17 607</td>
<td>40</td>
<td>216 (161-307)</td>
<td>284</td>
</tr>
<tr>
<td></td>
<td>1974</td>
<td>17 462</td>
<td>54</td>
<td>309 (227-391)</td>
<td>384</td>
</tr>
<tr>
<td>Shetland11</td>
<td>1954</td>
<td>18 715</td>
<td>25</td>
<td>134 (81-185)</td>
<td>142</td>
</tr>
<tr>
<td></td>
<td>1962</td>
<td>17 537</td>
<td>29</td>
<td>165 (105-226)</td>
<td>184</td>
</tr>
<tr>
<td></td>
<td>1970</td>
<td>17 327</td>
<td>31</td>
<td>179 (116-242)</td>
<td>216</td>
</tr>
<tr>
<td></td>
<td>1974</td>
<td>18 449</td>
<td>34</td>
<td>194 (122-246)</td>
<td>234</td>
</tr>
<tr>
<td>North East</td>
<td>1970</td>
<td>440 176</td>
<td>557</td>
<td>127 (116-137)</td>
<td>153</td>
</tr>
<tr>
<td>Scotland11</td>
<td>1973</td>
<td>440 227</td>
<td>634</td>
<td>144 (133-155)</td>
<td>175</td>
</tr>
<tr>
<td></td>
<td>1980</td>
<td>471 000</td>
<td>859</td>
<td>178 (165-190)</td>
<td>221</td>
</tr>
<tr>
<td>London Borough of Sutton</td>
<td>1985</td>
<td>169 600</td>
<td>195</td>
<td>115 (99-131)</td>
<td>129</td>
</tr>
</tbody>
</table>

*Based on prevalence rates in the 1961 Northern Ireland study.

for each sex and age group 15–34, 35–44, 45–54, 55–64 and 65 and over. Corresponding annual death and population data were collected for the nine standard English regions, for the period 1974–83.

Annual age and sex specific death rates per 100 000 population were calculated for England and Wales, Scotland and Northern Ireland for the period 1954–83. Standardised mortality ratios (SMRs) were calculated for England, Scotland and Northern Ireland for the same period, using 1974 death rates in the UK as standard.

Poisson regression models18 19 were used in assessing linear trends in mortality rates with calendar period, and in examining the relationship between variations with area, calendar period and age group. The model reported is equivalent to assuming that the number of observed deaths Oik in the jth age group (j = 1, . . . 6: 15–34, 35–44, 45–54, 55–64, 65–74, 75+) and kth country (j = 1, 2, 3: England and Wales, Scotland, Northern Ireland) and kth year (k = 1, . . . 30: 1954, . . . 1983) are independent Poisson variables whose means satisfy: log E (Oi k) = log (Pi k) + constant + αj + β1x + αj + β2x, where Pi k is the number of person years at risk20 in the jth category and x the time in years from 1953; autocorrelation between observations in successive years is thus ignored. Age group—calendar period of death—birth cohort effects were investigated by following a variety of approaches,11 21 using cohorts defined by 10 year age groups and calendar periods.

Results

MORTALITY BY AGE, SEX AND CALENDAR PERIOD OF DEATH

The number of MS deaths at age 15 and over recorded in England and Wales, Scotland and Northern Ireland from 1954–83 and corresponding crude death rates are shown in table 2. In all three countries the male:female mortality ratio is approximately 2:3, in accordance with previous accounts22 of the epidemiology of MS. Apparently higher rates in Scotland and Northern Ireland than in England and Wales agree with the latitudinal hypothesis.

However, as Figs 1 and 2 show there are clear time trends over the thirty year period and marked variations in mortality between age groups. From Fig 1 it is apparent that crude death rates have fallen over the thirty year period in the UK as a whole. The female death rate at ages 15 and over declined from 3-2 per 100 000 in 1954 to 2-45 in 1983, a fall of about 23%; the male death rate declined from 2-3 to 1-6, a fall of about 30%. These findings are confirmed by the decline in the number of deaths set out in table 3. From this table it is clear that the fall has been much more marked in Scotland (39% between the first and last five year periods shown) and possibly also in Northern Ireland (27%) than in England and Wales (10%).

The main features of the death rates for females in England and Wales in fig 2 are that 1) the highest death rates have been seen in the 45–64 year age group; 2) in both this group and the 15–44 age group death rates have been declining steadily through the period, but 3) rates in the 65+ group have been increasing.

Similar patterns appear to be present in the results for Scotland with the important exception that rates in the over 65s would seem to have declined somewhat, explaining the sharper overall decline seen in table 3. In Northern Ireland the scatter of annual rates is much wider, the rates being based on much smaller numbers than in England and Wales, and clear trends are difficult to discern. In the corresponding male mortality rates the separation of

Table 2 Number of deaths, and average annual death rates per 100 000 from multiple sclerosis at age 15 and over, 1954–83, by country and sex

<table>
<thead>
<tr>
<th>Country</th>
<th>Males Rate/100000 Deaths</th>
<th>Females Rate/100000 Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>England and Wales</td>
<td>1.77</td>
<td>9370</td>
</tr>
<tr>
<td>Scotland</td>
<td>2.79</td>
<td>1543</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>2.71</td>
<td>415</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1.91</td>
<td>11328</td>
</tr>
</tbody>
</table>

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rates in the 65+ and 45–64 age groups is generally not apparent and time trends much less marked except in the 15–44 age group, and perhaps in the older age groups in Scotland.

The use of the SMR as a summary measure in the presence of contrary time trends such as those in the age specific England and Wales death rates is potentially misleading but SMRs for every tenth year during the study period are presented for reference in table 4. Deaths at ages 65 and over account for about 22% of those at all ages from MS in the UK. Consequently whereas the overall impression of time trends in mortality rates in Scotland and Northern Ireland is downwards as the summary SMRs in table 4 indicate, in England and Wales the opposite age specific trend have largely compensated each other. The sharper decline in SMRs in Scotland and Northern Ireland than in England and Wales over the period corresponds to a narrowing of differentials in overall mortality over the period.

All of these descriptive results are confirmed and shown more clearly by the results of Poisson regression analysis of the data. The coefficients of a model for female mortality comparing age group, country, and time trend terms are shown in table 5. The intercept coefficients clearly show that death rates are higher in Scotland and Northern Ireland than in England and Wales, and suggest that they are highest in the 45–54 and 55–64 age groups.

There is evidence for an overall downward trend with time in all age groups except 65–74 and 75+ and steeper declines in Scotland and Northern Ireland than in England and Wales. Results of a corresponding model for male mortality are very similar.

**ANALYSIS OF BIRTH COHORT EFFECTS IN MORTALITY**

In the previous section analyses of variations in MS mortality rate with calendar period have been reported. However, without further possibly arbitrary assumptions such effects are not distinguishable from those attributable to variations between birth cohorts, and thus interpretation of the data and of the regression models may be problematical. (A linear drift is clearly identifiable, but second order non drift effects do not show a clear pattern.) Nonetheless, one interpretation of the results of a Poisson regression model incorporating only age and cohort terms is that mortality is considerably lower in cohorts whose birth centred around 1938, and in later cohorts, than in the earlier cohorts. This is consistent with the pattern of cohort specific rates for England and Wales presented by Li et al. 25

**CUMULATIVE MORTALITY**

Cumulative mortality for the five year periods 1954–58 and 1979–83 are presented in table 6. Whereas 60% of the MS population of the UK had died by age 55 in the earlier period, only 39% had died in the more recent period, suggesting longer survival. Estimated median ages at death were 52 in 1954–58, and 59 in 1979–83. Changes in cumulative mortality between 1954–58 and 1979–83 were similar in the three countries. Thus on the further assumption that median ages of onset are similar in each country, (estimated to be around 34 years in various prevalence surveys) and that the age at onset had not changed during the period of the survey, it follows that survival experiences have changed
Mortality rates from multiple sclerosis: geographical and temporal variations revisited

at approximately the same rate in all three countries.

MORTALITY BY REGION
Mortality data by standard region for each of the ten years 1974–83 by age group and sex as before have been examined in similar ways. Numbers of deaths by region are, however, so small that age specific trends are difficult to identify graphically. The results of Poisson modelling as before (with region replacing country) are summarised in Table 7. Standardised mortality ratios for the 10 year period by region are shown in table 8. Neither analysis offers evidence supporting the existence of a

north–south gradient in mortality within England, although the SMRs for Scotland are raised. Other differentials and trends in the model are consistent with those to be expected from the country based model in table 5. The most interesting feature of the SMRs in table 8 is the occurrence of apparently low levels of mortality from MS in the West Midlands and in Wales. There is some corroboration for these findings in the model results in table 7, although the strong upward trend with time in the West Midlands should be noted. The results of a corresponding model for male mortality are less clear.

MULTIPLE SCLEROSIS AS UNDERLYING AND CONTRIBUTORY CAUSE OF DEATH
The data used in this study are based on MS recorded as the underlying cause of death on the certificate. Other mentions of MS (as a contributory cause of death) have not been coded routinely throughout the study period and so do not appear in published data.

The coding of all mentions of a particular cause of death (multi-cause) began in 1972 in England and Wales on a sample of certificates. In 1977, for example, of 1030 certificates on which MS was mentioned as a cause of death, 707 had MS recorded as the underlying cause, suggesting that use of an underlying cause alone underestimates deaths of MS sufferers by about 30%. In 1985 the percentage of underlying deaths was again 70% of all mentions of MS on death certificates.24 In Scotland the percentage of MS mentions which are coded as underlying cause also appears to be quite constant over time, with 1017 out of 1970 (52%) being recorded as an underlying cause in the period 1975–84.25

Figure 3 Prevalence ratios and crude mortality rates per 100 000 by area over time.

Table 8 Standardised mortality ratios (and 95% confidence intervals) from multiple sclerosis by sex and region, 1974–83

<table>
<thead>
<tr>
<th>Region</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yorkshire</td>
<td>106 (94–118)</td>
<td>98 (89–107)</td>
</tr>
<tr>
<td>Northern</td>
<td>95 (82–110)</td>
<td>103 (92–116)</td>
</tr>
<tr>
<td>North West</td>
<td>96 (86–100)</td>
<td>96 (88–103)</td>
</tr>
<tr>
<td>East Midlands</td>
<td>96 (84–110)</td>
<td>97 (87–108)</td>
</tr>
<tr>
<td>West Midlands</td>
<td>84 (74–95)</td>
<td>88 (80–97)</td>
</tr>
<tr>
<td>East Anglia</td>
<td>95 (78–115)</td>
<td>104 (89–120)</td>
</tr>
<tr>
<td>South East</td>
<td>100 (94–106)</td>
<td>102 (97–107)</td>
</tr>
<tr>
<td>South West</td>
<td>92 (81–104)</td>
<td>100 (91–110)</td>
</tr>
<tr>
<td>Wales</td>
<td>86 (73–102)</td>
<td>75 (65–86)</td>
</tr>
<tr>
<td>Scotland</td>
<td>139 (126–154)</td>
<td>124 (114–134)</td>
</tr>
</tbody>
</table>

Table 5 Parameter estimates from Poisson regression models of observed deaths in females by country, year and age group

<table>
<thead>
<tr>
<th>Factor</th>
<th>Intercept (SE)</th>
<th>Time trend (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>-4.85 (0.06)</td>
<td>-0.03 (0.003)</td>
</tr>
<tr>
<td>Age group (vs 14–34 group)</td>
<td>1.49 (0.07)</td>
<td>0.006 (0.004)</td>
</tr>
<tr>
<td>35–44</td>
<td>1.91 (0.06)</td>
<td>0.017 (0.004)</td>
</tr>
<tr>
<td>45–54</td>
<td>1.83 (0.06)</td>
<td>0.029 (0.004)</td>
</tr>
<tr>
<td>55–64</td>
<td>1.44 (0.07)</td>
<td>0.041 (0.004)</td>
</tr>
<tr>
<td>65–74</td>
<td>0.91 (0.10)</td>
<td>0.047 (0.005)</td>
</tr>
<tr>
<td>Country (vs England and Wales)</td>
<td>0.55 (0.04)</td>
<td>-0.014 (0.003)</td>
</tr>
<tr>
<td>Scotland</td>
<td>0.53 (0.08)</td>
<td>-0.009 (0.005)</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>-0.53 (0.05)</td>
<td>-0.009 (0.005)</td>
</tr>
</tbody>
</table>

Deviance 634.5 on 524 df. (Null model deviance 10615 on 539 df).

Table 6 Cumulative mortality by age group and country for periods 1954–58 and 1979–83

<table>
<thead>
<tr>
<th>Cumulative percentage deaths 1954–58</th>
</tr>
</thead>
<tbody>
<tr>
<td>By age</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>35</td>
</tr>
<tr>
<td>45</td>
</tr>
<tr>
<td>55</td>
</tr>
<tr>
<td>65</td>
</tr>
<tr>
<td>75+</td>
</tr>
</tbody>
</table>

1979–83

<table>
<thead>
<tr>
<th>By age</th>
<th>Scotland (n = 492)</th>
<th>England and Wales (n = 3671)</th>
<th>Northern Ireland (n = 145)</th>
<th>United Kingdom (n = 4308)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>6</td>
<td>6</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>45</td>
<td>20</td>
<td>17</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>55</td>
<td>38</td>
<td>38</td>
<td>40</td>
<td>39</td>
</tr>
<tr>
<td>65</td>
<td>68</td>
<td>69</td>
<td>68</td>
<td>69</td>
</tr>
<tr>
<td>75+</td>
<td>90</td>
<td>91</td>
<td>88</td>
<td>91</td>
</tr>
</tbody>
</table>

Table 7 Parameter estimates from Poisson regression model of observed deaths in females by region, year and age group

<table>
<thead>
<tr>
<th>Factor</th>
<th>Intercept (SE)</th>
<th>Time trend (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>-5.51 (0.14)</td>
<td>-0.002 (0.021)</td>
</tr>
<tr>
<td>Age group (vs 14–35 group)</td>
<td>1.65 (0.16)</td>
<td>-0.026 (0.025)</td>
</tr>
<tr>
<td>35–44</td>
<td>2.96 (0.14)</td>
<td>-0.057 (0.023)</td>
</tr>
<tr>
<td>45–54</td>
<td>2.55 (0.14)</td>
<td>-0.013 (0.022)</td>
</tr>
<tr>
<td>55–64</td>
<td>2.44 (0.14)</td>
<td>-0.009 (0.023)</td>
</tr>
<tr>
<td>65–74</td>
<td>1.45 (0.17)</td>
<td>-0.026 (0.027)</td>
</tr>
<tr>
<td>Region (vs South East)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>North West</td>
<td>0.07 (0.10)</td>
<td>-0.026 (0.017)</td>
</tr>
<tr>
<td>East Midlands</td>
<td>-0.04 (0.13)</td>
<td>-0.02 (0.021)</td>
</tr>
<tr>
<td>West Midlands</td>
<td>0.04 (0.13)</td>
<td>0.045 (0.019)</td>
</tr>
<tr>
<td>East Anglia</td>
<td>-0.20 (0.17)</td>
<td>0.039 (0.027)</td>
</tr>
<tr>
<td>Yorkshire</td>
<td>-0.19 (0.11)</td>
<td>0.028 (0.027)</td>
</tr>
<tr>
<td>South West</td>
<td>-0.02 (0.11)</td>
<td>0.0001 (0.019)</td>
</tr>
<tr>
<td>Wales</td>
<td>-0.35 (0.16)</td>
<td>0.026 (0.026)</td>
</tr>
<tr>
<td>Northern</td>
<td>-0.13 (0.13)</td>
<td>0.026 (0.021)</td>
</tr>
<tr>
<td>Scotland</td>
<td>0.15 (0.13)</td>
<td>-0.003 (0.022)</td>
</tr>
</tbody>
</table>

Deviance 578.8 on 540 df. (Null model deviance 3708.4 on 569 df).
MORTALITY RATES AND PREVALENCE RATIOS BY
AREA AND TIME PERIOD
As fig 3 shows, although no overall relationship
between crude prevalence ratios reported in the
UK surveys summarised in table 1 and the best
current estimate of mortality in the same
area can be seen, there are some clear within
area time trends. These are particularly
apparent for the North (East) Scotland and
Orkney rates, but not for the Shetland rates. It
should be noted firstly, however, that the
mortality rates used for all of these area
comparisons are those for the \textit{whole} of Scotland
(more local rates being unobtainable, or subject
to large variance) and secondly that the
prevalence ratios are themselves subject to
wide sampling errors.

\section*{Discussion}

The most important findings of this study are:
1) an overall decline in mortality throughout
the UK of about 25% over the 30 year period
during in 1983; 2) a reduction in the mortality
differential between Scotland on the one hand
and England and Wales on the other; 3) no
positive correlation between morbidity and
mortality.

\section*{Overall Decline in MS Mortality}

This study has demonstrated an overall decline
in MS death rates for females of 23\% and for
males of 30\% over the 30 years of the survey.
One possible explanation for the decline in
mortality is that the observed trend may not be
real but artefactual. Changes may have occurred in the recognition or diagnosis of the
disease, in the way doctors certify MS, or in the
rules and procedures for the coding of the
disease. In fact there is no evidence to suggest
that any of these factors have contributed to the
decline. On the contrary, improvements in
diagnostic techniques and an increase in aware-
ness of the disease are more likely to have led to
an increase in the number of cases diagnosed.

Factors which would cause a real decline in
mortality include an improvement in survival over
the short term or a true decrease in the incidence of the disease. While the data used in
this survey do not permit a true calculation of
survival times because there is no clear and well
defined starting point, nevertheless, certain
inferences about survival can be made if one
assumes little change in the median age of onset
as Limburgh suggests.\cite{Limburgh} Moreover, a number of
UK prevalence surveys have shown the average
age of onset to be around 34 years,\cite{3,4,13}
and there is no clear evidence, to suggest any
significant change over time. Assuming then
the age of onset to be constant over the period
of the survey, the data in table 6 suggest an
improvement in median survival over the
period of the survey which would have con-
tributed to the overall decline in mortality.

\section*{Reduction in Mortality Differential
between Scotland, and England and Wales}

The fact that Scotland has relatively high rates
of MS compared with England and Wales is
consistent with Limburgh's latitudinal
hypothesis. In this survey, however, a clear
reduction in the mortality differential between
Scotland, and England and Wales has been
shown. The total number of deaths (table 3)
decreased by 39\% between 1954–58 and 1979–
83 in Scotland compared with a 10\% decline
for England and Wales. The estimated
improvement in survival over the period of the
study, however, is similar for both countries
(table 4), and so is unlikely to have contributed
to the reduction in mortality differential.

The possibility that artefactual factors, such as
changes in diagnostic criteria, disease aware-
ness, and in certifying and coding practice, play
a role again needs to be mentioned. It is
possible that differences in these factors have
led to biases in the collection of MS data
between England and Scotland which may
have contributed to the observed trends. A
validation study comparing death certification
with clinical data is needed to clarify this
question. Nevertheless, it remains possible that
a real decrease in the incidence of MS has
occurred in Scotland. If this is indeed the case
then it could provide an important aetiological
clue to the cause of MS. Moreover, in view of
the short time scale of change, any dissipating
aetiological agent responsible for the diminish-
ing latitudinal gradient is likely to be environ-
mental rather than genetic.

\section*{Relative Value of Mortality and Morbidity
Data}

Another major question that is raised by the
findings of this survey is the relative value of
mortality and morbidity data. In this study we
found no overall positive correlation between
mortality and morbidity data. The overall
trend in mortality during the period of study
showed a gradual decline in the numbers of MS
cases coded as underlying cause, the fall being
about 25\% over the 30 year period. Morbidity
surveys, on the other hand, demonstrated large
increases in incidence and prevalence during
the 30 years of the survey. In the north of
Scotland, for example, prevalence increased
threefold.\cite{Williams, McKeran} During the same time period
the SMR in Scotland fell by more than half. The
previously reported findings that mortality and
morbidity data do not correlate have not been con-
firmed by this survey.\cite{Reliance on mortality data may, however,
lead to underestimation of prevalence. Published mortality data are based on underlying
cause and where MS is certified as a contrib-
uting cause of death it is not routinely coded.
The resulting degree of underestimation was
shown to be around 30\% for England and
Wales and nearly 50\% for Scotland. As dem-
onstrated in this paper the proportion of under-
estimation appears to be consistent over time
for both countries, and so mortality data based
on underlying cause can be a valuable tool for
observing trends and uncovering geographical
difference.

Mortality data have two strengths: its com-
pleteness, as virtually all deaths are certified and
coded, and the reliability of the diagnosis
(the doctor is unlikely to mention MS on the
certificate unless the diagnosis has been estab-
Mortality rates from multiple sclerosis: geographical and temporal variations revisited

lished with reasonable certainty). A further obvious advantage is that mortality data is collected on a routine basis, and so are widely available.

Morbidity (prevalence) data, on the other hand, suffers from incomplete geographic availability and from the disadvantage of diagnostic uncertainty. This is especially likely to be a problem in early cases as there is no definite confirmatory test which is positive in all cases. It seems possible that, under survey conditions where the aim is to ascertain cases, there is a danger of over diagnosing. Therefore diagnostic bias as a result of case finding, although it has never been measured, remains a possibility. Changes in diagnostic habits and different methods of ascertainment make comparisons between population surveys carried out at different times extremely difficult to interpret.

LATITUDINAL GRADIENT?

In his paper on the prevalence of MS in northern Scotland, Sutherland suggested MS was more common in Scotland than elsewhere in the UK. This view has been generally accepted, having been supported by the numerous population studies which make Scotland the most surveyed area in the world. Recently, however, Williams and McKeran in studying prevalence in South London questioned the extent of the north-south gradient.

This review provides evidence that the differential in mortality between Scotland and England has been declining during the survey period. Also there is no clear evidence of a latitudinal gradient in mortality south of the Scottish border.

If it is accepted that at the beginning of the survey period a real north-south gradient existed, then it seems plausible that an environmental factor has been operating to cause the gradient, and that its effect has been dissipating over time, more markedly in Scotland than England. The possibility, however, that an artefact was responsible for the original mortality differential between England and Scotland cannot be excluded.

25 Scottish Registrar General. Personal communication.
Mortality rates from multiple sclerosis: geographical and temporal variations revisited.
E S Williams, D R Jones and R O McKeran

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