Original Research

Changing patterns of neurological mortality in the 10 major developed countries — 1979–2010

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SUMMARY

Objectives: To examine whether there is a continued increase in neurological deaths in the major developed countries over the period 1979–2010.

Study design: Analyzes changing patterns of neurological deaths and Total Mortality of people aged 55–74 years by sex.

Methods: Baseline WHO 3-year average mortality for 1979–81 were compared with changes in 2008–10, for Total Mortality and the neurological categories Nervous Disease, and Alzheimer & other Dementias deaths in rates per million. To control for different diagnostic practice, the focus is upon Total Neurological Deaths in relation to Total Mortality and Odds ratios are calculated. UK Motor Neuron Disease, Parkinson’s disease and variant CJD are explored as possible constituent categories of Nervous Disease for other countries.

Results: Total Mortality fell substantially in every country, conversely, Nervous Disease and Alzheimer’s rose in seven and six countries respectively. Total Neurological Deaths for males and females increased significantly in Australia, Canada, England & Wales, Italy, the Netherlands and especially the USA.

Unlike motor neurone disease, variant CJD’ deaths in England and Wales did not contribute substantially to the overall neurological increases found.

Odds ratios indicated that neurological deaths differentially increased significantly in every country compared to Total Mortality.

Conclusions: These results pose a major public health problem, as the epigenetic contribution to these changes, rather than longevity, have serious implications indicating earlier onset of neurological morbidity pressurizing families, health and social care services, with resource implications especially for Australia, Canada, Italy, Netherlands, Spain, the UK and the USA.

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Introduction

Neurological disease affects 2% of the general population in England and Wales and has increased in recent years. Until recently neurological deaths were mainly included within two global categories, namely ‘mental disorder deaths’, which are deaths due to the dementias, and ‘other diseases of the nervous system and sense organs deaths’. This latter category included such disparate conditions as Parkinson’s disease, motor neurone disease, hereditary neuromuscular conditions, prion disorders, degenerative diseases, as well as Creutzfeldt Jacob’s Disease and variant CJD. In 2012 however, the WHO has narrowed ‘other diseases of the nervous system’ down to Nervous Disease Deaths, which is the former category but minus deaths related to sensory organs and the WHO produced data specifically for Alzheimer & other Dementia deaths for the whole period between 1979 and 2010, enabling the analysis of the other Nervous Disease deaths separately from the analysis of Alzheimer and other Dementia deaths. Thus the new categories are far more precise than the earlier global categories reported in 2004 and 2008, which reported data up to 2006, whereas the new configuration for most countries and for Total Neurological Disease deaths contains data up to 2010.

Most neurological disorders have a complex aetiology. Only a very few are exclusively genetically determined and an aetiological model of genetic vulnerability that interacts with environmental factors seems best to explain clusters of disease. Studies examining Alzheimer type mortality rates, found that population density was a surrogate marker for environmental exposure; whilst a similar link found was in relation to cancer deaths and there are reports of increasing dementia rates in some countries, as well as ‘early onset dementias’ as well as increasing younger aged motor neurone disease patients.

A previous examination of neurological deaths between 1979 and 1997 in ten major developed countries found evidence for notable rises in neurological mortality, indicating that these conditions may have been starting earlier. The 2012 WHO Mortality database now permits a later and much more accurate analysis of these trends up to 2010. This study has two a priori working null hypotheses, namely that between 1979–81 and 2008–10:

1. there would be no significant differences between Total Mortality and the combined Nervous Disease and Alzheimer’s & other Dementia deaths in the ten major developed countries; and
2. there would be no evidence of increases in the two categories of neurological deaths over the period.

Method

WHO format standardized mortality data were utilized to examine changes between baseline years (1979–81) and index years (2008–10) to be contrasted with Total Mortality, i.e. ‘All Causes of Death’ as a quasi ‘control’ group to compare the two neurological mortalities, Nervous Disease deaths and the separately reported Alzheimer’s & other Dementia deaths over the intervening years.
change for the neurological deaths by the ratio of changes for general mortality.

A simple example best illustrates the process. The UK male 55–74-year old Total Mortality Rate fell over the period giving a ratio of change of 0.45, whilst Total Neurological Deaths rose giving a ratio of 1.32. Dividing the ratios of change of 1.32 by 0.45 yields an Odds ratio of 2.93:1, indicating that compared to ordinary deaths neurological deaths rose very substantially over the period.

The Total Mortality rates are the context in which to contrast any changes over the period between general mortality and Total Neurological Disease deaths, which includes both Nervous Disease and Alzheimer’s & other Dementia deaths in people aged between 55 and 74 years, an age which is below the life-expectancy of most Western countries.39

The original 10 major developed countries, were chosen on the basis of their relatively larger populations, the smallest being the Netherlands at 16.6 million, ranging through Australia 20.4 million, UK 60.9 million and Germany 81.8million, to the US at 301.6 million. Of the other 10 smaller Western countries only Greece, Belgium and Portugal have populations in excess of 10 million, with five countries populations being fewer than 6 million, which are smaller than many American states.3 However, it was decided to take advantage of the new configuration, and whilst the focus remains upon the 10 major developed countries, data for the ten smaller Western states were also analyzed. It is acknowledged that amongst the 10 major countries reviewed; Australia, Canada, France, Germany, Italy, Japan, Netherlands, Spain, the UK and the USA, all have different types of healthcare systems; the USA being markedly different from the others in terms of the source of GDP expenditure on health mainly coming from ‘private’ sources.39 Indeed recent comparative research into cancer and general mortality outcomes for these 10 countries highlighted that there were markedly different outcomes, which appeared to reflect structural factors in patterns of health service provision.20,21

Some studies have suggested that apparent changes in neurological deaths may be due to recording or changes or improvements in diagnosis22-24 whilst conversely, some argued that there is an under-reporting of neurological deaths.1,5,23 To resolve this possible dilemma arising from possible diagnostic changes, whilst each neurological category is presented separately, the core comparative analysis will be between Total Mortality and Total Neurological Disease deaths, which include the separately calculated Nervous Disease and the Alzheimer’s and other Dementia deaths to determine are there any substantial changes over the period.

**Component diseases in Nervous Disease deaths**

There are many constituent conditions in the Nervous Disease category, many relatively very rare and the WHO does not report these separately. However, motor neurone disease and Parkinson’s disease rates, which are included in Nervous Diseases have shown an upward trend and that it may be that a ‘substantial percentage of neurological deaths are missed’,24 suggesting any changes found here might be an underestimate as these two sub-categories are a major constituent of Nervous Diseases. Another minority constituent would be all forms of Creutzfeld-Jakob Disease, which attracted considerable interest in Britain a decade or more ago, so CJD, motor neurone and Parkinson’s disease data are extrapolated,25,26 to determine whether these conditions might have contributed to the changes in the UK. The measurement of these three constituent disorders in the UK might serve as a surrogate indicator for the other countries possible constituent Nervous Disease deaths. All age rates for Creutzfeld–Jacob’s Disease had to be used25 as there was no matching of the WHO age bands so the eventual rates may be a slight overestimate.

**Statistical analysis**

Ratios of change in the death rates between the baseline and index years are produced, from which Odds ratios are calculated to demonstrate the degree to which Total Neurological Deaths and Total Mortality may have varied between 1979 and 2010. Spearman rank order correlations (Rho) are used to explore linkages between rates and ratio of change between the sexes and between total increases in the 2004–06 and 2008–10 outcomes.

**Results**

**Nervous Disease Deaths (minus Alzheimer’s) 1979–2010: Table 1** shows the rates per million (rpm) of Nervous Disease deaths by sex in the 10 developed countries between 1979–81 and 2008–10.

**Males:** Currently France has the highest male rate at 262 pm, followed by the UK at 242 pm and Germany at 239 pm, down to lows of 130 pm in Japan, 154 pm in Spain and 172 pm in the Netherlands, overall average being 203 pm.

**Ratios of change increased substantially in seven countries over the period, ranging from Japan at 1.60 to the three highest, Germany 3.85, Australia up 2.18, the UK 1.85 and the USA up 1.66, with an overall average of 203 pm, equivalent to a rise of 41% over the period. Conversely, there were notable falls in Italy 0.86 and the Netherlands 0.88.**

**Females:** Highest female deaths were in Canada 173 pm, the UK 169 pm and Germany at 157 pm, the lowest being in Japan at 78 pm, Spain 104 pm and the Netherlands at 109 pm, with an overall average of 137 pm.

**Ratios of change rose substantially for six countries the highest being Australia 2.72, Canada 1.88 and the UK 1.71, the USA 1.61 and notably, albeit from a low base rate, Japan up 1.53, then overall average was 137 pm which was equivalent to an increase of 32% over the period. However, there were falls in the Netherlands 0.84 and Italy 0.87.**

There were significant positive correlations between the sexes in regard to rates over the period (Rho = +0.802, P < 0.005) and ranked ratios of change (Rho = +0.564, P < 0.05).

**Alzheimer’s & Other Dementia deaths: Table 2** shows the changing pattern of Alzheimer type deaths over the period by sex.

**Males:** The highest mortality rate was again found in the USA currently at 186 pm, followed by Spain at 178 pm and Canada 150 pm, down to lows of 43 pm in Japan, 106 pm in
Australia and 109 pm in Germany. There was an overall average of 130 pm. Over the period Male ratios of change increased significantly in five countries and there were notable increases in Spain 2.70 and Italy 2.12 more than doubling and the USA at 1.65.

Conversely there were notable falls in Japan, Germany and Australia with ratios of change down 0.53–0.67.

Females: Again the USA had the highest rate at 187 pm, Spain 160 pm and the UK 146 pm, with lows in Japan 30 pm, Germany 88 pm and 101 pm in Australia, averaging in the ten countries 123 pm.

Over the period seven countries had clinically substantial rises in their ratio of change. Ratios of change more than doubled in three countries with substantial increases in Spain 3.70, Italy 2.57 and 2.27 in the USA, other notable increases were the Netherlands 1.49, Canada 1.38 and the UK 1.28. There were falls of 0.56 in Japan and 0.84 in Australia.

### Table 1 – Nervous diseases (minus Alzheimer's) deaths by sex rates per million [rpm].

<table>
<thead>
<tr>
<th>Country, latest comparative years</th>
<th>Rank of ratios of change</th>
<th>Total Nervous Disease deaths males</th>
<th>Total Nervous Disease deaths females</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008–10</td>
<td></td>
<td>239</td>
<td>157</td>
</tr>
<tr>
<td>Ratio of change</td>
<td></td>
<td>3.85</td>
<td>1.42</td>
</tr>
<tr>
<td>2] Australia 1979–81</td>
<td></td>
<td>85</td>
<td>50</td>
</tr>
<tr>
<td>2004–06</td>
<td></td>
<td>188</td>
<td>136</td>
</tr>
<tr>
<td>Ratio of change</td>
<td></td>
<td>2.18</td>
<td>2.72</td>
</tr>
<tr>
<td>3] UK 1979–81</td>
<td></td>
<td>131</td>
<td>99</td>
</tr>
<tr>
<td>2008–10</td>
<td></td>
<td>242</td>
<td>169</td>
</tr>
<tr>
<td>Ratio of change</td>
<td></td>
<td>1.85</td>
<td>1.71</td>
</tr>
<tr>
<td>2002–04</td>
<td></td>
<td>210</td>
<td>173</td>
</tr>
<tr>
<td>Ratio of change</td>
<td></td>
<td>1.49</td>
<td>1.88</td>
</tr>
<tr>
<td>5] USA 1979–81</td>
<td></td>
<td>134</td>
<td>97</td>
</tr>
<tr>
<td>2005–07</td>
<td></td>
<td>223</td>
<td>156</td>
</tr>
<tr>
<td>Ratio of change</td>
<td></td>
<td>1.66</td>
<td>1.61</td>
</tr>
<tr>
<td>2006–08</td>
<td></td>
<td>154</td>
<td>104</td>
</tr>
<tr>
<td>Ratio of change</td>
<td></td>
<td>2.17</td>
<td>1.06</td>
</tr>
<tr>
<td>7] Japan 1979–81</td>
<td></td>
<td>81</td>
<td>51</td>
</tr>
<tr>
<td>2007–09</td>
<td></td>
<td>130</td>
<td>78</td>
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<tr>
<td>Ratio of change</td>
<td></td>
<td>1.60</td>
<td>1.53</td>
</tr>
<tr>
<td>8] France 1979–81</td>
<td></td>
<td>295</td>
<td>165</td>
</tr>
<tr>
<td>2006–08</td>
<td></td>
<td>262</td>
<td>154</td>
</tr>
<tr>
<td>Ratio of change</td>
<td></td>
<td>0.90</td>
<td>0.93</td>
</tr>
<tr>
<td>9] Italy 1979–81</td>
<td></td>
<td>243</td>
<td>157</td>
</tr>
<tr>
<td>2006–08</td>
<td></td>
<td>208</td>
<td>136</td>
</tr>
<tr>
<td>Ratio of change</td>
<td></td>
<td>0.86</td>
<td>0.87</td>
</tr>
<tr>
<td>10] Netherlands 1979–81</td>
<td></td>
<td>196</td>
<td>130</td>
</tr>
<tr>
<td>2008–10</td>
<td></td>
<td>172</td>
<td>109</td>
</tr>
<tr>
<td>Ratio of change</td>
<td></td>
<td>0.88</td>
<td>0.84</td>
</tr>
<tr>
<td>Average 1979–81</td>
<td></td>
<td>144</td>
<td>104</td>
</tr>
<tr>
<td>2008–10</td>
<td></td>
<td>203</td>
<td>137</td>
</tr>
<tr>
<td>Ratio of change</td>
<td></td>
<td>1.41</td>
<td>1.32</td>
</tr>
</tbody>
</table>

Ranked by highest increases in ratios of change.

Male vs Female rates Rho = +0.8024, P < 0.005.

Male vs Female Ranked increases Rho = +0.5636, P < 0.05.

a Clinically significant results in **BOLD**.

### Table 2 – Alzheimer’s & other dementia deaths of 55–74-year olds rates per million [rpm].

<table>
<thead>
<tr>
<th>Country &amp; years 1979–81 vs latest comparative years</th>
<th>Males rpm</th>
<th>Females rpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1] Spain 1979–81</td>
<td>66</td>
<td>53</td>
</tr>
<tr>
<td>2006–08</td>
<td>178</td>
<td>160</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>2.70</td>
<td>3.02</td>
</tr>
<tr>
<td>2] Italy 1979–81</td>
<td>58</td>
<td>44</td>
</tr>
<tr>
<td>2006–08</td>
<td>123</td>
<td>113</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>2.12</td>
<td>2.57</td>
</tr>
<tr>
<td>3] USA 1979–81</td>
<td>113</td>
<td>82</td>
</tr>
<tr>
<td>2005–07</td>
<td>186</td>
<td>187</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.65</td>
<td>2.27</td>
</tr>
<tr>
<td>4] Netherlands 1979–81</td>
<td>114</td>
<td>94</td>
</tr>
<tr>
<td>2008–10</td>
<td>125</td>
<td>140</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.10</td>
<td>1.49</td>
</tr>
<tr>
<td>5] Canada 1979–81</td>
<td>135</td>
<td>104</td>
</tr>
<tr>
<td>2002–04</td>
<td>150</td>
<td>144</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.11</td>
<td>1.38</td>
</tr>
<tr>
<td>6] UK 1979–81</td>
<td>137</td>
<td>114</td>
</tr>
<tr>
<td>2008–10</td>
<td>138</td>
<td>146</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.01</td>
<td>1.28</td>
</tr>
<tr>
<td>7] France 1979–81</td>
<td>154</td>
<td>128</td>
</tr>
<tr>
<td>2006–08</td>
<td>140</td>
<td>122</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.91</td>
<td>0.95</td>
</tr>
<tr>
<td>8] Germany 1980–82</td>
<td>191</td>
<td>74</td>
</tr>
<tr>
<td>2004–06</td>
<td>106</td>
<td>101</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.67</td>
<td>0.84</td>
</tr>
<tr>
<td>10] Japan 1979–81</td>
<td>81</td>
<td>54</td>
</tr>
<tr>
<td>2007–09</td>
<td>43</td>
<td>30</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.53</td>
<td>0.56</td>
</tr>
<tr>
<td>Average 1979–81</td>
<td>128</td>
<td>86</td>
</tr>
<tr>
<td>2008–10</td>
<td>130</td>
<td>123</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.02</td>
<td>1.43</td>
</tr>
</tbody>
</table>

Ranked by highest increases in ratios of change.

Male and Female rates Rho = +0.9578, P < 0.001.

Male vs Female Ranked increases Rho = +0.9515, P < 0.001.

a Clinically significant results in **BOLD**.
There were very strong positive correlations in regard to the gender for both rates (Rho = +0.958, P < 0.001) and ranked ratios of change (Rho = +0.952, P < 0.001).

**Total Mortality rates contrasted with Total Neurological Deaths**

Total Mortality: Table 3a juxtaposes Total Mortality deaths (i.e. all deaths by all causes, by gender in columns 2 and 3) with Total Neurological Deaths (combined Nervous Disease and Alzheimer type deaths) and the ratios of change over the period.

Males: German Males had the highest Totally Mortality rates at 16360 pm, the USA 16288 pm and France 14776 pm to the lowest three countries Australia at 12061 pm, Japan 12700 pm and the Netherlands at 13017 pm, an overall average of 14158 pm, representing an overall reduction of 45%.

Every country’s male rates fell substantially, with the biggest reductions being in the UK falling 55%, in Australia by 54% and by 49% in the Netherlands, whilst the smallest declines were in Germany, 36%, Japan 37% and the USA 40%.

Females: US females had the highest female Total Mortality rate at 10635 pm, followed by the UK 9131 pm and Canada 8845 pm, the lowest being Japan 5501 pm, Spain 6164 pm and

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**Table 3a – Total mortality vs total neurological deaths by sex rates per million [rpm] and ratios of change.**

<table>
<thead>
<tr>
<th>Country, latest years &amp; combined rank</th>
<th>Total Mortality Deaths males</th>
<th>Total Mortality Deaths females</th>
<th>Total Neurological Deaths males</th>
<th>Total Neurological Deaths females</th>
</tr>
</thead>
<tbody>
<tr>
<td>1] USA</td>
<td>26981</td>
<td>14370</td>
<td>247</td>
<td>179</td>
</tr>
<tr>
<td>1979–81</td>
<td>16288</td>
<td>10635</td>
<td>409</td>
<td>343</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.60</td>
<td>0.74b</td>
<td>1.66</td>
<td>1.92b</td>
</tr>
<tr>
<td>2] Spain</td>
<td>22469</td>
<td>11746</td>
<td>217</td>
<td>151</td>
</tr>
<tr>
<td>1979–81</td>
<td>14571</td>
<td>6164</td>
<td>332</td>
<td>264</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.65</td>
<td>0.52</td>
<td>1.53</td>
<td>1.75b</td>
</tr>
<tr>
<td>3] Canada</td>
<td>24799</td>
<td>12696</td>
<td>276</td>
<td>196</td>
</tr>
<tr>
<td>1979–81</td>
<td>14278</td>
<td>8845</td>
<td>360</td>
<td>317</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.58</td>
<td>0.69b</td>
<td>1.30</td>
<td>1.62b</td>
</tr>
<tr>
<td>4] UK</td>
<td>31146</td>
<td>17153</td>
<td>288</td>
<td>213</td>
</tr>
<tr>
<td>1979–81</td>
<td>14005</td>
<td>9131</td>
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<tr>
<td>Ratio of change</td>
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<td>0.53b</td>
<td>1.32</td>
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</tr>
<tr>
<td>4] Germany</td>
<td>25734</td>
<td>17926</td>
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<tr>
<td>1988–90</td>
<td>16360</td>
<td>7191</td>
<td>348</td>
<td>245</td>
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<tr>
<td>Ratio of change</td>
<td>0.64</td>
<td>0.40</td>
<td>1.38</td>
<td>1.42b</td>
</tr>
<tr>
<td>6] Australia</td>
<td>26087</td>
<td>13286</td>
<td>244</td>
<td>170</td>
</tr>
<tr>
<td>1979–81</td>
<td>12061</td>
<td>7092</td>
<td>291</td>
<td>237</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.46</td>
<td>0.53b</td>
<td>1.20</td>
<td>1.39b</td>
</tr>
<tr>
<td>7] Italy</td>
<td>27257</td>
<td>13669</td>
<td>301</td>
<td>201</td>
</tr>
<tr>
<td>1979–81</td>
<td>13522</td>
<td>7044</td>
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<td>249</td>
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<tr>
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<td>0.50</td>
<td>0.52b</td>
<td>1.10</td>
<td>1.24b</td>
</tr>
<tr>
<td>8] Japan</td>
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<td>11018</td>
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<td>105</td>
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<td>1979–81</td>
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<td>5501</td>
<td>173</td>
<td>108</td>
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<td>0.63</td>
<td>0.50</td>
<td>1.07</td>
<td>1.03</td>
</tr>
<tr>
<td>9] Netherlands</td>
<td>25615</td>
<td>12092</td>
<td>310</td>
<td>224</td>
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<td>1979–81</td>
<td>13017</td>
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<tr>
<td>Ratio of change</td>
<td>0.51</td>
<td>0.69b</td>
<td>0.96</td>
<td>1.11b</td>
</tr>
<tr>
<td>10] France</td>
<td>26049</td>
<td>11948</td>
<td>445</td>
<td>293</td>
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<tr>
<td>1979–81</td>
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<td>276</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.57</td>
<td>0.56</td>
<td>0.90</td>
<td>0.91b</td>
</tr>
<tr>
<td>Average</td>
<td>25620</td>
<td>13591</td>
<td>275</td>
<td>101</td>
</tr>
<tr>
<td>1979–81</td>
<td>14158</td>
<td>6195</td>
<td>332</td>
<td>260</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.55</td>
<td>0.46</td>
<td>1.21</td>
<td>1.29b</td>
</tr>
</tbody>
</table>

a Clinically significant increases in **BOLD**.

b Countries with female increased ratios higher than males.
France 6651 pm, with an overall average of 6195, representing a reduction of 54% over the period.

Every country’s female rate fell substantially, the biggest fall being in Japan 50%, and Italy and Spain by 48%, the smallest reductions being in the USA 26%, and Canada and the Netherlands by 31%.

It should be noted that women’s ratios of change were higher than males in six countries.

Total Neurological Death rates

Columns 4 and 5 of Table 3a gives the combined rates followed by ratios of change, which were used to calculate Odds ratios between changes in Total Mortality and Neurological Deaths.

It should be noted that in nine of the ten countries female Nervous Disease death ratio of change was higher than their male ratios.

There was no significant correlation between the sexes in regards to Total Mortality but there was a strong positive correlation between the rates of neurological deaths between the gender (Rho = +0.876, P < 0.001). There was a positive correlation between ratios of change between both Total deaths and the Total Neurological Deaths (Rho = +0.8758, P < 0.005).

Odds ratios of Total Mortality: neurological deaths

Table 3b shows the examination of the Odds ratios that indicate the degree to which neurological deaths have worsened compared to Total Mortality in each of the major developed countries over 20 and more years.

Males: The male Total Mortality: neurological Odds ratios were quite dramatic led by the UK at 1:2.93, the USA 1:2.77 and Australia 1: 2.61, with a further four countries having Odds ratios more than 1:2.0. Even less substantial Odds ratios, such as found in Japan (1:1.70) and France (1: 1.58) indicate that neurological deaths have worsened, relative to total mortality in the countries under review.

Females: Female Odds ratios showed an even greater divergence between Total Deaths and Neurological mortality than Male, led by Germany 1:3.55, Spain 1:3.37 and the UK at 1:2.79, with five other countries having ratios of more than 1:2.0 and the remaining countries having neurological mortality worsening compared to Total deaths.

When combing the Male and Female Odds ratios, the UK, Germany and Spain were equal first 1:2.86 followed by the USA 1:2.68, with relative lows for France 1:1.60, the Netherlands 1:1.75 and Japan 1:1.88.

Smaller Western Countries Total Mortality & Total Neurological Deaths

Table 4a shows that the outcomes found in the major developed countries are mirrored in these 10 smaller nations. They all experienced substantial falls in Total Mortality whilst the majority, eight, had increases in their Total Neurological Deaths. These ranged from male rate of 748 pm in Finland to 223 pm in Austria, with an overall average of 381 pm. In regard to females the range went from 484 pm in Finland down to 135 pm in Greece, averaging 256 pm. It should be noted that women’s ratio of change was higher than their males in six countries.

Smaller Western Countries Total Mortality: Neurological Deaths Odds ratios

Table 4b lists the Total Mortality to total Neurological Odds ratios over the period. Similar to the major countries, seven countries had Odds ratios of greater than 1.90:1 for both sexes.

The results from these smaller countries add to the validity of the findings from the major developed countries.

Previous configuration of neurological deaths in 55–64- and 65–74-year olds

Table 5 is based upon the pervious configuration of combined Other Neurological Disease deaths and Mental Disorder deaths from 1979 up to 2004–06 period, where the current 55–74-year old formulation was split between 55–64- and 65–74-year olds in rates per million (rpm).

The point to note is that amongst the 55–64-year olds clinical significant increases were found in this younger age
In respect to the younger females, there were increases in the USA of 95%, by 37% in Spain, 29% in Italy, 24% in the UK and by 17% and 12% respectively in the Netherlands and Canada.

In both the 55–64- and 65–74-year age bands, women’s rates rose more than men’s in nine of the ten countries.

Correlating the ranked ratios of change between the 2004–06 and 2008–10 for both sexes there was an overall significant correlation between the two periods (P < 0.05), indicating there is a continuation of the increases noted in the earlier period.

Some constituents of Nervous Disease Deaths: i] Creutzfeld Jakob’s Disease (CJD) and Variant CJD (VCJD), ii) Motor Neurone and Parkinson’s Disease deaths in England & Wales. i] Extrapolating CJD mortality for England & Wales, no separate gender or age bands were given, hence the data is for all CJD deaths in England for people aged from 20 to 75+ years. Variant CJD was not reported until after 1994 when in 1995–97 VCJD averaged 0.14 per million in with a total incidence of 1.07 pm, rising to a peak in 2001–03 of 0.3 pm for VCJD in a total incidence of 1.62 pm. By 2004–06 VCJD fell to 0.09 pm and total CJD to 1.32 pm, indicating that at least in England and Wales, these prion type deaths did not contribute greatly to an increase in Nervous Disease deaths in the UK.

Motor Neurone Disease (MND) and Parkinson’s Disease (PD) deaths (Table 6): MND 55–74-year old males rose to 111 pm a ratio of change of 1.56 and women’s 1.65 up to 81 pm. The remaining elderly group aged 75+ are shown with increases up to

<table>
<thead>
<tr>
<th>Country, latest years &amp; combined rank</th>
<th>Total Mortality male</th>
<th>Total Mortality female</th>
<th>Total Neurological Deaths male</th>
<th>Total Neurological Deaths female</th>
<th>Total Deaths: Neurological Deaths Odds ratio male–female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1] Portugal</td>
<td>29748</td>
<td>15878</td>
<td>228</td>
<td>102</td>
<td>2.12* 2.79–4.42</td>
</tr>
<tr>
<td>2008–10</td>
<td>16021</td>
<td>7599</td>
<td>370</td>
<td>216</td>
<td></td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.54</td>
<td>0.48</td>
<td>1.62</td>
<td>2.12*</td>
<td></td>
</tr>
<tr>
<td>2] Finland</td>
<td>30300</td>
<td>10798</td>
<td>422</td>
<td>238</td>
<td></td>
</tr>
<tr>
<td>1987–89</td>
<td>17093</td>
<td>7291</td>
<td>748</td>
<td>484</td>
<td></td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.56</td>
<td>0.68</td>
<td>1.75</td>
<td>2.04</td>
<td></td>
</tr>
<tr>
<td>3] New Zealand</td>
<td>29264</td>
<td>16556</td>
<td>238</td>
<td>243</td>
<td></td>
</tr>
<tr>
<td>1979–81</td>
<td>12004</td>
<td>8370</td>
<td>331</td>
<td>279</td>
<td></td>
</tr>
<tr>
<td>Ratio of change</td>
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<td>0.51</td>
<td>1.39</td>
<td>1.15</td>
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<tr>
<td>4] Belgium</td>
<td>30803</td>
<td>15556</td>
<td>342</td>
<td>228</td>
<td></td>
</tr>
<tr>
<td>1979–81</td>
<td>16392</td>
<td>8739</td>
<td>427</td>
<td>336</td>
<td></td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.53</td>
<td>0.56</td>
<td>1.25</td>
<td>1.47*</td>
<td></td>
</tr>
<tr>
<td>5] Sweden</td>
<td>20529</td>
<td>10958</td>
<td>172</td>
<td>206</td>
<td></td>
</tr>
<tr>
<td>1987–89</td>
<td>11971</td>
<td>7153</td>
<td>312</td>
<td>233</td>
<td></td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.58</td>
<td>0.65</td>
<td>1.82</td>
<td>1.13</td>
<td></td>
</tr>
<tr>
<td>6] Austria</td>
<td>20137</td>
<td>15289</td>
<td>195</td>
<td>170</td>
<td></td>
</tr>
<tr>
<td>1979–81</td>
<td>15144</td>
<td>7718</td>
<td>223</td>
<td>203</td>
<td></td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.75</td>
<td>0.49</td>
<td>1.14</td>
<td>1.19*</td>
<td></td>
</tr>
<tr>
<td>7] Ireland</td>
<td>32363</td>
<td>14591</td>
<td>400</td>
<td>256</td>
<td></td>
</tr>
<tr>
<td>1979–81</td>
<td>18668</td>
<td>8591</td>
<td>471</td>
<td>262</td>
<td></td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.58</td>
<td>0.59</td>
<td>1.18</td>
<td>1.04</td>
<td></td>
</tr>
<tr>
<td>8] Denmark</td>
<td>24297</td>
<td>15292</td>
<td>316</td>
<td>145</td>
<td></td>
</tr>
<tr>
<td>1994–96</td>
<td>16566</td>
<td>11512</td>
<td>353</td>
<td>179</td>
<td></td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.68</td>
<td>0.75</td>
<td>1.12</td>
<td>1.23*</td>
<td></td>
</tr>
<tr>
<td>9] Greece</td>
<td>21933</td>
<td>10543</td>
<td>279</td>
<td>174</td>
<td></td>
</tr>
<tr>
<td>1979–81</td>
<td>11408</td>
<td>6893</td>
<td>251</td>
<td>135</td>
<td></td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.52</td>
<td>0.65</td>
<td>0.90</td>
<td>0.78</td>
<td></td>
</tr>
<tr>
<td>10] Switzerland</td>
<td>19380</td>
<td>9577</td>
<td>396</td>
<td>206</td>
<td></td>
</tr>
<tr>
<td>1995–97</td>
<td>11907</td>
<td>7153</td>
<td>328</td>
<td>233</td>
<td></td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.61</td>
<td>0.75</td>
<td>0.83</td>
<td>1.13*</td>
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</tr>
<tr>
<td>Average</td>
<td>25875</td>
<td>13504</td>
<td>299</td>
<td>197</td>
<td></td>
</tr>
<tr>
<td>1979–81</td>
<td>14717</td>
<td>8102</td>
<td>352</td>
<td>256</td>
<td></td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.57</td>
<td>0.60</td>
<td>1.18</td>
<td>1.30*</td>
<td></td>
</tr>
</tbody>
</table>

Clinically significant increases in BOLD.
Table 4b — Total Mortality & Total Neurological Disease Deaths Odds ratio 1979–2010. Ranked by highest average odds ratios.

<table>
<thead>
<tr>
<th>Country &amp; rank of Odds ratios</th>
<th>Male Total Mortality: neurological deaths Odds ratios</th>
<th>Females Total Mortality: neurological deaths Odds ratios</th>
<th>Average Odds Ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td>1] Portugal</td>
<td>2.79</td>
<td>4.42</td>
<td>3.61</td>
</tr>
<tr>
<td>2] Finland</td>
<td>3.12</td>
<td>3.00</td>
<td>3.06</td>
</tr>
<tr>
<td>3] New Zealand</td>
<td>3.39</td>
<td>2.25</td>
<td>2.82</td>
</tr>
<tr>
<td>4] Belgium</td>
<td>2.36</td>
<td>2.63</td>
<td>2.50</td>
</tr>
<tr>
<td>5] Sweden</td>
<td>3.14</td>
<td>1.74</td>
<td>2.44</td>
</tr>
<tr>
<td>6] Austria</td>
<td>1.52</td>
<td>2.43</td>
<td>1.98</td>
</tr>
<tr>
<td>7] Ireland</td>
<td>2.03</td>
<td>1.76</td>
<td>1.90</td>
</tr>
<tr>
<td>8] Denmark</td>
<td>1.65</td>
<td>1.64</td>
<td>1.65</td>
</tr>
<tr>
<td>9] Greece</td>
<td>1.73</td>
<td>1.20</td>
<td>1.47</td>
</tr>
<tr>
<td>10] Switzerland</td>
<td>1.36</td>
<td>1.51</td>
<td>1.44</td>
</tr>
<tr>
<td>Average</td>
<td>2.31</td>
<td>2.26</td>
<td>2.29</td>
</tr>
</tbody>
</table>

378 pm for men indicative that MND might well have contributed to the overall rises in UK Nervous Disease deaths. Amongst the 55–74-year old age band for men and 167 pm for women rises equivalent of 294% and 255% over the period.

In regard to PD, there was no change for males aged 55–74 a fall for women, equivalent to 23% but older males rose 213% and females up 172% over the period.

Discussion

It seems reasonable to reject the working null hypotheses because there were substantial differences between Total Mortality and Total Neurological Disease deaths over the period. The previous finding of an increasing and relatively earlier onset of such deaths between 1979 and 1997 and up to 2004–06 was shown to be continuing and the 2010 results appear to conform these trends, which have serious public health implications.

What the study adds

The original study was the first-ever comparative international analysis of changing patterns of neurological disease deaths in the ten major developed countries between 1979 and 1997. This study, by taking the review up to 2010, confirms the increase in actual neurological deaths of people aged 55–74-years in the majority of countries; an observation which is given further validity from finding similar results in eight of the ten smaller (<11.3 millions) countries (population less than 11.3 million). It shows that relative to the reductions in cancer deaths for the same age bands, which have been associated with major increases in funding specifically to cancer services in the West, there does not appear to have been the same priority given to neurological diseases, leading to a reduced death rate. The new configuration that identified Alzheimer and other Dementia separately has confirmed clinical studies of increased Alzheimer deaths. At an international level, it has also shown that there have been substantial rises in the other neurological deaths i.e. the Nervous Disease deaths minus the Alzheimer’s, raising serious public health questions in all the nations reviewed.

Study limitations

The main limitation is that the current results based upon the 2012 WHO re-configuration cannot be compared directly with the earlier 2004 and 2008 versions, albeit the Nervous Disease and Alzheimer’s and Other Dementias data which are far more precise than the previous formulations. Another limitation was that by merging the 55–64 year-old age bands into the wider 55–74-year age bands, it is less easy to highlight the rises in the relatively younger 55–64 years group.

A minor limitation was that under the old configuration the data covered by two Editions of the ICD, meant that the previously used Mental Disorder deaths had varied slightly between editions. This new version is based entirely upon the 10th ICD edition and covers the whole period under review and resolves this satisfactorily. Furthermore, expanding the analysis to twenty Western countries, gives further weight to the overall outcomes.

A further limitation may arise from the categorization of neurological deaths, where there may have been greater willingness to report such deaths than before, but by focussing on Total Nervous Disease deaths, which are the combined neurological deaths to include the non-Alzheimer Nervous Disease deaths and the other Nervous Disease mortalities, any such problems are reduced.

Although whilst some studies have found little change in regard to Motor Neurone Disease, attributing any rises to improved categorization, other research has unequivocally reported an upward trend in Motor Neurone Disease deaths, as shown from the Anglo-Welsh data, there appears to be unequivocal rises in MND for males up to 65%, which may well be the case in other developed countries. Although others have argued that the problem lies in differentiating between underlying contributory and final cause of death, which is said to be linked to under-reporting neurological mortality. However, the rise in specific MND mortalities may be due to a greater accuracy in death certification rather than a true rise in MND or the inclusion of MND as a contributory cause in some countries.

Data for constituent OND sub-categories were only available for England and Wales, which includes the highly publicized ‘outbreak’ of Variant CJD in Britain yet when transposing the annual numbers of total Variant CJD into rates, at their peak all types of CJD never exceeded 1.62 pm, so did not contribute significantly to an increase in Anglo-Welsh OND deaths. Whilst rises in MND suggest that some of the increases may arise from increases in MND, the 10 major developed countries over a relative short period and should be a matter of some concern.

One feature that might have influenced the results is the different healthcare system of the countries reviewed. This is a complex issue where for example, against media expectations and analysis of Total Mortality in 20 Western nations
showed that despite being one of the lowest funded countries for health care, the UK was the second most effective and efficient in reducing deaths under 74 years. Equally, the UK had a similar successful outcome in reducing cancer deaths compared with other countries but were relatively less successful in regard to reducing child mortality, although the NHS relatively achieved more with comparatively far less funding than most other countries. These results reflected differential impacts of not just a nation’s GDP health expenditure but how the system were configured. In respect to child mortality, the worst results are for children in the USA, and it was clear that relative poverty impacted upon the outcomes as the USA had the worst relative poverty in the West. The UK had the third highest relative poverty levels, and relatively poor results of child mortality were also seen for the UK. Such factors need to be considered when comparing the results between countries and whether similar increases in resource allocation and priority given to cancer services might equally benefit the neurological field.

Another difficulty is that this study cannot explain particular variations in some of the countries. For example the Alzheimer’s deaths rose considerably in Italy and the

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Table 5 – Earlier Global Configuration: ‘Other Neurological Diseases’ (OND) & ‘Mental Disorder Deaths’ (MDD) by sex for 55–64-year olds & 65–74-year olds 1979–81 vs 2004–06. Countries where female ratios higher than males. Ranked by highest increased ratios of change by both sexes in 2004–06.

<table>
<thead>
<tr>
<th>Country – years</th>
<th>OND males 55–64</th>
<th>OND females 55–64</th>
<th>MDD males 65–74</th>
<th>MDD females 65–74</th>
</tr>
</thead>
<tbody>
<tr>
<td>1] USA</td>
<td>1979–81</td>
<td>271</td>
<td>135</td>
<td>540</td>
</tr>
<tr>
<td></td>
<td>2003–05</td>
<td>335</td>
<td>263</td>
<td>925</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.24</td>
<td>1.95*</td>
<td>1.71</td>
<td>2.36*</td>
</tr>
<tr>
<td>2] Spain</td>
<td>1979–81</td>
<td>176</td>
<td>90</td>
<td>399</td>
</tr>
<tr>
<td></td>
<td>2003–05</td>
<td>203</td>
<td>123</td>
<td>787</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.15</td>
<td>1.37*</td>
<td>1.97</td>
<td>2.18*</td>
</tr>
<tr>
<td>3] Italy</td>
<td>1979–81</td>
<td>164</td>
<td>92</td>
<td>429</td>
</tr>
<tr>
<td></td>
<td>2001–03</td>
<td>169</td>
<td>119</td>
<td>673</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.03</td>
<td>1.29*</td>
<td>1.57</td>
<td>2.68*</td>
</tr>
<tr>
<td>4] Netherlands</td>
<td>1979–81</td>
<td>146</td>
<td>117</td>
<td>515</td>
</tr>
<tr>
<td></td>
<td>2004–06</td>
<td>220</td>
<td>137</td>
<td>749</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.51</td>
<td>1.17</td>
<td>1.45</td>
<td>1.91*</td>
</tr>
<tr>
<td>5] Canada</td>
<td>1979–81</td>
<td>281</td>
<td>73</td>
<td>641</td>
</tr>
<tr>
<td></td>
<td>2002–04</td>
<td>256</td>
<td>82</td>
<td>931</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>0.98</td>
<td>1.12*</td>
<td>1.45</td>
<td>1.97*</td>
</tr>
<tr>
<td></td>
<td>2004–06</td>
<td>152</td>
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<td>687</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.31</td>
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<td>1.51</td>
<td>1.45</td>
</tr>
<tr>
<td>7] Australia</td>
<td>1979–81</td>
<td>210</td>
<td>119</td>
<td>556</td>
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<td>2001–03</td>
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<td>706</td>
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<td>0.97</td>
<td>1.11*</td>
<td>1.27</td>
<td>1.50*</td>
</tr>
<tr>
<td>8] Germany</td>
<td>1980–82</td>
<td>333</td>
<td>158</td>
<td>596</td>
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<td></td>
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<td>1.10</td>
<td>0.96</td>
<td>1.09</td>
<td>0.97</td>
</tr>
<tr>
<td>9] France</td>
<td>1979–81</td>
<td>452</td>
<td>180</td>
<td>1122</td>
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<td>2003–05</td>
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<td>1010</td>
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<tr>
<td>Ratio of change</td>
<td>0.96</td>
<td>1.06*</td>
<td>0.90</td>
<td>0.98*</td>
</tr>
<tr>
<td>10] Japan</td>
<td>1979–81</td>
<td>120</td>
<td>76</td>
<td>314</td>
</tr>
<tr>
<td></td>
<td>2004–06</td>
<td>105</td>
<td>55</td>
<td>276</td>
</tr>
<tr>
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<td>0.81</td>
<td>0.72</td>
<td>0.88</td>
<td>0.78</td>
</tr>
<tr>
<td>Average</td>
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<td>557</td>
</tr>
<tr>
<td></td>
<td>2004–06</td>
<td>249</td>
<td>125</td>
<td>739</td>
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<tr>
<td>Ratio of change</td>
<td>1.08</td>
<td>1.09*</td>
<td>1.33</td>
<td>1.59*</td>
</tr>
</tbody>
</table>

Ranked by total increases 2006 vs 2010, Rho = +0.6152, P < 0.05. Male 2004–06 vs 2008–10 increase, Rho = +0.4546, P < 0.1 trend. Female 2004–06 vs 2008–10 Rho = +0.6242, P < 0.05.
Clinically significant increases in BOLD.

Netherlands but at the same time fell for the Nervous diseases. Another apparent anomaly was France, whose neurological mortality was highest and whilst still second highest amongst males, their overall rates have seen a small decline. Nothing in the study however can explain these apparent inconsistencies and only country-specific research can explain the results.

What is unequivocal is that in contrast to major reductions in general mortality in all 20 countries, Total Neurological Deaths actually rose substantially between 1980 and 2010 in both sexes in 16 of the twenty Western countries.

**Potential explanations**

Neurological diseases are considered to be diseases of older people and as people live longer they develop diseases which previously they had not lived long enough to develop, this is called the 'Gompertzian effect' – i.e. that as people live longer, they have diseases that previously they would not have lived long enough to develop.56 The question posed therefore is whether these substantial changes, occurring over a relatively short period, are mainly due to the Gompertzian effect? The explanation for example that arises in cancer deaths is mainly due to having proportionately more people living longer. This is not a Gompertzian prediction, for example breast cancers are increasingly occurring in increasingly younger women under 40 years old,21 and the Gompertzian does not account for changes between countries and gender.10,23,24 Moreover, in respect to cancers, whilst increases in the incidence of new cases of cancer have slowed down over the past decade in many countries, the incidence does still continue to rise, across all age bands and in particular the under 40-year olds – hardly a Gompertzian effect.21,26

Other possible explanations for these changes might be related to improved diagnostic techniques and the re-categorization of deaths, but the new configuration is even more precise than the earlier one and moreover, whilst in the early treatment stage of some of these conditions there may have been early doubts about diagnosis but by the time of death, it would be fairly clear that it was a neurological disease, and the new Nervous Disease death category covers that much better than before.3 Moreover, looking back 30 or more years the concept of early onset dementia or the need for the creation of a Young Parkinson’s Disease society in Britain would have seemed a tautology.

A major explanation for the increases must be in regard to the major life-style changes in Western countries, especially amongst women and the fact that changes in Total Neurological Deaths were overall worst amongst females in the majority of countries – a factor also found in many countries in regard to cancers in women,3,24 which suggests the rises in female neurological deaths are indicator of environmental factors.35–37 Furthermore increasing deaths from Parkinson’s Disease and Motor Neurone Disease cannot be attributable to longevity, bearing in mind the relatively short-time period, and cannot explain the 55–64-year old mortality rises up to 2006. Clearly other influences must be operating, though in no way does this deny the importance of hereditary factors but rather strongly points towards an epigenetic explanation, that is negative environmental triggers impacting upon underlying genetic predispositions.1,6–9,23,35–37

The nature of any environmental factors are uncertain but there have been major environmental changes; including increased population, economic activity, air and road traffic, and increased home technology involving increased background electro-magnetic fields (mobile phones, micro-wave ovens, computers, etc),9,13,27,31,35,36 which are unique to these later years. Such an interpretation is strengthened by the fact that since the late 1970’s more women are entering the work force,39 in areas that previously were virtually male, so it is only now that women are increasingly exposed to background electro-magnetic fields, petro-chemical etc as previously only men have been.

More research is needed to assess the potential impact of these environmental changes upon neurological deaths and the wider aspects of human health, especially when considering how, relative to general mortality, neurological deaths have disproportionately increased.

**Implications**

Within the context of increased longevity, rising numbers of people with dementia and surviving strokes will add further pressure on already stretched health and social care services. The earlier onset of neurological disorders will have profound implications for patients, families and front-line services. Crucially, relative to other specialities, the present configuration of services may require re-organization, especially for specialist neurological services and for community psycho-social provision, to meet the challenge of more ‘disabled’ people in the community.

There are lessons to be drawn from reduced cancer mortality over the period. Every Government of the countries under review have made major additional investments in cancer services and research and this needs to be done in the field of neurology.

Finally, a new British study showing that age-related cognitive decline was earlier than first thought but acknowledged that some of their findings ‘could simply be the correlates of a disease process’ and this might be an early indicator of initial stages of neuro-degenerative diseases, which may be another indicator that the dementias are starting earlier.

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**Table 6**

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Males 55–74</th>
<th>Females 55–74</th>
<th>Males 75+</th>
<th>Females 75+</th>
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<tbody>
<tr>
<td>Motor neuron</td>
<td>1979–81</td>
<td>71</td>
<td>49</td>
<td>96</td>
</tr>
<tr>
<td>2010</td>
<td>111</td>
<td>81</td>
<td>378</td>
<td>167</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.56</td>
<td>1.65</td>
<td>3.94</td>
<td>3.55</td>
</tr>
<tr>
<td>Parkinson’s</td>
<td>1979–81</td>
<td>76</td>
<td>47</td>
<td>505</td>
</tr>
<tr>
<td>2010</td>
<td>76</td>
<td>30</td>
<td>1579</td>
<td>593</td>
</tr>
<tr>
<td>Ratio of change</td>
<td>1.00</td>
<td>0.77</td>
<td>3.13</td>
<td>2.72</td>
</tr>
</tbody>
</table>

*Source: ONS (2012).*
Author statements

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Ethical approval

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Competing interests

None declared.

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