Neurological deaths of American adults (55–74) and the over 75’s by sex compared with 20 Western countries 1989–2010: Cause for concern

Colin Pritchard, Emily Rosenorn-Lanng

Emily Rosenorn-Lanng Research Officer, Faculty of Health and Social Sciences, Psychiatric Social Work, 1Bournemouth University, Bournemouth BH1 3LT, UK

E-mail: *Colin Pritchard - cpritchard@bournemouth.ac.uk; Emily Rosenorn-Lanng - elanng@bournemouth.ac.uk

*Corresponding author

Received: 21 November 14 Accepted: 06 May 15 Published: 23 July 15

This article may be cited as:
Pritchard C, Rosenorn-Lanng E. Neurological deaths of American adults (55–74) and the over 75’s by sex compared with 20 Western countries 1989–2010: Cause for concern. Surg Neurol Int 2015;6:123.

http://surgicalneurologyint.com/surgicalint_articles/Neurological-deaths-of-American-adults-(55–74)-and-the-over-75’s-by-sex-compared-with-20-Western-countries-1989–2010:-Cause-for-concern/

Access this article online
Website: www.surgicalneurologyint.com
DOI: 10.4103/2152-7806.161420
Quick Response Code:

Copyright: © 2015 Pritchard C. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

**Background:** Have USA total neurological deaths (TNDs) of adults (55–74) and the over 75’s risen more than in twenty Western Countries?

**Methods:** World Health Organization TND data are compared with control mortalities cancer mortality rates (CMRs) and circulatory disease deaths (CDDs) between 1989–1991 and 2008–2010 and odds ratios (ORs) and confidence intervals calculated.

**Results:** Neurological Deaths – Twenty country (TC) average 55–74 male rates per million (pm) rose 2% to 503 pm, USA increased by 82% to 627 pm. TC average females rose 1% to 390 pm, USA rising 48% to 560 pm. TC average over 75’s male and female increased 117% and 143%; USA rising 368% and 663%, significantly more than 16 countries. Cancer mortality – Average 55–74 male and female fell 20% and 12%, USA down 36% and 18%. TC average over 75’s male and female fell 13% and 15%, the USA 29% and 2%. Circulatory deaths – TC average 55–74 rates fell 60% and 46% the USA down 54% and 53%. Over 75’s average down 46% and 39%, USA falling 40% and 33%. ORs for rose substantially in every country. TC average 75’s ORs for CMR: TND male and females were 1:2.83 and 1:3.04 but the USA 1:5.18 and 1:6.50. The ORs for CDD: TND male and females TC average was 1:3.42 and 1:3.62 but the USA 1:6.13 and 1:9.89.

**Conclusions:** Every country’s neurological deaths rose relative to the controls, especially in the USA, which is a cause for concern and suggests possible environmental influences.

**Key Words:** Age, gender, international comparison, neurological deaths

INTRODUCTION

Neurological disease has increased in recent years throughout the developed world. Neurological deaths are reported by the World Health Organization (WHO) in two global categories, Alzheimer and other dementias, and nervous disease deaths, which enables us to calculate a total neurological death (TND) rate per million (pm) of population. Thus, TND include such disparate conditions as Parkinson’s disease, motor neuron disease (MND), hereditary neuromuscular...
conditions, prion disorders, degenerative diseases, including Creutzfeldt Jacob’s disease (CJD), and new variant CJD,[20] though the incidence of the later appears to have relatively stabilized, returning close to pre-2000 levels.[9,30,41]

Earlier research found that dementia morbidity was occurring earlier and had disproportionately increased in some Western countries in people aged 45–74 years, with relatively larger increases in women[26,38,40] as women’s TND rates had risen relatively more than male rates in every country. As Western women’s lifestyles have changed more than men's this suggests possible interactive environmental contributions.[6,10,22,32,38,41,44] This view is supported by studies of neurological mortality that found population density was a surrogate marker for environmental exposure[13,46] and a similar link has been found in relation to incidence of cancer,[39] with substantial increases in two specific neurological conditions, MND,[1,6,12,19,23] and “early-onset dementias.”[29,33,38,36,38,41,49]

However, as neurological diseases are classically “diseases of the elderly,” it has been argued that the Gompertzian theory on longevity was operating, namely people are now living longer to develop diseases that they would not have lived long enough to have acquired in previous times.[7,14,42] However, while this process might partially account for the some of the rises, the disproportionate rises in the incidence over a relatively short time suggest other factors, both in respect to the cancer and neurological morbidity.[1,7,21,35,38,41,49] While a number of researchers have acknowledged that the longevity Gompertzian effect may be a factor, they argued that environmental factors probably played a larger part.[24,25,42,45] Furthermore, increases in neurological morbidity in the less economically developed countries, would not appear to be mainly attributable to the Gompertzian explanation.[15,24,25,31,38,41,42,44,44]

Conversely, changes or improvements in diagnosis have been thought to be a possible factor,[18,23] but other reviews suggest this is not a major issue, as current brain imagining and better biomarkers allows diagnosis to be more accurate and, therefore, the figures are essentially more reliable.[23] while some USA studies showed that dementia deaths are under-reported.[21,26,35,36]

Previous work that highlighted earlier dementia deaths,[18,41] spanned a 30 years period and two International Classification of Diseases (ICDs) editions, whereas this study covers only 20 years and one ICD edition.[50] This limits the likelihood of any changes being related to differences in reporting and also reduces the Gompertzian explanation.

However, to try to account for the Gompertzian effect, other “diseases of the elderly,” cancer mortality rates (CMRs) and circulatory disease deaths (CDDs),[37] are used as controls to be contrasted against TND. It is however, recognized that there have been major health campaigns in many countries to reduce the toll of circulatory and cancer diseases, which have not been matched in the neurological field.

Theoretically therefore, if the two biggest classical diseases of old age, are mainly due to longevity and not changes in lifestyle, treatment advances and the environment, it would be expected that there would be little difference in the patterns of neurological, cancer, and circulatory deaths over the period under review.

The latest available WHO data (July 2014) for the USA is data up to 2010,[47] which will be the index year for this international comparison.

There are two working null hypothesis, that between baseline 1989–1991 and index 2008–10 years there would be no significant differences between:

- TND and cancer and circulatory diseases death rates by age or sex in each country, and
- Between the USA and the other 20 Western in regard to TNDs.

**METHODS**

World Health Organization standardized mortality data[20] is used to examine any changes between 3 years average baseline data, covering the years 1989–1991, compared to the index years of 2008–2010 for the USA and the other 20 Western countries for TND, CMR and CDD mortalities. This is based upon the 10th edition of the ICD editions,[50] making it a more uniform analysis than the earlier studies.[38,41]

One important change in the current WHO reporting is that the previously separate age groups of 55–64 and 65–74 have now been combined into the 55–74 age band[47] so the separate age bands can no longer be compared as was possible previously. TNDs are based upon combining the WHO categories nervous disease deaths and the Alzheimer and other dementia deaths into rates per million of the population for two age bands, the 55–74 and the over 75’s.

Cancer mortality rate and CDD rates by age bands and gender are contrasted against TND over the period first to compare each country against itself and then with the USA, twenty country (TC) average being calculated for of each of the age bands and mortalities.

However, when using multi-national data it has to be acknowledged that there are inherent problems in terms of reporting, possible “fashions” in diagnosis and the problem of concomitant diagnoses across different disease conditions. Moreover, when comparing three broad diagnostic categories such as these, raises the
issue of different countries having varied health policy strategies, which to a degree might influence treatment priorities and therefore changes of mortality rates over time. In part, this is controlled for by measuring each country against itself which provide a degree of reliability of each country’s results over the period. The WHO acknowledges that some countries, but not usually the 21 countries review here, can have problems of reporting, while lead times are usually 4 or more years behind the year of publication, example, WHO report up to 2010 published in July 2014. Furthermore, it is stressed that “it is the underlying cause of death in accordance with the rules of the ICDs that is, reported and data included only for countries reporting data properly code” (sited in WHO mortality database documentation document), which seems as accurate as is feasible, not least because of the uniformity of collation. Moreover, the controversy over diagnosis which can occur at the beginning of any disease process is resolved at death, and while 100% accuracy can never be determined in dealing with human phenomena, bearing these limitations in mind, the WHO data, collated in a consistent and uniform manner and using the latest ICD edition, remains the best comparative international data available.

**Statistical analysis**

The three mortalities are presented for each age band by sex, and a ratio of change is calculated for any changes over the period. Odds ratios (ORs) are calculated to explore whether TNDs and CMR and CDD have changed proportionally over the 21 years.

A TC average death rate is calculated to be compared with changes in the USA mortality rates over the period.

Confidence intervals (CIs) to ± 95% level of significance are used to determine any statistical significant difference between the USA and each of the other TCs.

**RESULTS**

**Total neurological deaths 55–74**

The highest current male 55–74 TND rates ranged from Finland at 1106 pm, down to Japan 219 pm. In 1989–1991, the TC average rate was 495 pm, increasing to 503 pm over the period, equivalent to a 2% rise.

Initially, the USA rate was 344 pm, and was 17th highest out of 21 countries but is now second highest at 627 pm, and had the biggest increase of all countries at 82%.

Females aged 55–74 current TND rates ranged from Finland 816 pm to Greece and Japan 198 pm. The TC average 1989–1991 was 387 pm rising to 560 pm, an increase of 48% over the period, which was third largest rise, only Greece had a bigger increase but from a much lower baseline [Table 1].

| Country 1989-1991 versus 2008-2010 | TND       | 1989-1991 | 2008-2010 | Ratio |
|-----------------------------------|-----------|-----------|-----------|-------|
| Males                             | Females   | Males     | Females   |       |
| 1-1 = Finland                     | 657       | 646       |           |       |
| 2008-2010                         | 1106      | 816       |           |       |
| Ratio                             | 1.68      | 1.26      |           |       |
| 2-17 = USA                        | 344       | 378       |           |       |
| 2008-2010                         | 627       | 560       |           |       |
| Ratio                             | 1.82      | 1.48      |           |       |
| 3-17 = Denmark                    | 344       | 378       |           |       |
| 2008-2010                         | 569       | 468       |           |       |
| Ratio                             | 1.66      | 1.24      |           |       |
| 4-4 = Norway                      | 525       | 540       |           |       |
| 2008-2010                         | 556       | 513       |           |       |
| Ratio                             | 1.06      | 0.95      |           |       |
| 5-10 = Sweden                     | 485       | 430       |           |       |
| 2008-2010                         | 546       | 478       |           |       |
| Ratio                             | 1.13      | 1.11      |           |       |
| 6-2 = Belgium                     | 654       | 521       |           |       |
| 2008-2010                         | 542       | 503       |           |       |
| Ratio                             | 0.83      | 0.96      |           |       |
| 7-6 = Canada                      | 522       | 441       |           |       |
| 2007-2009                         | 525       | 439       |           |       |
| Ratio                             | 1.01      | 1.00      |           |       |
| 7-4 = France                      | 525       | 407       |           |       |
| 2008-2010                         | 525       | 388       |           |       |
| Ratio                             | 1.00      | 0.95      |           |       |
| 9-3 = UK                          | 604       | 525       |           |       |
| 2008-2010                         | 518       | 460       |           |       |
| Ratio                             | 0.86      | 0.88      |           |       |
| 10-13 = Spain                     | 453       | 356       |           |       |
| 2008-2010                         | 515       | 385       |           |       |
| Ratio                             | 1.14      | 1.08      |           |       |
| 11-8 = Switzerland                | 518       | 466       |           |       |
| 2008-2010                         | 506       | 467       |           |       |
| Ratio                             | 0.98      | 1.00      |           |       |
| 12-15 = Germany 1990-1992         | 403       | 340       |           |       |
| 2008-2010                         | 481       | 394       |           |       |
| Ratio                             | 1.19      | 1.00      |           |       |
| 13-11 = Ireland                   | 511       | 413       |           |       |
| 2008-2010                         | 483       | 408       |           |       |
| Ratio                             | 0.95      | 0.99      |           |       |
| 14-12 = Australia                 | 454       | 365       |           |       |
| 2008-2010                         | 456       | 380       |           |       |
| Ratio                             | 1.00      | 1.04      |           |       |
| 15-11 = Italy                     | 456       | 367       |           |       |
| 2008–2010                         | 463       | 371       |           |       |
| Ratio                             | 1.02      | 1.01      |           |       |
| 16-14 = New Zealand               | 428       | 421       |           |       |
| 2007-2009                         | 455       | 411       |           |       |
| Ratio                             | 1.06      | 0.98      |           |       |

Contd...
Total neurological death over 75’s

Current male over 75’s TND rates were highest in Finland 19,887 pm to the lowest in Greece 1166 pm, with the TC average rising by 114% with rates more than doubling in 11 countries.

The USA rate increased from 3336 pm to 12,271 pm, more than a two-fold (368%) rise over the period and had the biggest increase than all countries.

Current female

The over 75’s TND rates ranged from Finland 24,797 pm to lowest in Greece at 1479 pm, with the TC average increasing by 185%, with a doubling of rates in 17 countries. It should be noted that in every country female rates rose more than males over the period.

The USA rate rose from 3206 pm to 21,253 pm, a more than five-fold (663%) increase, which was the largest rise of all countries under review [Table 2].

Control mortalities

Cancer mortality rates 55–74

Male CMR fell in every country, the TC average fell from 7501 pm to 6008 pm, a 20% decrease. USA rates went from 7938 pm to 5080 pm, a 36% reduction.

The final column in Table 3 refers to the ORs of CMR: TND, which will be discussed below.

USA male 55–74 TND to cancer deaths ratio in 1989–1991 was one to 27.08 cancer deaths by 2008–2010 this had narrowed to 1:8.1.

Female 55–74 average

Apart from the Netherlands, Portugal, and Spain female CMR fell in 18 countries, as the TC average went from 4414 pm to 3705 pm, decrease of 16%. The USA rates fell from 5191 pm to 4241 pm, an 18% reduction.

USA female TND to cancer deaths ratio in 1989–1991 was 1:13.73 by 2008–2010 this had reduced to 1:7.6.

Cancer mortality rate people over 75’s+

The TC male over 75’s CMR moved from 22,666 pm to 19,831 pm, a reduction of 13%. The US rates fell from 20,919 pm to 14,872 pm a fall of 29%.

USA male TND to CMR ratios initially were 1:6.3 by the index years they had narrowed to 1:1.2.

Female over 75’s CMR for the TC average fell from 13,038 pm down to 10,989 pm, a 16% reduction. USA over 75’s female went from 11,277 pm to 11,040 pm, a 2% decline.

USA TND to CMR ratios in 1989–1991 had been 1:3.53 but by the 2008–2010 this had been reversed so that for every female over 75 cancer death there were 1.85 neurological deaths [Table 4].

Table 1: Contd...

| Country 1989-1991 rank | TND | Current and 1989-1991 rank | Males | Female |
|------------------------|-----|---------------------------|-------|--------|
| 17-7=Netherlands        | 520 | 354                       | 2008-2010 | 443 |
| 18-19=Portugal          | 246 | 204                       | 2008-2010 | 416 |
| 19-16=Austria           | 367 | 316                       | 2009-2011 | 357 |
| 20-21=Greece            | 154 | 115                       | 2008-2010 | 274 |
| 21-20=Japan             | 206 | 150                       | 2008-2010 | 219 |
| Ratio                  | 1.69 | 1.48                      | 2008-2010 | 1.06 |
| Ratio                  | 1.78 | 1.72                      | 2008-2010 | 1.32 |

TND: Total neurological deaths, OR: Odds ratio

Table 2: Elderly (75+) TND (rates per million) OR 1989-1991 versus 2008-2010: Ranked highest male cancer deaths

| Country 1989-1991 versus latest year | TND | Current and 1989-1991 rank | Males | Female |
|--------------------------------------|-----|---------------------------|-------|--------|
| 1-2=Finland                          | 6463 | 7564                      | 2008-2010 | 19,887 |
| 2-11=USA                             | 3336 | 3206                      | 2008-2010 | 12,271 |
| 3-1=Switzerland                      | 6946 | 7422                      | 2008-2010 | 9811 |
| 4-4=Canada                           | 5246 | 4715                      | 2007-2009 | 9400 |
| 5-16=Denmark                         | 2599 | 2251                      | 2008-2010 | 8810 |
| 6-7=France                           | 4358 | 4279                      | 2008-2010 | 8586 |
| 7-14=Sweden                          | 3006 | 3518                      | 2008-2010 | 8508 |
| 8-10=Spain                           | 3368 | 3007                      | 2008-2010 | 8445 |
| 9-13=Norway                          | 3221 | 3025                      | 2008-2010 | 8316 |
| 10-6=Australia                       | 4372 | 4436                      | 2008-2010 | 8102 |

Contd...
### Table 2: Contd...

| Country 1989-1991 versus latest year | TND |  |  |
|-------------------------------------|-----|--|---|
| Current and 1989-1991 rank | Male | Female |
| Ratio | 1.85 | 2.44 |
| 11-3=Belgium | 5766 | 6175 |
| 2008-2010 | 7953 | 9558 |
| Ratio | 1.38 | 1.55 |
| 12-8=Netherlands | 3598 | 3158 |
| 2009-2011 | 7699 | 11,283 |
| Ratio | 2.14 | 3.57 |
| 13-12=New Zealand | 3227 | 3289 |
| 2007-2009 | 7038 | 9075 |
| Ratio | 2.18 | 2.76 |
| 14-5=UK | 4785 | 4662 |
| 2008-2010 | 6862 | 9144 |
| Ratio | 1.43 | 1.96 |
| 15-9=Ireland | 3403 | 3282 |
| 2008-2010 | 6035 | 7100 |
| Ratio | 1.77 | 2.16 |
| 16-15=Italy | 2761 | 2466 |
| 2008-2010 | 5806 | 6960 |
| Ratio | 2.10 | 2.82 |
| 17-17=Germany 1990-1992 | 2378 | 1805 |
| 2008-2010 | 4472 | 5091 |
| Ratio | 1.88 | 2.82 |
| 18-18=Austria | 1978 | 1465 |
| 2008-2010 | 4238 | 4455 |
| Ratio | 2.14 | 3.03 |
| 19-20=Portugal | 1050 | 817 |
| 2008-2010 | 4093 | 4042 |
| Ratio | 3.90 | 4.96 |
| 20-21=Japan | 844 | 729 |
| 2008-2010 | 1540 | 1480 |
| Ratio | 1.82 | 2.03 |
| 21-19=Greece | 1127 | 1045 |
| 2008-2010 | 1166 | 1479 |
| Ratio | 1.03 | 1.42 |

Elderly male and female combined neurological death $p=0.0487$, $P<0.001$. TND: Total neurological deaths, OR: Odds ratio

### Table 3: Contd...

| Country 1989-1991 versus latest year | CMR | CMR:TND |
|-------------------------------------|-----|---------|
| Current and 1989-1991 rank | Males | Females | Males OR | Female OR |
| 3-1=Denmark | 8741 | 6729 | 1:2.33 | 1:1.68 |
| 2008-2010 | 6206 | 4948 |  |  |
| Ratio | 0.71 | 0.74 | | |
| 4-2=Italy | 8735 | 3977 | 1:1.46 | 1:1.16 |
| 2008-2018 | 6158 | 3449 |  |  |
| Ratio | 0.70 | 0.87 | | |
| 5-13=Germany 1990-1992 | 7293 | 4553 | 1:1.42 | 1:1.15 |
| 2008-2010 | 6099 | 3873 |  |  |
| Ratio | 0.84 | 0.87 | | |
| 6-6=Belgium | 8163 | 4195 | 1:1.12 | 1:1.10 |
| 2008-2010 | 6067 | 3654 |  |  |
| Ratio | 0.74 | 0.87 | | |
| 7-19=Portugal | 6287 | 3377 | 1:1.76 | 1:0.956 |
| 2008-2010 | 6047 | 5211 |  |  |
| Ratio | 0.96 | 1.54 | | |
| 8-20=Greece | 6281 | 3073 | 1:1.87 | 1:1.89 |
| 2008-2010 | 5985 | 2789 |  |  |
| Ratio | 0.95 | 0.91 | | |
| 9-4=Netherlands | 8536 | 4629 | 1:1.21 | 1:0.87 |
| 2009-2011 | 5954 | 5568 |  |  |
| Ratio | 0.70 | 1.20 | | |
| 10-5=UK | 8490 | 5832 | 1:1.25 | 1:1.16 |
| 2008-2010 | 5879 | 4412 |  |  |
| Ratio | 0.69 | 0.76 | | |
| 11-7=Ireland | 8114 | 5487 | 1:1.38 | 1:1.29 |
| 2008-2010 | 5620 | 4201 |  |  |
| Ratio | 0.69 | 0.77 | | |
| 12-11=Austria | 7511 | 4473 | 1:1.31 | 1:1.08 |
| 2008-2010 | 5547 | 3664 |  |  |
| Ratio | 0.74 | 0.77 | | |
| 13-18=Japan | 6524 | 3020 | 1:1.25 | 1:1.52 |
| 2008-2010 | 5532 | 2633 |  |  |
| Ratio | 0.85 | 0.87 | | |
| 14-9=Canada | 7841 | 4874 | 1:1.49 | 1:1.30 |
| 2007-2009 | 5305 | 3735 |  |  |
| Ratio | 0.68 | 0.77 | | |
| 15-10=New Zealand | 7667 | 5774 | 1:1.58 | 1:1.07 |
| 2007-2009 | 5101 | 5327 |  |  |
| Ratio | 0.67 | 0.92 | | |
| 16-8=USA | 7938 | 5191 | 1:2.84 | 1:1.80 |
| 2008-2010 | 5087 | 4241 |  |  |
| Ratio | 0.64 | 0.82 | | |
| 17-14=Australia | 7231 | 4453 | 1:1.49 | 1:1.42 |
| 2008-2010 | 4861 | 3248 |  |  |
| Ratio | 0.67 | 0.73 | | |
| 18-15=Norway | 6910 | 4706 | 1:1.51 | 1:1.13 |
| 2008-2010 | 4838 | 3936 |  |  |
| Ratio | 0.70 | 0.84 | | |
Changes over the period odds ratios cancer mortality rate to total neurological death

Neurological to cancer deaths

In Table 3 the final column shows the ORs of TND to CMR for both sexes.

55–74-year-old

Male 55–74 CMR: TND ratios of >1:1.20 occurred in 20 countries, with a TC average OR of 1:1.53 over the period.

The USA CMR: TND OR was 2.84 and had the widest OR of all countries.

Female 55–74 CMR: TND ORs of >1:1.20 occurred in 9 countries, the TC average OR was 1:1.25.

Table 3: Contd...

| Country 1989-1991 versus latest year | CMR | CMR:TND |
|-------------------------------------|-----|---------|
|                                     |     |         |
|                                     | Males | Females | Males OR | Female OR |
| 19–16 = Finland                      | 6844  | 3954    | 1.24    | 1.37     |
| 2008-2010                            | 4629  | 3642    | 1.28    | 1.37     |
| Ratio                               | 0.68  | 0.82    |         |          |
| 20–17 = Switzerland                 | 6650  | 4049    | 1.14    | 1.15     |
| 2008-2010                            | 4624  | 3532    | 1.15    | 1.16     |
| Ratio                               | 0.70  | 0.87    |         |          |
| 21–21 = Sweden                      | 6132  | 4515    | 1.19    | 1.63     |
| 2008-2010                            | 3476  | 3084    | 1.15    | 1.68     |
| Ratio                               | 0.57  | 0.68    |         |          |

55–74 years male and female circulatory deaths $\rho = +0.2949$, $P < 0.1$ trend. CMR: Cancer mortality rate, TND: Total neurological deaths, OR: Odds ratio

Table 4: Contd...

| Country 1989-1991 versus latest year | CMR | CMR:TND |
|-------------------------------------|-----|---------|
|                                     |     |         |
|                                     | Males | Females | Males OR | Female OR |
| 55–74 years male and female circulatory deaths $\rho = +0.2949$, $P < 0.1$ trend. CMR: Cancer mortality rate, TND: Total neurological deaths, OR: Odds ratio

Table 4: CMR 75+ people, OR CMR:TND (rates per million) ratios 1989-2010: Ranked highest male CMR

| Country 1989-1991 versus latest year | CMR | CMR:TND |
|-------------------------------------|-----|---------|
|                                     |     |         |
|                                     | Males | Females | Males OR | Female OR |
| 1–6 = France                        | 24,259 | 11,455 | 1:2.10  | 1:2.85    |
| 2008-2010                            | 22,904 | 9,970   | 1:2.30  | 1:3.07    |
| Ratio                               | 0.94  | 0.87    |         |          |
| 2–9 = Ireland                       | 23,613 | 14,024 | 1:1.86  | 1:2.18    |
| 2008-2010                            | 22,523 | 13,495 | 1:1.63  | 1:2.30    |
| Ratio                               | 0.95  | 0.99    |         |          |
| 3–5 = UK                            | 25,004 | 13,495 | 1:1.63  | 1:1.88    |
| 2008-2010                            | 22,100 | 12,488 | 1:1.53  | 1:1.97    |
| Ratio                               | 0.88  | 0.87    |         |          |
| 4–4 = Denmark                       | 25,453 | 14,468 | 1:3.94  | 1:5.51    |
| 2008-2010                            | 21,882 | 11,083 | 1:3.21  | 1:4.22    |
| Ratio                               | 0.71  | 0.93    |         |          |
| 5–10 = Italy                        | 22,856 | 13,822 | 1:2.25  | 1:2.44    |
| 2008-2010                            | 20,571 | 12,499 | 1:2.25  | 1:2.44    |
| Ratio                               | 0.97  | 1.13    |         |          |
| 6–13 = New Zealand                  | 20,571 | 12,499 | 1:2.10  | 1:2.85    |
| 2008-2010                            | 19,914 | 9,780   | 1:1.77  | 1:2.05    |
| Ratio                               | 0.97  | 1.03    |         |          |
| 7–17 = Japan                        | 20,559 | 9,579  | 1:2.10  | 1:2.85    |
| 2008-2010                            | 19,914 | 9,780   | 1:1.77  | 1:2.05    |
| Ratio                               | 0.97  | 1.03    |         |          |
| 8–16 = Spain 89-91                  | 20,814 | 9,792  | 1:2.56  | 1:3.52    |
| 2008-2010                            | 20,394 | 9,579  | 1:2.56  | 1:3.52    |
| Ratio                               | 0.98  | 0.97    |         |          |
| 9–11 = Australia                    | 21,538 | 10,839 | 1:1.97  | 1:2.30    |
| 2008-2010                            | 20,335 | 11,504 | 1:1.97  | 1:2.30    |
| Ratio                               | 0.94  | 1.06    |         |          |
| 10–3 = Canada                       | 25,464 | 12,567 | 1:2.27  | 1:2.79    |
| 2007-2009                            | 20,089 | 12,479 | 1:2.27  | 1:2.79    |
| Ratio                               | 0.79  | 0.99    |         |          |
| 11–2 = Belgium                      | 27,988 | 12,749 | 1:1.86  | 1:1.74    |
| 2008-2010                            | 19,947 | 11,361 | 1:1.86  | 1:1.74    |

Contd...
The USA female OR was 1:1.80 and was the highest of all the countries.

**Over 75’s**

Male CMR: TND ORs for over 75’s was >1:2.00 in 14 countries, with a TC average of 1:2.83.

The USA CMR: TND ratio was 1:5.18 and was highest of all countries under review.

Over 75’s female ORs more than doubled in 17 countries, the TC average being 1:3.04.

The USA cancer to neurological death for the over 75’s female OR was 1:6.50 and was the largest of all countries.

**Circulatory disease deaths 55–74**

Male 55–74 CDD TC average of 10,103 pm fell to 3936 pm a 61% reduction, the USA fell from 10,165 pm to 4685 pm a 54% reduction.

In the baseline years, USA TND to CDD was one to 29 (1:29.6) by 2008–10 they had narrowed to <1 in 8 (1:7.5).

Female 55–74 CDD TC average rates fell from 4343 pm to 2361 pm, a decline of 46%. American female rates fell from 5191 pm to 2461 pm a 53% reduction.

In the baseline years, female USA TND to CDD had been 1:13.73 at the end of the period they were 1:4.39 [Table 5].

**Circulatory disease death the over 75’s**

Male over 75’s TC average CDD rates went from 49,784 pm to 29,429 pm a fall of 41% and rates fell by than 25% in every country. The USA male CDD rate fell from 48,792 pm to 29,439 pm a 40% reduction.

In 1989–1991 USA 75’s TND to CDD had been 1:14.63 and now is 1:2.40.

Female over 75’s rates also fell substantially (>22%) in every country, the TC average was 44,378 pm and fell to became 28,505 pm a decline of 361%, with USA rates falling from 41,079 pm to 27,553 pm, a 33% reduction.

In 1989–1991 female USA over 75’s TND to CDD ratio was 1:12.85 by 2008–2010 it is 1:1.65 [Table 6].

**Neurological to circulatory deaths odds ratios of total neurological death: Circulatory disease death [Tables 5 and 6]**

**Odds ratios 55–74**

Male 55–74 TND: CDD ORs have more than doubled in 18 countries, an average of 1:2.83. The USA was 1:3.96, which was fifth largest of 21 countries.

Female 55–74 TND to CDD ORs more than doubled in 19 countries with an average OR of 1:2.74, while USA female was 1:3.15 and was the ninth largest.

---

**Table 5: Circulatory deaths 55-74 by gender rates per million and CDD:TND (rates per million) OR 1989-2010**

| Country 1989-1991 and latest year | 55-74 | CDD: TND |
|-----------------------------------|-------|----------|
| Current and 1989-1991 rank | Male | Female | Male | Female |
| 1-2 = Finland | 13,289 | 5871 | 1:4.00 | 1:4.34 |
| 2008-2010 | 5610 | 1715 | \(0.42\) | \(0.29\) |
| Ratio | | | \(0.42\) | \(0.29\) |
| 2-15 = Greece | 7924 | 4833 | 1:2.87 | 1:3.82 |
| 2008-2010 | 4950 | 2154 | \(0.62\) | \(0.45\) |
| Ratio | | | \(0.62\) | \(0.45\) |
| 3-7 = USA | 10,165 | 5191 | 1:3.96 | 1:3.15 |
| 2008-2010 | 4685 | 2461 | \(0.46\) | \(0.47\) |
| Ratio | | | \(0.46\) | \(0.47\) |
| 4-9 = Germany 1990-1992 | 9856 | 5070 | 1:2.53 | 1:2.50 |
| 2008-2010 | 4633 | 2006 | \(0.47\) | \(0.40\) |
| Ratio | | | \(0.47\) | \(0.40\) |
| 5-3 = UK | 12,329 | 6198 | 1:2.28 | 1:2.75 |
| 2008-2010 | 4318 | 1998 | \(0.35\) | \(0.32\) |
| Ratio | | | \(0.35\) | \(0.32\) |
| 6-1 = Ireland | 13,873 | 6450 | 1:3.06 | 1:3.54 |
| 2008-2010 | 4307 | 1785 | \(0.31\) | \(0.28\) |
| Ratio | | | \(0.31\) | \(0.28\) |
| 7-8 = Austria | 9904 | 4758 | 1:2.31 | 1:2.24 |
| 2008-2010 | 4155 | 1747 | \(0.42\) | \(0.37\) |
| Ratio | | | \(0.42\) | \(0.37\) |
| 8-6 = Sweden | 10,546 | 4267 | 1:3.14 | 1:2.85 |
| 2008-2010 | 3835 | 1648 | \(0.36\) | \(0.39\) |
| Ratio | | | \(0.36\) | \(0.39\) |
| 9-5 = New Zealand | 10,918 | 5674 | 1:3.12 | 1:3.16 |
| 2007-2009 | 3761 | 1761 | \(0.34\) | \(0.31\) |
| Ratio | | | \(0.34\) | \(0.31\) |
| 10-16 = Belgium | 7210 | 3581 | 1:1.63 | 1:2.00 |
| 2008-2010 | 3704 | 1763 | \(0.51\) | \(0.48\) |
| Ratio | | | \(0.51\) | \(0.48\) |
| 11-11 = Portugal | 9240 | 5255 | 1:4.45 | 1:4.63 |
| 2008-2010 | 3481 | 1628 | \(0.38\) | \(0.32\) |
| Ratio | | | \(0.38\) | \(0.32\) |
| 12-14 = Canada | 8124 | 3575 | 1:2.40 | 1:3.38 |
| 2007-2009 | 3407 | 1518 | \(0.42\) | \(0.42\) |
| Ratio | | | \(0.42\) | \(0.42\) |
| 13-10 = Denmark | 9395 | 4417 | 1:4.61 | 1:3.44 |
| 2008-2010 | 3387 | 1578 | \(0.36\) | \(0.36\) |
| Ratio | | | \(0.36\) | \(0.36\) |
| 14-17 = Italy | 7105 | 3382 | 1:2.13 | 1:2.20 |
| 2008-2010 | 3376 | 1561 | \(0.48\) | \(0.46\) |
| Ratio | | | \(0.48\) | \(0.46\) |
| 15-19 = Spain | 6128 | 3212 | 1:2.24 | 1:2.84 |
| 2008-2010 | 3130 | 1229 | \(0.51\) | \(0.38\) |
| Ratio | | | \(0.51\) | \(0.38\) |
| 16-13 = Netherlands | 9161 | 3786 | 1:2.58 | 1:2.74 |

Contd...
In regard to the over 75’s TND to CDD ORs males more than doubled in 20 countries, with an average of 1:3.84.

The USA OR was 1:6.13 and was third highest of all countries.

Female over 75’s OR doubled in every countries, overall ORs were 1:5.05.
The USA OR at 1:9.89 was the third biggest of all countries.

Comparison of USA total neurological death rates versus other countries

Table 7 presents the CI at the 95% level of significance in comparisons of each country against the USA neurological deaths for both gender and age bands. The table shows that the USA had significantly bigger rises in TND rates for both sexes and age groups than 16 other countries.

DISCUSSION

Main findings

The first null hypothesis, that there would be no significant differences between neurological and the control mortalities over the period can be rejected for both sexes and age bands. The control mortalities fell in every country, whereas the TND, for male and female over 75’s rates rose considerably and more than doubled in 13 and 17 countries, respectively.

The second null hypothesis that the USA would not be significantly different from the other countries can also be largely rejected, as USA 55–74 male neurological rates had been equal 17th highest but had risen to being second highest, while USA females went from 10th to being highest out of 21 countries. Moreover, apart from Portugal, over the 20 years the USA had statistically significant greater rises in TND than 16 other countries, indicating disproportionate changes in neurological morbidity and mortality in American adults (55–74) and the over 75’s.

Limitations

- A core limitation in any study of international mortality rates is the reliability in the reporting of the causes of death and diagnoses where there may be changes in fashion or recording methods. For example, WHO mortality data was previously reported in separate age bands 55–64 and 65–74 but since 2008 they have been combined into 55–74, which made it impossible to directly compare the earlier rates for 55–64-year-olds, which had risen significantly in some countries. Nonetheless, the WHO international data is the most reliable available as it is collated in a consistent and uniform manner.
- The differential changes over the period of the three mortalities will likely have been influenced by local health priorities for treatment and the differentials between the neurological deaths and the other mortalities. This would have also been affected by the advances in health policy and treatment of cancer and the circulatory disease and perhaps by a higher priority given to these conditions compared to the neurological. Country specific research would be needed to determine such influences.

Table 7: 20 Western countries versus USA TND by age and gender CI

| Country versus USA | Male 55-74 | Male 75+ | Female 55-74 | Female 75+ |
|--------------------|-----------|---------|-------------|-----------|
|                    | Lower     | OR      | Lower       | OR        | Lower      | OR      | Lower      | OR        |
| Australia          | 1:1.49    | 1:1.79  | 1:2.15      | 1:1.89    | 1:1.99     | 1:2.1    |
| Austria            | 1:1.54    | 1:1.87  | 1:2.28      | 1:1.68    | 1:1.8      | 1:1.92   |
| Belgium            | 1:1.85    | 1:2.2   | 1:2.62      | 1:2.53    | 1:2.67     | 1:2.81   |
| Canada             | 1:1.52    | 1:1.81  | 1:2.17      | 1:1.95    | 1:2.05     | 1:2.16   |
| Denmark            | 1:0.93    | 1:1.13  | 1:1.36      | 1:1.07    | 1:1.13     | 1:1.2    |
| Finland            | 1:1.03    | 1:1.21  | 1:1.43      | 1:1.14    | 1:1.2      | 1:1.25   |
| France             | 1:1.52    | 1:1.82  | 1:2.18      | 1:1.77    | 1:1.87     | 1:1.97   |
| Germany            | 1:1.24    | 1:1.49  | 1:1.8       | 1:1.72    | 1:1.83     | 1:1.95   |
| Greece             | 1:0.82    | 1:1.04  | 1:1.31      | 1:3.41    | 1:3.74     | 1:4.1    |
| Ireland            | 1:1.61    | 1:1.93  | 1:2.31      | 1:1.96    | 1:2.07     | 1:2.2    |
| Italy              | 1:1.49    | 1:1.8   | 1:2.16      | 1:1.65    | 1:1.75     | 1:1.86   |
| Japan              | 1:1.3     | 1:1.64  | 1:2.06      | 1:1.61    | 1:1.76     | 1:1.93   |
| New Zealand        | 1:1.42    | 1:1.71  | 1:2.07      | 1:1.59    | 1:1.69     | 1:1.78   |
| Netherlands        | 1:1.78    | 1:2.14  | 1:2.57      | 1:1.63    | 1:1.72     | 1:1.82   |
| Norway             | 1:1.36    | 1:1.62  | 1:1.93      | 1:1.34    | 1:1.41     | 1:1.49   |
| Portugal           | 1:0.92    | 1:1.13  | 1:1.38      | 1:0.97    | 1:1.05     | 1:1.13   |
| Spain              | 1:1.33    | 1:1.59  | 1:1.91      | 1:1.48    | 1:1.57     | 1:1.66   |
| Sweden             | 1:1.35    | 1:1.62  | 1:1.94      | 1:1.23    | 1:1.3      | 1:1.38   |
| Swiss              | 1:1.56    | 1:1.87  | 1:2.23      | 1:2.48    | 1:2.6      | 1:2.74   |
| UK                 | 1:1.78    | 1:2.13  | 1:2.53      | 1:2.43    | 1:2.56     | 1:2.71   |

CI: Confidence interval; OR: Odds ratio; TND: Total neurological deaths
• Research on MND, which is part of TND, has yielded some inconsistencies for while some studies found little change in MND rates, and some attributed to the rises to improved categorization,²¹ but others demonstrated what appears to be an unequivocal upward trend in MND in a number of countries.²³⁻²⁵,²⁷⁻²⁹,³⁵,⁴⁶,⁴⁸ Furthermore, some have shown that because of problems differentiating between underlying contributory causes of death, this may have led to an under-reporting of neurological mortality.¹³⁻²³,²⁵,⁴⁴ However, by comparing a country’s mortality rates against itself, this maintains a degree of internal reliability although there might have been a greater willingness to highlight neurological pathology and etiology than before.

• The disproportionate rises in TND compared to CMR and CDD might be attributed to more effective treatment of these conditions, as there have been national campaigns to reduce these diseases in many countries, so the possible main reason for the divergence has been more effective treatments? However, would this account for the doubling of TND in most countries in such a relatively short-time, and for the remarkable rises in the USA?

• Possible interactive factors that have contributed to the increases in TND may be related to the emerging increase in “early-onset dementia,” that could be related to lifestyle changes, rather than wider environmental factors, such as greater alcohol dependence and possible drug-related neurological disturbances⁴⁶ but would this have so markedly affected the over 75’s rates?²⁶⁻²⁹,⁴⁸ Moreover, the extent of “early dementias,” often seen in people under 60, was virtually unknown 30 or more years ago and the more than doubling of the over 75’s TND rates in the US within just 20 years, suggests that interactive multiple environmental and lifestyle factors are operating.

• Neurological diseases are considered to be “diseases of the elderly”⁴⁷ and that possibly the rises are essentially due to the “Gompertzian effect”-that is, that as people live longer, they have diseases that previously they would not have lived long enough to develop.⁷⁻¹⁴,⁴⁹ This appears to have some validity, but the question is whether such substantial changes, occurring over a relatively short period, are mainly due to the Gompertzian effect? However, international changes in regard to cancer deaths⁴¹,⁴² do not accord with a Gompertzian prediction, nor does this explanation account for changes between countries and gender especially in the USA, as other studies, while acknowledging an element of Gompertzian process, have suggested that environmental factors play a larger part.²⁻²⁶,²⁵,⁴¹,⁴⁵ Finally, life expectancies have continued to rise over the past 30, between ICD editions in every country under review, but with relatively little differences between the countries, though women on average continue to outlive men,⁴⁷ which would possibly be a contributing factor to the sex differences found. Though while caution is required interpreting these results, the extent of the changes must be a cause of concern and require answers.

Overall, therefore, despite the above limits, the neurological changes found when contrasted against cancer and CDDs, all of whom shared the multiple environmental changes, are suggestive that multiple interactive factors are affecting human neurology.

There is much this study cannot explain, seen in three brief examples; the marked differences between countries over time; women’s older rate increasing more than males and what accounts for the remarkable two and five-fold increases in older American neurological deaths, which should stimulate a range of hypotheses, which again will require country-specific research. Nonetheless, despite the relatively short period of 20 years, paradoxically, with the relative decline of CMR and CDD deaths, especially in the older group, what if anything has opened the way for any possible latent neurological pathology to develop, we just do not know but is an area for future research.

**CONCLUSIONS**

The Gompertzian explanation appears limited, not least because it does not explain the USA position, but we avoid the temptation to speculate but point toward a number of studies indicating possible epigenetic factors influencing neurological morbidity,³⁻⁵,¹⁵,²²⁻²⁴,²⁶⁻²⁹,³²⁻³⁶ suggesting that possible nongenetic influences on gene expression, may be entertained.⁴⁻⁶,¹⁰⁻¹²,¹₃⁻¹₆,¹⁹⁻³₂,⁴¹

The nature of any environmental factors are uncertain but there have been major environmental changes; including increased population, economic activity, substantial rises in road and air travel; increased home technology involving background electromagnetic fields (mobile phones, microwave ovens, computers), which are unique to these later years and these possible environmental factors cannot be ignored, especially as they probably interact.⁶⁻¹⁰,²⁷⁻²₉,³₃ This list of possible features might be described as “modern living” and the USA is the epitome of “modern living.”

**IMPLICATIONS**

The recognition that increased longevity carries new problems is well accepted, however, the extent of the disproportionate increase in neurological morbidity in comparison with other diseases of the elderly, puts further pressure on already stretched health and social care services but may not yet be fully recognized in regard
to neurology. The substantial earlier onset of neurological disorders will have profound psychosocial and economic implications for patients, families, and front-line services that must add to the burden of disease within society, with inevitable psycho-socioeconomic impact upon all involved.[1,3,11,21,29,33,36,48] There is growing concern about the “burden of disease of older people”, with improvements in longevity.[37] A new major international study confirmed that it is the cardiovascular and cancer diseases (45%) that are greatest burden of diseases, and they report only 6.6% related to neurological disorders.[38] However, in a systematic international review of the “cost-of-illness” related to dementia in a number of countries, it showed the new extent of the considerable cost drivers linked to dementia, impacting upon patient and families, with new pressures upon healthcare systems.[45] With the above result indicating that neurological morbidity in continuing to rise disproportionately, these costs for family and society are likely to increase. A stark example of this is seen in a recently created British charity “Young Dementia UK,” whose clients are mainly people in their late 40’s and early 50’s, which reflect the human cost of earlier studies showing that the dementia are starting earlier.[35,48]

Crucially therefore, relative to other specialties, the present configuration of services may require re-organization, especially for specialist neurological services and for community psychosocial provision, to meet the challenge. While increases in Alzheimer disease is recognized in many Western countries, there have also been rises in other neurological diseases,[12,4,12,29,31-33,38,41,48] that need to be brought to national attention. Indeed, there are lessons to be drawn from reduced cancer mortality as every government has made major additional investments in cancer services to respond to wider public concern,[1] which led to major research and treatment resources. This level of commitment, investment, and research needs to be matched in the field of neurology to meet the new challenge, especially in the USA, as with their disproportionate increases in neurological morbidity and mortality, this must be a major cause for concern.

REFERENCES

1. Alonso A, Logrosino G, Jick SS, Hernán MA. Incidence and lifetime risk of motor neuron disease in the United Kingdom: A population-based study. Eur J Neurolo 2009;16:745-51.
2. Alonso V, Villaverde-Hueso A, Hens MJ, Morales-Piga A, Abaitua I, de la Paz MP. Increase in motor neuron disease mortality in Spain: Temporal and geographical analysis (1990-2005). Amyotroph Lateral Scler 2011;12:192-8.
3. Alzheimer’s Association. Alzheimer’s disease facts and figures. Alzheimer’s Dement 2013;9:208-45.
4. Bergen DC, Silberberg D. Nervous system disorders: A global epidemic. Arch Neurol 2002;59:1194-6.
5. Callaghan B, Feldman D, Gruijs K, Feldman E. The association of exposure to lead, mercury, and selenium and the development of amyotrophic lateral sclerosis and the epigenetic implications. Neurodegener Dis 2011;8:1-8.
6. Chang PA, Wu YJ. Motor neuron diseases and neurotoxic substances: A possible link? Chem Biol Interact 2009;180:127-30.
7. Chio A, Magnani C, Sflquier D. Gompertzian analysis of ALS mortality in Italy 1957-1987: Application to birth cohorts. Neuroepidemiology 1995;14:269-77.
8. Cima V, Logrosino G, D’Ascenzo C, Palmieri A, Volpe M, Biani C, et al. Epidemiology of ALS in Padova district, Italy, from 1992 to 2005. Eur J Neurolo 2009;16:920-4.
9. CJD Surveillance Unit. CJD Figures. 2010. Available from: http://www.cjd.ac.uk/figures.htm. [Last accessed on 2014 Jun 06]
10. Costa LG, Giordano G, Faustman EM. Domoic acid as a developmental neurotoxin. Neurotoxicology 2010;31:409-23.
11. D’Alton S, Hunter S, Whitehouse P, Brayne C, George D. Adapting to dementia in society: A challenge for our lifetimes and a charge for public health. J Alzheimers Dis 2014;42:151-63.
12. Day TG, Scott M, Perrin R, Doyle P. Motor neuron disease mortality in Great Britain continues to rise: Examination of mortality rates 1975 – 2004. Amyotroph Lateral Scler 2007;8:337-42.
13. Diekstra FP, Beleza-Meireles A, Leigh NP, Shaw CE, Al-Chalabi A. Interaction between PON1 and population density in amyotrophic lateral sclerosis. Neuroreport 2009;20:186-90.
14. Easton DM. Gompertzian growth and decay: A powerful descriptive tool for neuroscience. Physiol Behav 2005;86:407-14.
15. Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, et al. Global prevalence of dementia: A Delphi consensus study. Lancet 2005;366:211-27.
16. Flint-Richter P, Sadezki S. Genetic predisposition for the development of radiation-associated meningioma: An epidemiological study. Lancet Oncol 2007;8:403-10.
17. Forbes RB, Colville S, Parratt J, Swinger RJ. The incidence of motor neuron disease in Scotland. J Neurol 2007;254:866-9.
18. Goldacre MJ, Duncan M, Griffith M, Turner MR. Trends in death certification for multiple sclerosis, motor neuron disease, Parkinson’s disease and epilepsy in English populations 1979-2006. J Neurol 2010;257:706-15.
19. Gordon PH, Artaud F, Aubia A, Laurent F, Meininger V, Elbaz A. Changing mortality for motor neuron disease in France (1968-2007): An age-period-cohort analysis. Eur J Epidemiol 2011;26:729-37.
20. Graham AJ, Macdonald AM, Hawkes CH. British motor neuron disease twin study. J Neurol Neurosurg Psychiatry 1997;62:562-9.
21. Hebert LE, Weuve J, Scherr PA, Evans DA. Alzheimer disease in the United States (2010-2050) estimated using the 2010 census. Neurology 2013;80:1778-83.
22. Horton R. GBD 2010: Understanding disease, injury, and risk. Lancet 2012;380:2053-4.
23. Hugo J, Ganguli M. Dementia and cognitive impairment: Epidemiology, diagnosis, and treatment. Clin Geriatr Med 2014;30:421-42.
24. Imazumi Y. Longitudinal gompertzian analysis of mortality from prostate cancer, Japan, 1955–1996. Cancer Detect Prev 2000;24:473-84.
25. Imazumi Y. Longitudinal Gompertzian analysis of Parkinson’s disease mortality in Japan, 1950-1993. Mech Ageing Dev 1995;88:15-23.
26. James BD, Leurgans SE, Hebert LE, Scherr PA, Yaffe K, Bennett DA. Contribution of Alzheimer disease to mortality in the United States. Neurology 2014;82:1045-50.
27. Johansen C. Electromagnetic fields and health effects – Epidemiologic studies of cancer, diseases of the central nervous system and arrhythmia-related heart disease. Scand J Work Environ Health 2004;30 Suppl 1:1-30.
28. Kasai M, Nakamura K, Meguro K. Alzheimer’s disease in Japan and other countries: Review of epidemiological studies in the last 10 years. Brain Nerve 2010;62:667-78.
29. Kelley BJ, Boeve BF, Josephs KA, Zabetian CP. The association of exposure to lead, mercury, and selenium and the development of amyotrophic lateral sclerosis and the epigenetic implications. Neurodegener Dis 2011;8:1-8.
30. Kermoianis P, Ioannidis P, Konstantinopoulos E, Karacostas D. Early onset dementias: Demographic characteristics and etiological classification in a
34. Mercy L, Hodges JR, Dawson K, Barker RA, Brayne C. Incidence of early-onset dementias in Cambridgeshire, United Kingdom. Neurology 2008;71:1496-9.
35. Murphy M, Quinn S, Young J, Parkinson J. Increasing incidence of ALS in Canterbury, New Zealand: A 22-year study. Neurology 2008;71:1889-95.
36. Panegyres PK, Chen HY, Coalition against Major Diseases (CAMD). Early-onset Alzheimer's disease: A global cross-sectional analysis. Eur J Neurol 2014;21:1149-54, e64.
37. Prince MJ, Wu F, Guo Y, Gutierrez Robledo LM, O'Donnell M, Sullivan R, et al. The burden of disease in older people and implications for health policy and practice. Lancet 2015;385:549-62.
38. Pritchard C, Baldwin D, Mayers A. Changing patterns of adult (45-74 years) neurological deaths in the major Western world countries 1979-1997. Public Health 2004;118:268-83.
39. Pritchard C, Evans B. Population density and cancer mortality by gender and age in England and Wales and the Western World 1963-93. Public Health 1997;111:215-20.
40. Pritchard C, Hickish T. Comparing cancer mortality and GDP health expenditure in England and Wales with other major developed countries from 1979 to 2006. Br J Cancer 2011;105:1788-94.
41. Pritchard C, Mayers A, Baldwin D. Changing patterns of neurological mortality in the 10 major developed countries – 1979-2010. Public Health 2013;127:357-68.
42. Retsky MW, Swartzendruber DE, Bame PD, Wardwell RH. Computer model challenges breast cancer treatment strategy. Cancer Invest 1994;12:559-67.
43. Riggs JE, Schochet SS Jr. Rising mortality due to Parkinson's disease and amyotrophic lateral sclerosis: A manifestation of the competitive nature of human mortality. J Clin Epidemiol 1992;45:1007-12.
44. Rizzi L, Rosset I, Roriz-Cruz M. Global epidemiology of dementia: Alzheimer's and vascular types. Biomed Res Int 2014;2014:908915.
45. Rose MR, Rauzer CL, Mueller LD, Benford G. A revolution for aging research. Biogerontology 2006;7:269-77.
46. Schaller S, Mauskopf J, Kriza C, Wahister P, Kolominsky-Rabas P. Pay me now or pay me later: Dementia and the cost of health care. Int J Geriatr Psychiatry 2015;30:111-29.
47. Scott KM, Abhinav K, Wijesekera L, Ganesalingam J, Goldstein LH, Janssen A, et al. The association between ALS and population density: A population based study. Amyotroph Lateral Scler 2010;11:435-8.
48. Woodburn KJ, Johnstone EC. Early-onset dementia in Lothian, Scotland: An analysis of clinical features and patterns of decline. Health Bull (Edinb) 1999;57:384-92.
49. World Health Organization. International Classification of Diseases. 10th ed. Geneva: World Health Organization; 1992.
50. World Health Organization. World Statistical Annual 1980-2008. Geneva, Switzerland: World Health Organization; 2014. Available from: http://www.who.int/whosis/mort/table 1. process.cfm.