

Neurological Deaths in the 21st Century in 21 Western Countries: Demographics or Environmental Causes

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Abstract

Introduction: There is evidence of rising neurological deaths in the Western world. This study examines any changes during the 21st century to indicate whether the causes are primarily demographic or environmental.

Method: All data based upon WHO mortality rates per million (pm) for WHO mortality categories Nervous Disease Deaths (NDD) and Alzheimer and Other Dementias Deaths (AlzD) to calculate a Combined Neurological Mortality rate for people aged 55-74 Year Olds (lower than Western life-expectancy) and AGE-STANDARDISED-DEATH-RATES (ASDR) (pm) for both sexes. Over75's neurological deaths and population numbers analyzed to determine if increased mortality mainly due to an ageing population.

Results: 55-74Year Olds: NDD rates were higher than AlzD in every country. Combined rates rose substantially in ten countries, although Canadian and French rates fell. Total ASDR: NDD and AlzD increased substantially in all countries. Highest combined rates rose from 476 per million (pm) to 973pm in Finland, followed by America 336 pm to 592 pm and UK 205 pm to 553 pm. Notable increases in numbers of deaths of 55-74-year-olds, below Western life-expectancy olds, were Austria 77%, Germany 52%, Sweden 48%, Finland 44%, America 39%, Japan 36% the UK 32% in just 16 years. Examples of major rises in Total neurological deaths was in Britain going from 24,601 to 103,550 and in America from 174,708 to 436,43, whilst Over75's neurological deaths substantially outstripped population increases.

Conclusions: Neurological death rates are accelerating at an unprecedented rate, challenging the Gompertzian hypothesis that these increases are primarily due demographics, strongly indicating multiple interactive environmental causes.

Key words: Neurological; Mortality; Accelerating; International; Environment.

INTRODUCTION

Whilst the incidence of cardiovascular, cancer and neurological disease are strongly age-related in most developed countries, cardiovascular and cancers mortality rates have continued to fall over the past 25 years in every-one of the 21 Western Developed Countries (WDC) [1-3]. The reverse has been the case in regard to neurological disease-related mortality in spite of substantial increases in overall life expectancy [3,4-8]. This includes conditions such as Alzheimer's Disease, Motor Neurone Disease and Parkinson's Disease as well as the much rarer Multiple System Atrophy and Progressive Supra-nuclear Palsy [6-8], though in regard to Motor Neurone Disease some authorities stated that

the increases were mainly due to better diagnosis [9]. However, a range of other studies have found statistical associations between various neurological conditions and occupations such as chemicals, engineering, electronics and wider environmental influences [4,6,10-17]. The inference being that the reported increases are strongly influenced by multiple interactive environmental factors, impacting on any under-lying genetic predispositions.

Others have argued that the rises were mainly due to demographic changes and rises in longevity, postulating the Gompertzian hypothesis. This hypothesis states that as people are living longer, they are now able to develop age-related diseases that they were not old enough to develop previously and therefore the apparent rises are

an artefact [18,19]. However, the Gompertzian hypothesis has been challenged as it cannot account for the differences between the sexes and especially the big rises in early-onset-dementias, although there are underlying genetics factors associated with early dementias [20-25]. Nonetheless, in the media health correspondents often reflect the Gompertzian view by inferring the reasons for neurological increases are demographic and are mainly due to rises in the elderly (75+years) population. However, this study pays special attention to people aged 55-74years is below current life expectancy in the developed world. Hence mortality in this age-band might be considered as premature deaths.

This study builds upon earlier work [26] and asks whether the earlier reported increases in neurological death rates are accelerating in the 21st century in the twenty-one Western-Developed-Countries (WDC) [27]. These countries are Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Japan, Netherlands, New Zealand, Norway, Portugal Spain, Sweden, Switzerland, UK and the USA.

There is one working null hypothesis, that there will be no substantial rise in neurological mortality for both 55-74-year-olds and total all age neurological ASDR between 2000 and 2015.

METHODOLOGY

This study draws upon the separate WHO global neurological diagnostic categories of Nervous Disease Deaths (NDD), and, Alzheimer's and Other Dementia Deaths (AlzD) [27], which together produces the Combined Neurological Mortality (CNM) rates per million (pm) and examines changes over the relatively short period of 2000 to 2015. In addition, WHO Age-Standardised-Death-Rates (ASDR) are examined which are deaths across all age-bands, controlled for age, gender and population for NDD and AlzD mortalities producing the Combined Neurological Mortality (CNM) rate over the period [27].

Any substantial rises are defined by any increases that produce an Odds Ratio (O.R) of >1:1.20, equivalent to +20% in NDD, AlzD or CNM over the 15-year period. 'Notable' rises occur if an Odds Ratios reaches >1:1.30 that is equivalent to a 30% increase.

We compare each of the 21 WDC neurological mortality rates for the year 2000 with the latest WHO date available, which for most WDC is 2015. Canada, France, New Zealand and Portugal had earlier index years, noted in the tables, whilst Austria, Netherlands and Sweden

had data for 2016 but to maintain consistency across the majority of countries we use these nation's 2015 outcomes [27].

Neurological disease mortality is reported in two global WHO mortality categories [27], Nervous Disease Deaths (NDD), coded G00-G99, and Alzheimer' and the Dementias Deaths (AlzD), coded F01, F03, G30-31. We compare WHO Age-Standardised-Death-Rates (ASDR), which are based upon world population to provide a standardised total death rate, thus controlling for population. The NDD and AlzD ASDR rates are combined to produce the Combined Neurological Mortality (CNM) rate. A key focus is upon mature adults, people aged 55-74year of both sexes for NDD and AlzD categories. The 55-74 rates are obtained by examining the numbers of NDD and AlzD deaths divided by the 55-74-year-old population of that country to produce mortality rates per million (pm) and summing the NDD and AlzD rates provides the Combined Neurological Mortality (CNM) rates. Each country is its own control by comparing their baseline with their index years, from which a series of ratios of change are calculated.

In order to compare between countries of markedly different population sizes, it is necessary to use death rates. To some extent this can mask the practice reality of the extent of any subsequent rises and how this might impact upon the neurological and community services. So, the Numbers of neurological deaths of people aged 55-74 and total numbers of neurological deaths are also reported and compared with the changes in the numbers of the 55-74 and total populations in each country. Ratios of change are then determined over the period for both age bands from which population to Combined Neurological Mortality (CMN) odds ratios are calculated.

RESULTS

55-74-Year-olds

Table 1 is for the 55-74year olds data, ranked by highest CNM rates, which rose substantially (>20%) in eleven countries over the sixteen years 2000-2015.

The separate category of NDD were higher than AlzD in every country both in year 2000 and 2015. There were substantial rises in twelve countries for NDD and eleven countries for AlzD.

There was notable (>30%) rises in CNM in Austria up 77%, Australia 34%, Denmark 33%, Finland 44%, Germany 52%, Japan 36%, Sweden 48%, UK 32% and USA 39% in the century.

Conversely, French rates fell for both NDD and AlzD an overall 23% decline for CNM. Belgium and Canada CNM rates fell 5% and 10% respectively. Conversely, there were falls in AlzD in Greece, Italy, Japan and Portugal although their overall CNM rates had increased over the period.

Total ASDR

A perusal of Table 2 shows that All but three country's NDD rates rose more than 25% over the period, nine by more than 50%, Canada was the only nation to have a small decline, 10% in their NDD rates. Every country,

Table 1: Nervous Disease Deaths (NDD) & Alzheimer & Other Dementia Deaths (Alz) are Combined Neurological Mortality (CNM) 55-74-year-olds rates per million 2000-2015 % Change. Ranked by Highest CNM rates.

Country and % Change	NDD 55-74 2000-2015	Alzh 55-74 2000-2015	CNM 55-74 2000-2015
Finland % change	394-642 63%	305-364 19%	699-1006 44%
USA % change	364-455 25%	147-255 73%	511-710 39%
UK % change	256-399 56%	164-254 55%	420-653 32%
Sweden % change	267-387 45%	157-239 52%	424-626 48%
Netherland % change	350-379 8%	116-223 92%	466-602 29%
Denmark % change	339-398 17%	115-204 77%	454-602 33%
Norway % change	365-390 7%	125-176 39%	490-566 16%
Belgium % change	377-383 2%	206-172 -17% #	583-555 -5% #
Switzerland % change	297-356 20%	141-180 28%	438-536 22%
Ireland % change	291-345 19%	174-176 1%	465-521 12%
Spain % change	299-329 10%	195-179 -8% #	494-508 3%
Australia %change	272-335 23%	105-171 63%	377-506 34%
Canada 2013 % change	376-318 -15 #	159-165 4%	535-483 -10% #
Germany % change	254-342 35%	60-136 127%	314-478 52%
New Zealand 2013 % change	279-314 13%	129-161 25%	408-475 16%
Italy % change	266-327 23%	186-133 -28% #	452-460 2%
Portugal % change	230-290 26%	144-142 -1 % #	374-432 16%
France % change	397-321 -19 % #	173-119 -31% #	570-440 -23% #
Austria % change	160-286 79%	74-129 74%	234-415 77%
Greece % change	213-279 31%	121-99 -18% #	334-378 13%
Japan % change	123-180 46%	28-26 -7 % #	151-206 36%

rate fell over the period.

Table 2: Nervous Disease Deaths (NDD) & Alzheimer & Other Dementia Deaths (Alz) Total Age-Standardised-Death-Rates (ASDR) are Combined Neurological Mortality (CNM)per million 2000-2015 Ranked by Highest Rates.

Country and % Change	NDD ASDR 2000-2015	Alzh ASDR 2000-2015	CNM ASDR 2000-2015
Finland % change	165-492 198%	311-481 55%	476-973 104%
USA % change	187-281 50%	149-311 109%	336-592 76%
UK % change	109-205 88%	96-348 262%	205-553 170%
Netherland % change	110-190 73%	164-297 81%	274-487 78%
Sweden % change	101-175 73%	156-261 67%	257-436 70%
Ireland % change	130-186 43%	78-225 188%	208-411 98%
Switzerland % change	151-171 13%	142-239 68%	293-410 40%
Spain % change	132-188 42%	166-215 30%	298-403 35%
Denmark % change	122-173 42%	100-227 127%	222-400 80%
Norway % change	123-172 40%	85-224 163%	208-396 90%
Belgium % change	144-190 32%	144-197 37%	288-387 34%
Australia % change	136-172 26%	106-213 101%	242-385 59%
Canada 2013 % change	188-168 -11% #	167-233 40%	355-401 13%
New Zealand 2013 % change	138-152 10%	124-196 58%	262-348 33%
France % change	169-182 8%	135-154 14%	304-336 11%
Germany % change	104-135 30%	33-147 345%	137-282 106%
Italy % change	111-148 33%	103-133 29%	214-281 31%
Portugal % change	89-135 52%	52-121 133%	141-256 82%
Austria % change	78-134 72%	27-80 196%	106-214 102%
Greece % change	74-132 78%	38-52 37%	112-184 64%
Japan % change	44-71 61%	15-41 173%	59-112 nb90%

except France AlzD rates rose by >50%. The average rise in NDD over the period was 52% and 110% for AlzD.

Every nation's CNM increased by >30% except France up 11% and Canada by 13%.

Combined rates rose by more than 100% in Finland, Germany and the UK and by more than 75% in Denmark, Ireland, Japan, the Netherlands, Portugal and the USA.

Population and Neurological Deaths in the Over 75's

Table 3 presents WHO data for increases in population and

CNM in the Over 75's from which population to CNM Odds Ratios are calculated. The elderly population average rise was 33%, up 30% in 15 countries but CNM rises averaged 120%, rose and more than doubled in twelve.

Apart from Canada, at 1:0.98, every nation's population to CNM Odds Ratio was positive fifteen countries had ratios of more than 1:1.20. Whilst Odds Ratios more than doubled in the UK at 1:3.26, Norway 1:2.74, Austria 1:2.54, Ireland 1:2.32, Denmark 1:2.07, with other notable rises in Finland 1:1.95, Germany and, Portugal 1:78, Sweden 1:1.98 and the USA 1:1.83.

Table 3: Over-75's Population and Combined Neurological Mortality rates per million 2000-2015. Ratio of change Population to CNM then Odds Ratios. Ranked by highest Widest Population: CNM Odds Ratio.

Country and Widest Odds Ratio Rank	Population Millions	Ratio of Change	Rate CNM	Ratio of Change	Population: CNM Odds Ratio
UK 2000 2015	4.406 5.19	1.18	4005 15438	3.85	01:03.3
Norway 2000 2015	0.35 0.358	1.02	4200 11735	2.79	01:02.7
Austria 2000 2016	0.568 0.752	1.32	1674 5570	3.33	01:02.5
Ireland 2000 2014	0.184 0.24	1.3	3592 10812	3.01	01:02.3
Denmark 2000 2015	0.378 0.42	1.11	4838 11122	2.3	01:02.1
Sweden 2000 2016	0.788 0.83	1.05	6626 13801	2.08	1:1.98
Finland 2000 2015	0.336 0.467	1.28	12506 31246	2.5	01:01.9
USA 2000 2015	16.601 19.621	1.18	8346 18056	2.16	01:01.8
Germany 2000 2015	5.854 8.459	1.44	2511 6422	2.56	01:01.8
Portugal 2000 2014	0.69 1.003	1.45	2152 5551	2.58	01:01.8
Netherlands 2000 2016	0.965 1.282	1.33	7078 14868	2.1	01:01.6
Japan 2000 2015	8.98 15.896	1.77	880 2682	2.57	01:01.4
Australia 2000 2014	1.069 1.496	1.4	5722 11064	1.93	01:01.4
Belgium 2000 2015	0.747 0.998	1.34	6593 10771	1.63	01:01.2
Switzerland 2000 2015	0.515 0.675	1.31	8074 12693	1.57	01:01.2
New Zealand 2000 2013	0.203 0.265	1.31	6379 9844	1.54	01:01.2
France 2000 2014	4.307 5.853	1.36	7530 11177	1.48	01:01.1
Italy 2000 2015	4.473 6.595	1.47	4641 7319	1.58	01:01.1
Spain 2000 2015	2.902 4.298	1.48	7524 11920	1.58	01:01.1
Greece 2000 2015	0.669 1.158	1.73	1239 2261	1.81	01:01.0
Canada 2000 2013	1.716 2.357	1.37	9185 12235	1.33	01:01.0

Mortality Numbers for Practice Implications

To provide an indication of possible implications for services, actual numbers of deaths are reported. Table 4 gives the increases in millions of populations and rises in numbers of CNM and the percentage of change.

In respect to the 55-74-year-olds, except for Belgium, Canada and France, every countries CNM rose greater than any population rises. Whilst France was the major outlier, having a 4% fall in their numbers of deaths as against a 31% rise in the numbers of population. Overall population rises for the 55-74years averaged 29% over the period but average neurological deaths rise was 67%.

Four countries had 100% increases namely the Netherlands 133%, USA 120%, Australia 108% and Finland 100%, whilst elven had increases of more than 50%. In twelve countries 55-75 population to neurological deaths were greater than 1:1.30.

In regard to the numbers of all neurological deaths seventeen countries rose by more than 100%, more than doubling in Norway 375%, the UK 321%, Japan

299%, Finland 239%, Austria 236%, Germany 225% and Ireland 213%. Average rises in total population were 9% as against 175% rise in all neurological deaths over the period. In fourteen countries population to CMN numbers produced odds ratio of more than 1:2.00 over the period.

The widest total population to CMN odds ratios were in Norway at 1:4.09 who were tenth highest, whilst Japan, with the lowest rates had the second biggest rise over the period with an odds ratio of 1:4.03.

Three countries in particular merit further comment. The outlier country France, neurological deaths of people aged 55-74 deaths fell from 6,236 down to 5,997, an odds ratio of 1:0.73. Whereas their total neurological deaths went from 40,594 to 71,543, yielding an odds ratio of 1:61.

The UK, who were second highest, their 55-74-Year-olds deaths rose from 4,650 to 9,019, an odds ratio of 1:1.55 and total deaths rose from 24,601 to a remarkable 103,550, producing an odds ratio of 1:3.86 over the period.

Table 4: Numbers-Both Sexes 55-74 and Total Combined Neurological Mortality (CNM) 2000-15. % Population (in millions). Percentage Change for Population and CMN. Ranked by Biggest Total Pop:CMN Odds Ratio

Country 55-74, CNM Population	2000-2015 55-74years	Ratio Change	Odd Ratio	2000-2015 Total CNM	Ratio Change	Odd Ratio
Norway Population	371-616 0.757-1.088	1.66 1.44	1.15	1096-5203 4.470-5.189	4.75 1.16	4.09
Japan Population	4438-8099 29.392-33.471	1.82 1.14	1.6	14023-56027 125.612-125.319	3.99 0.99	4.03
UK Population	4650-9019 11.065-13.792	1.94 1.25	1.55	24601-103550 59.704-65.110	4.21 1.09	3.86
Germany Population	5790-9332 18.424-19.491	1.61 1.06	1.52	22543-73310 82.188-81.687	3.25 0.99	3.28
Austria Population	369-702 1.571-1.901	1.9 1.21	1.57	1519-5107 8.011-8.629	3.36 1.08	3.11
Finland Population	692-1385 0.991-1.377	2 1.39	1.45	5063-17155 5.176-5.482	3.23 1.06	3.1
Ireland Population	262-445 0.565-0.616	1.74 1.09	1.6	1080-3384 3.789-3.979	3.13 1.05	2.98
Portugal Population	779-1037 2.084-2.409	1.33 1.16	1.15	2842-7775 10.290-10.401	2.74 1.01	2.71
Netherlands Population	1026-2389 2.799-3.813	2,33 1.36	1.71	8279-21931 15.925-16.939	2.65 1.06	2.5
Denmark Population	465-798 1.023-1.325	1.72 1.30	1.32	2460-5925 5.337-5.678	2.41 1.06	2.27
Australia Population	1155-2407 3.072-4.749	2.08 1.55	1.34	7846-21594 19.153-23.781	2.75 1.24	2.22
USA population	21818-48047 42.666-67.380	2.2 1.58	1.39	174708-436438 281.421-319.929	2.5 1.14	2.19
Italy deaths Population	5693-6542 12.598-14.231	1.68 1.13	1.49	27554-61678 56.924-60.731	2.24 1.07	2.09
Greece Population	788-927 2.357-2.452	1.18 1.04	1.13	2092-4741 10.917-10.871	2.27 1.09	2.08
Spain Population	3892-5007 7.888-9.876	1.29 1.25	1.03	26679-62871 40.174-46.410	2.35 1.16	2.03
Sweden Population	743-1355 1.754-2.209	1.82 1.26	1.46	6159-13110 8.872-9.696	2.13 1.09	1.95
Belgium Population	1179-1363 2.020-2.462	1.16 1.22	0.95	6400-13054 10.251-11.266	2.04 1.10	1.85
Switzerland Population	601-972 1.373-1.814	1.62 1.32	1.23	4904-10225 7.209-8.320	2.09 1.15	1.82
N. Zealand Population	240-414 0.588-0.872	1.73 1.48	1.17	1689-3199 3.887-4.442	1.89 1.14	1.66
France Population	6236-5997 10.628-13.956	0.96 1.31	0.73	40594-71543 58.898-64.129	1.76 1.09	1.61
Canada Population	2649-3652 0.496-0.761	1.38 1.53	0.9	19293-35091 30.791-35.255	1.82 1.14	1.6

The third highest country was the USA whose 55-74 numbers of deaths went from 21,818 to 48,047, giving an odds ratio of 1:1.39. American total neurological deaths rising from 174,708 to 436,438 producing an odds ratio of 1:2.19 in just sixteen years.

DISCUSSION

Limitations

The limits in international comparative studies are due to how reliable are the data and the effect of the different configurations of each nation's health-care system upon their mortality outcomes. However, the WHO database is the most consistent and reliable available and has annually reported data from 1968 and online from 1979 onwards [27]. Moreover, by using each nation's baseline and index year's statistics as a control provides a degree of internal reliability, especially over such a short period of time. The main limit is that this study cannot explain the changes between the countries and especially the 55-74 outcomes of the outlier countries Canada, France and, to a lesser extent, Belgium. One explanation may be that their people either developed their neurological condition later or survived into an older age-band, as eventually Belgium and France had substantial increases in their total neurological deaths than rises in population. Nonetheless, the study provides a baseline for future research to explore the any subsequent acceleration of neurological mortality.

The null hypothesis is rejected as the majority of WDC substantially increased its neurological mortality for people aged 55-74, indicating that some neurological diseases are starting earlier, with eleven nations having substantial increases in 'premature deaths of the 55-74-year-old. Moreover, total mortality ASDR more than doubled in Austria, Finland, Germany and the UK, whilst fifteen nations combined rates rose by more than 30% over the century 2000-2015.

The speed of these changes poses a serious challenge to the general Gompertzian explanation [18,19], especially when considering the rises in early-onset-dementia, often occurring in people in their forties and fifties [21-26]. This is not to gainsay that there will be no Gompertzian elements as well as genetic and epigenetic factors contributing to the results. Indeed, we recall the first Professor of Genetics at Oxford in 1970, Sir Walter Bodmer's famous adage "genetics loads the gun but the environment pulls the trigger" [28]. This in part explains why one particular environmental exposure, depending upon the under-lying genetic predisposition, appears to

lead to different diseases, exemplified by the association of electromagnetism with the development of both cancer and neurological diseases [26,29-32]. The idea that these neurological increases are due to improved diagnosis and demographics [9]. [18,19] may well have a role to play but unlikely to be at such an accelerating pace in just sixteen years. The more likely explanation is that environmental and occupational factors impact upon under-lying genetic factors, creating oxidative stress that contributes to neuro-degeneration [3,4,10,11,13-17,29-32]. One strong indicator of the influence of multiple-interactive environmental factors is Finland, with its known genetic weighting for neurological disease which nevertheless doubled its rate in such a short time, whilst the USA who in 1989 were 15th highest of the twenty-one developed countries but in the space of twenty-five years rose to become the second highest in the Western world 3. Such a marked change surely suggests environmental influence and can no longer be ignored.

A practical indication of accelerating neurological morbidity in Britain is the development of two new charities, 'Young Dementia UK' and 'The Young Person's section' of 'The Parkinson's Disease Society', suggesting both community and hospital services may be overwhelmed. Exemplified in the numbers of total neurological deaths, rising from under 30,000 in the UK to more than 100,000 and in America from 174,000 to more than 436,000.

Our concern is that there may be a parallel evolving, similar to what occurred with asbestosis, which often took twenty years to develop serious symptom from initial exposure. At the moment, the impact of the asbestos crisis is still being seen in major increases in mesothelioma cases going through the age-bands who were exposed earlier in the 20th century [33-35]. But more importantly, following Governmental preventative measures the incidence of mesothelioma began to decline [36]. Therefore, it seems self-evident that with the accelerating numbers of neurological patients there will be a need for enhanced services as well as prevention.

It is feared that any necessary response could be hampered by the false assumption that increased neurological disease is largely due to demography rather than dis-proportionately more people developing neurological disease and at an earlier age. There is not only a need to determine what is causing these changes over such a short time span, but also a need for urgent action to prevent, treat and upgrade services accordingly.

Every major unsolved problem in science is usually nonlinear. This means that any discipline laboring in its own silo of science is very unlikely to find answers to problems which by their very nature-our human nature-cross several disciplines. Consilience in research now is vital. The laws of physics and the laws of unintended consequences demand that we address the complex non-linear multifactorial problems which appear to be increasing exponentially. Whatever the interactive multiplicity of factors that had led to this acceleration, in view of the speed of change it must be predominately environmental reflecting the profound changes that have occurred in the last thirty years ranging from the possible inter-action of petro-chemical, endocrine chemicals, food additives, increased air, food and water pollution and the new digital world. That were new levels of background low exposure electro-magnetism water, then many of us would be living in a faint mist [26].

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