

## Original Article

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

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## 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**Access this article online****Website:**[www.surgicalneurologyint.com](http://www.surgicalneurologyint.com)**DOI:**

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## INTRODUCTION

Neurological disease has increased in recent years throughout the developed world.<sup>[1-4,8,12,15,17,19,21,26,28,31,33,35-38,41,44]</sup> Neurological deaths are reported by the World Health Organization (WHO) in

two global categories, Alzheimer and other dementias, and nervous disease deaths<sup>[47,50]</sup> 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<sup>[50]</sup> though the incidence of the later appears to have relatively stabilized, returning close to pre-2000 levels.<sup>[9,30,41]</sup>

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<sup>[26,38,40]</sup> 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.<sup>[6,11,22,32,38,41,44]</sup> This view is supported by studies of neurological mortality that found population density was a surrogate marker for environmental exposure<sup>[13,46]</sup> and a similar link has been found in relation to incidence of cancer,<sup>[39]</sup> with substantial increases in two specific neurological conditions, MND,<sup>[1,6,8,12,19,23]</sup> and “early-onset dementias.”<sup>[29,33,34,36,38,41,49]</sup>

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.<sup>[7,14,42]</sup> 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.<sup>[1,7,21,35,38,41,49]</sup> 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.<sup>[24,25,42,45]</sup> Furthermore, increases in neurological morbidity in the less economically developed countries, would not appear to be mainly attributable to the Gompertzian explanation.<sup>[15,24,25,31,38,41,42,44,45]</sup>

Conversely, changes or improvements in diagnosis have been thought to be a possible factor,<sup>[18,23]</sup> but other reviews suggest this is not a major issue, as current brain imaging and better biomarkers allows diagnosis to be more accurate and, therefore, the figures are essentially more reliable,<sup>[23]</sup> while some USA studies showed that dementia deaths are under-reported.<sup>[21,26,33,36]</sup>

Previous work that highlighted earlier dementia deaths,<sup>[38,41]</sup> spanned a 30 years period and two International Classification of Diseases (ICDs) editions, whereas this study covers only 20 years and one ICD edition.<sup>[50]</sup> 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),<sup>[37]</sup> 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,<sup>[47]</sup> 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<sup>[20]</sup> 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 10<sup>th</sup> edition of the ICD editions,<sup>[50]</sup> making it a more uniform analysis than the earlier studies.<sup>[38,41]</sup>

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<sup>[47]</sup> 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 are 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.<sup>[49,50]</sup> Moreover, the controversy over diagnosis which can occur at the beginning of any disease process is resolved at death,<sup>[18]</sup> 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  $\pm$  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 17<sup>th</sup> 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 390 pm, up 1% whereas the USA rate went from 378 pm 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].

**Table 1: 55-74 years TND (rates per million) OR 1989-1992 versus 2008-2020 ranked by highest male deaths (current and past ranks)**

Country 1989-1991 versus 2008-2010 Current and 1989-1991 rank	TND	
	Males	Female
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...

**Table 1: Contd...**

Country 1989-1991 versus 2008-2010 Current and 1989-1991 rank	TND	
	Males	Female
17-7=Netherlands	520	354
2008-2010	443	369
Ratio	0.85	1.04
18-19=Portugal	246	204
2008-2010	416	302
Ratio	1.69	1.48
19-16=Austria	367	318
2009-2011	357	263
Ratio	0.97	0.83
20-21=Greece	154	115
2008-2010	274	198
Ratio	1.78	1.72
21-20=Japan	206	150
2008-2010	219	198
Ratio	1.06	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 Current and 1989-1991 rank	TND	
	Male	Female
1-2=Finland	6463	7564
2008-2010	19,887	24,797
Ratio	3.08	3.28
2-11=USA	3336	3206
2008-2010	12,271	21,253
Ratio	3.68	6.63
3-1=Switzerland	6946	7422
2008-2010	9811	12,322
Ratio	1.41	1.66
4-4=Canada	5246	4715
2007-2009	9400	12,996
Ratio	1.79	2.76
5-16=Denmark	2599	2251
2008-2010	8810	11,665
Ratio	3.39	5.18
6-7=France	4358	4279
2008-2010	8586	10,593
Ratio	1.97	2.48
7-14=Sweden	3006	3518
2008-2010	8508	11,869
Ratio	2.83	3.37
8-10=Spain 1989-1991	3368	3307
2008-2010	8445	11,263
Ratio	2.51	3.41
9-13=Norway	3221	3025
2008-2010	8316	10,773
Ratio	2.58	3.56
10-6=Australia	4372	4436
2008-2010	8102	10,846

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**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 3703 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 2: Contd...**

Country 1989-1991 versus latest year Current and 1989-1991 rank	TND	
	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  $\rho=+0.9487, P<0.001$ . TND: Total neurological deaths, OR: Odds ratio

**Table 3: CMR 55-74 people 1989-1991 versus 2008-2012 (rates per million). OR 1989 versus 2010 of CMR to TND countries ranked by highest male cancer deaths**

Country 1989-1991 versus latest year Current and 1989-1991 rank	CMR		CMR:TND	
	Males	Females	Males OR	Female OR
1-3=France	8703	3502	1:1.33	1:1.07
2008-2010	6520	3151		
Ratio	0.75	0.89		
2-12=Spain	7361	3207	1:1.33	1:0.53
2008-2010	6300	6547		
Ratio	0.86	2.04		

**Table 3: Contd...**

Country 1989-1991 versus latest year Current and 1989-1991 rank	CMR		CMR:TND	
	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	4453	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		

Contd...

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**Table 3: Contd...**

Country 1989-1991 versus latest year	CMR		CMR:TND	
	Males	Females	Males OR	Female OR
19-16=Finland	6844	3954	1:2.47	1:1.37
2008-2010	4629	3642		
Ratio	0.68	0.92		
20-17=Switzerland	6650	4049	1:1.40	1:1.15
2008-2010	4624	3532		
Ratio	0.70	0.87		
21-21=Sweden	6132	4515	1:1.98	1:1.63
2008-2010	3476	3084		
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: 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	
	Male	Female	Males OR	Female OR
1-6=France	24,259	11,455	1:2.10	1:2.85
2008-2010	22,904	99,701		
Ratio	0.94	0.87		
2-9=Ireland	23,613	14,024	1:1.86	1:2.18
2008-2010	22,523	13,862		
Ratio	0.95	0.99		
3-5=UK	25,004	13,495	1:1.63	1:1.88
2008-2010	22,100	14,065		
Ratio	0.88	1.04		
4-4=Denmark	25,453	14,468	1:3.94	1:5.51
2008-2010	21,882	13,589		
Ratio	0.86	0.94		
5-10=Italy	22,856	11,852	1:2.31	1:3.07
2008-2010	20,824	10,912		
Ratio	0.91	0.92		
6-13=New Zealand	21,154	11,382	1:2.25	1:2.44
2007-2009	20,571	12,849		
Ratio	0.97	1.13		
7-17=Japan	19,914	9780	1:1.77	1:2.05
2008-2010	20,559	96,769		
Ratio	1.03	0.99		
8-16=Spain 89-91	20,814	9792	1:2.56	1:3.52
2008-2010	20,394	9525		
Ratio	0.98	0.97		
9-11=Australia	21,538	10,839	1:1.97	1:2.30
2008-2010	20,335	11,504		
Ratio	0.94	1.06		
10-3=Canada	25,546	12,567	1:2.27	1:2.79
2007-2009	20,089	12,479		
Ratio	0.79	0.99		
11-2=Belgium	27,988	12,749	1:1.86	1:1.74
2008-2010	19,947	11,361		

Contd...

**Table 4: Contd...**

Country 1989-1991 versus latest year	CMR		CMR:TND	
	Male	Female	Males OR	Female OR
Ratio	0.74	0.89		
12-8=Austria	23,809	13,270	1:2.71	1:3.48
2008-2010	18,829	11,587		
Ratio	0.79	0.87		
13-20=Portugal	14,543	7804	1:3.07	1:3.44
2008-2010	18,404	11,252		
Ratio	1.27	1.44		
14-7=Germany 1990-1992	24,083	13,459	1:2.51	1:3.44
2008-2010	17,987	11,083		
Ratio	0.75	0.82		
15-19=Greece	17,505	8224	1:1.02	1:1.25
2008-2010	17,603	93,948		
Ratio	1.01	1.14		
16-1=Netherlands	28,724	13,429	1:3.51	1:3.84
2008-2010	17,490	12,488		
Ratio	0.61	0.93		
17-14=Finland	21,149	11,203	1:3.85	1:3.73
2008-2010	16,893	9897		
Ratio	0.80	0.88		
18-15=US 1989-1991	20,919	12,277	1:5.18	1:6.5
2008-2010	14,872	11,459		
Ratio	0.71	1.02		
19-12=Norway	21,167	11,151	1:3.85	1:3.04
2008-2010	14,095	12,451		
Ratio	0.67	1.17		
20-18=Sweden	18,739	10,882	1:4.22	1:3.21
2008-2010	12,572	114,442		
Ratio	0.67 ck	1.05		
21-21=Switzerland	12,237	11,523	1:45	1:2.00
2008-2010	11,918	95,616		
Ratio	0.97	0.83		

75+ male and female cancer deaths  $\rho=+5909$   $P<0.005$ . CMR: Cancer mortality rate, OR: Odds ratio, TND: Total neurological deaths

## 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.

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 CCD 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 Current and 1989-1991 rank	55-74		CDD:TND	
	Male	Female	Male	Female
1-2=Finland 2008-2010	13,289 5610	5871 1715		
Ratio	0.42	0.29		
2-15=Greece 2008-2010	7924 4950	4833 2154	1:2.87	1:3.82
Ratio	0.62	0.45		
3-7=USA 2008-2010	10,165 4685	5191 2461	1:3.96	1:3.15
Ratio	0.46	0.47		
4-9=Germany 1990-1992 2008-2010	9856 4633	5070 2006	1:2.53	1:2.50
Ratio	0.47	0.40		
5-3=UK 2008-2010	12,329 4318	6198 1998	1:2.28	1:2.75
Ratio	0.35	0.32		
6-1=Ireland 2008-2010	13,873 4307	6450 1785	1:3.06	1:3.54
Ratio	0.31	0.28		
7-8=Austria 2008-2010	9904 4155	4758 1747	1:2.31	1:2.24
Ratio	0.42	0.37		
8-6=Sweden 2008-2010	10,546 3835	4267 1648	1:3.14	1:2.85
Ratio	0.36	0.39		
9-5=New Zealand 2007-2009	10,918 3761	5674 1761	1:3.12	1:3.16
Ratio	0.34	0.31		
10-16=Belgium 2008-2010	7210 3704	3581 1763	1:1.63	1:2.00
Ratio	0.51	0.48		
11-11=Portugal 2008-2010	9240 3481	5255 1682	1:4.45	1:4.63
Ratio	0.38	0.32		
12-14=Canada 2007-2009	8124 3407	3575 1518	1:2.40	1:38
Ratio	0.42	0.42		
13-10=Denmark 2008-2010	9395 3387	4417 1578	1:4.61	1:3.44
Ratio	0.36	0.36		
14-17=Italy 2008-2010	7105 3376	3382 1561	1:2.13	1:2.20
Ratio	0.48	0.46		
15-19=Spain 2008-2010	6128 3130	3212 1229	1:2.24	1:2.84
Ratio	0.51	0.38		
16-13=Netherlands	9161	3786	1:2.58	1:2.74

Contd...

**Table 5: Contd...**

Country 1989-1991 and latest year	55-74		CDD:TND	
	Male	Female	Male	Female
<b>Current and 1989-1991 rank</b>				
2008-2010	3028	1448		
Ratio	0.33	0.38		
17-4=Norway	11,937	4852	1:4.24	1:3.80
2008-2010	3008	1236		
Ratio	0.25	0.25		
18-21=Japan	4570	2607	1:1.66	1:3.00
2008-2010	2922	1154		
Ratio	0.64	0.44		
19-18=Switzerland	6271	2515	1:2.00	1:2.13
2008-2010	2883	1191		
Ratio	0.46	0.47		
20-20=France	5144	2079	1:1.92	1:1.98
2008-2010	2666	1007		
Ratio	0.52	0.48		
21-11=Australia	9240	4461	1: 3.57	1:4.00
2008-2010	2626	1154		
Ratio	0.28	0.26		

55-74 years male and female circulatory deaths  $\rho=+0.5835$ ,  $P<0.005$ . OR: Odds ratio, CDD: Circulatory-disease-deaths, TND: Total neurological deaths

**Table 6: Circulatory deaths 75+ years by gender rates per million and CDD:TND (rates per million) OR 1989-2010**

Country 1989-1991 and latest year	Male	Female	CDD:TND	
			Male	Female
<b>Current and 1989-1991 rank</b>				
1-6=Sweden	58,550	46,686	1:4.22	1:4.38
2008-2010	39,212	35,773		
Ratio	0.67	0.77		
2-2=Austria	63,108	56,212	1:3.51	1:4.21
2008-2010	38,229	40,411		
Ratio	0.61	0.72		
3-3=Finland	61,637	49,489	1:5.22	1:4.97
2008-2010	36,365	32,644		
Ratio	0.59	0.66		
4-4=Ireland	61,475	48,520	1:3.22	1:3.38
2008-2010	33,849	30,854		
Ratio	0.55	0.64		
5-1=Germany 1990-1992	66,243	55,822	1:3.69	1:4.27
2008-2010	33,488	36,875		
Ratio	0.51	0.66		
6-8=Greece	55,154	56,343	1:1.75	1:2.25
2008-2010	32,688	35,306		
Ratio	0.59	0.63		
7-11=Italy	51,052	43,551	1:3.44	1:4.09
2008-2010	31,168	30,199		
Ratio	0.61	0.69		
8-7=Norway	56,909	43,984	1:4.78	1:5.31
2008-2010	30,934	29,251		
Ratio	0.54	0.67		

Contd...

**Table 6: Contd...**

Country 1989-1991 and latest year	Male	Female	CDD:TND	
			Male	Female
<b>Current and 1989-1991 rank</b>				
9-16=Switzerland	47,706	41,456	1:2.20	1:12.37
2008-2010	30,515	28,888		
Ratio	0.64	0.70		
10-12=New Zealand	49,464	41,552	1:3.57	1:3.68
2007-2009	30,286	31,219		
Ratio	0.61	0.75		
11-10=UK	52,003	43,514	1:2.51	1:3.16
2008-2010	29,658	27,194		
Ratio	0.57	0.62		
12-13=USA	48,792	41,079	1:6.13	1:9.89
2008-10	29,439	27,553		
Ratio	0.60	0.67		
13-9=Denmark	53,089	43,365	1:6.28	1:8.78
2008-2010	28,614	25,695		
Ratio	0.54	0.59		
14-5=Portugal	59,723	54,438	1:8.48	1:10.1
2008-2010	27,668	26,782		
Ratio	0.46	0.49		
15-17=Belgium	46,279	39,091	1:2.30	1:2.35
2008-2010	27,651	25,690		
Ratio	0.60	0.66		
16-14=Australia	48,596	43,577	1:3.49	1:4.07
2008-2010	25,619	25,953		
Ratio	0.53	0.60		
17-15=Netherlands	47,724	37,424	1:4.04	1:5.58
2008-2010	25,429	23,823		
Ratio	0.53	0.64		
18-19=Canada	43,026	35,265	1:3.14	1:4.38
2007-2009	24,653	22,293		
Ratio	0.57	0.63		
19-21=France	36364	31,776	1:3.13	1:4.00
2008-2010	23,066	19,829		
Ratio	0.63	0.62		
20-18=Spain	44,716	44,148	1:5.46	1:6.43
2008-2010	20,521	23,619		
Ratio	0.46	0.53		
21-20=Japan	37,024	31,352	1:3.43	1:3.63
2008-2010	19,494	17,538		
Ratio	0.53	0.56		

75+ male and female  $\rho=+0.9558$ ,  $P<0.001$ . TND: Total neurological deaths, CDD: Circulatory-disease-deaths, OR: Odds ratio

#### Odds ratios over 75's

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 17<sup>th</sup> highest but had risen to being second highest, while USA females went from 10<sup>th</sup> 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.<sup>[38]</sup> 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						Female					
	55-74			75+			55-74			75+		
	Lower	OR	Upper	Lower	OR	Upper	Lower	OR	Upper	Lower	OR	Upper
Australia	1:1.49	1:1.79	1:2.15	1:1.89	1:1.99	1:2.1	1:1.27	1:1.55	1:1.89	1:2.62	1:2.75	1:2.9
Austria	1:1.54	1:1.87	1:2.28	1:1.68	1:1.8	1:1.92	1:1.45	1:1.79	1:2.21	1:2.05	1:2.19	1:2.35
Belgium	1:1.85	1:2.2	1:2.62	1:2.53	1:2.67	1:2.81	1:1.28	1:1.53	1:1.84	1:4.08	1:4.28	1:4.5
Canada	1:1.52	1:1.81	1:2.17	1:1.95	1:2.05	1:2.16	1:1.24	1:1.49	1:1.79	1:2.29	1:2.41	1:2.53
Denmark	1:0.93	1:1.13	1:1.36	1:1.07	1:1.13	1:1.2	1:0.99	1:1.2	1:1.44	1:1.26	1:1.33	1:1.41
Finland	1:1.03	1:1.21	1:1.43	1:1.14	1:1.2	1:1.25	1:1.08	1:1.27	1:1.5	1:1.93	1:2.02	1:2.12
France	1:1.52	1:1.82	1:2.18	1:1.77	1:1.87	1:1.97	1:1.28	1:1.55	1:1.88	1:2.54	1:2.68	1:2.82
Germany	1:1.24	1:1.49	1:1.8	1:1.72	1:1.83	1:1.95	1:1.17	1:1.42	1:1.73	1:2.04	1:2.18	1:2.32
Greece	1:0.82	1:1.04	1:1.31	1:3.41	1:3.74	1:4.1	1:0.62	1:0.81	1:1.05	1:5.15	1:5.64	1:6.17
Ireland	1:1.61	1:1.93	1:2.31	1:1.96	1:2.07	1:2.2	1:1.24	1:1.5	1:1.81	1:2.9	1:3.06	1:3.24
Italy	1:1.49	1:1.8	1:2.16	1:1.65	1:1.75	1:1.86	1:1.21	1:1.47	1:1.78	1:2.21	1:2.35	1:2.49
Japan	1:1.3	1:1.64	1:2.06	1:1.61	1:1.76	1:1.93	1:0.62	1:0.79	1:1	1:2.55	1:2.8	1:3.08
New Zealand	1:1.42	1:1.71	1:2.07	1:1.59	1:1.69	1:1.78	1:1.26	1:1.52	1:1.83	1:2.28	1:2.4	1:2.54
Netherland	1:1.78	1:2.14	1:2.57	1:1.63	1:1.72	1:1.82	1:1.17	1:1.42	1:1.73	1:1.76	1:1.86	1:1.96
Norway	1:1.36	1:1.62	1:1.93	1:1.34	1:1.41	1:1.49	1:1.18	1:1.4	1:1.67	1:1.66	1:1.75	1:1.85
Portugal	1:0.92	1:1.13	1:1.38	1:0.97	1:1.05	1:1.13	1:0.81	1:1.01	1:1.26	1:1.31	1:1.42	1:1.55
Spain	1:1.33	1:1.59	1:1.91	1:1.48	1:1.57	1:1.66	1:1.11	1:1.35	1:1.64	1:1.94	1:2.05	1:2.17
Sweden	1:1.35	1:1.62	1:1.94	1:1.23	1:1.3	1:1.38	1:1.11	1:1.33	1:1.6	1:1.86	1:1.96	1:2.07
Swiss	1:1.56	1:1.87	1:2.23	1:2.48	1:2.6	1:2.74	1:1.23	1:1.48	1:1.78	1:3.81	1:3.99	1:4.19
UK	1:1.78	1:2.13	1:2.53	1:2.43	1:2.56	1:2.71	1:1.41	1:1.69	1:2.03	1:3.21	1:3.38	1:3.56

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,<sup>[1,18,19,23]</sup> but others demonstrated what appears to be an unequivocal upward trend in MND in a number of countries.<sup>[2,6,8,12,19,35,46,48]</sup> 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.<sup>[4,8,23,26,44]</sup> 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 disturbances<sup>[48]</sup> but would this have so markedly affected the over 75's rates.<sup>[26,29,34,48]</sup> 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"<sup>[37]</sup> 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.<sup>[7,14,43]</sup> 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 deaths<sup>[41,42]</sup> 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.<sup>[2,24,25,41,45]</sup> 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,<sup>[47]</sup> 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,<sup>[3-5,15,22,24-26,32,36,44]</sup> suggesting that possible nongenetic influences on gene expression, may be entertained.<sup>[4-6,10,12,13,16,20,32,41]</sup>

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.<sup>[6,10,27,28,33]</sup> 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.<sup>[3,11,21,29,33,36,48]</sup> There is growing concern about the “burden of disease of older people”, with improvements in longevity.<sup>[37]</sup> 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.<sup>[37]</sup> 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.<sup>[45]</sup> 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.<sup>[38,48]</sup>

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,<sup>[1,2,4,12,29,33-35,38,41,48]</sup> 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,<sup>[5]</sup> 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.

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