

Trends of mortality from Alzheimer's disease in the European Union, 1994-2013

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Abstract

Background: In many countries, Alzheimer's disease (AD) has gradually become a relevant disease in elderly populations. The aim of this study was to analyse trends of mortality caused by AD in the 28 member countries in the European Union (EU) over the last two decades.

Methods: We extracted data for AD deaths for the period 1994-2013 in the EU from the Eurostat and World Health Organization database. Age-standardised mortality rates per 100,000 were computed. Joinpoint regression was used to analyse the trends and compute the annual percent change (APC) in the EU as a whole and by country. Analyses by gender and by European regions were conducted.

Results: Throughout the study period, mortality from AD has risen in the EU. Most of the countries showed upward trends, with the sharpest increases in Slovakia, Lithuania and Romania. In men and women, we recorded a 4.7% and 6.0% statistically significant increase in mortality rates in the whole EU, respectively. Several countries showed changing trends during the study period. According to the regional analysis, Northern and Eastern countries showed the steepest increases, while in the latter years in Western countries mortality has declined.

Conclusions: Our findings provide evidence that AD mortality has increased in the EU, especially in Eastern and Northern European countries and in the female population. Our results could be a reference for the development of primary prevention policies.

Keywords: Alzheimer's disease; Mortality; Trends; European Union; Joinpoint analysis

Introduction

Alzheimer's disease (AD) is defined by the World Health Organization (WHO) as a degenerative cerebral disease of unknown etiology, with characteristic neuropathological and neurochemical features [1].

With the progressive increase in life expectancy, AD has become an increasing public health issue. In 2013, the Global Burden of Disease Study found that AD was one of the top 50 global causes of years of life lost which experienced a more pronounced increase in the past years [2], and it has been estimated the disease will be the seventh cause of death in high income countries in the year 2030 [3].

Previous studies described increasing trends in mortality from AD in the United States, where the mortality rate rose from 45.3 in 1999 to 50.0 per 100,000 in 2008 [4], and in Canada, where the crude mortality rate for men and women increased from 10.1 to 11.5 per 100,000 and 24.4 to 25.4 per 100,000, respectively, between 2004 and 2011 [5].

However, to date, no studies have been conducted at a European level using a consistent methodology, estimating significant changes in trends. Therefore, the aim of this study was to analyse trends of mortality caused by AD in the European Union (EU) in the period 1994-2013.

Methods

Data from men and women over 50 years of age from the 28 member countries of the EU in the period 1994-2013 were extracted from the statistical office of the EU (Eurostat) (<http://ec.europa.eu/eurostat/data/database>) [6]. The WHO database was used when data were not available (<http://data.euro.who.int/dmdb/>) [7], extracting data from Belgium (2000-2002), Denmark (2010), Germany (1998-2008), France (2011), Croatia

(1995-1998), The Netherlands (1996-2006), Poland (1999-2004), and Slovakia (1994-1995). Databases were updated in April 2016 and December 2015, respectively. Both databases receive data from each country's statistical authorities, and no further analyses are conducted. Thus we assume data do not differ substantially, and do not have a significant effect on the results.

During the study period, two different revisions of the International Classification of Diseases (ICD) were used (ICD 9th and 10th revisions). AD deaths were recorded according to the ICD-9 code 331.0 and ICD-10 code G30.

Estimates of resident population, based on official censuses, were also extracted from the Eurostat database (updated on April 2016) [6]. Due to the study design, no approval by an institutional review board was needed.

The 28 EU member countries and their available data included: Belgium (1998-2013), Bulgaria (2005-2013), Czech Republic (1994-2013), Denmark (1994-2013), Germany (1998-2013), Estonia (1997-2013), Ireland (1997-2013), Greece (1994-2013), Spain (1994-2013), France (metropolitan) (1994-2011), Croatia (1995-2013), Italy (2001-2003, 2006-2013), Cyprus (2004-2013), Latvia (1996-2013), Lithuania (1994-2013), Luxembourg (1998-2013), Hungary (1994-2013), Malta (1995-2011, 2013), the Netherlands (1996-2013), Austria (1994-2013), Poland (1999-2013), Portugal (1994-2000, 2002-2013), Romania (1999-2013), Slovenia (1995-2013), Slovakia (1994-2013), Finland (1996-2013), Sweden (1994-2013), and the United Kingdom (1994-2013). Unfortunately, data for one or more calendar years were missing from a few countries. No extrapolation was made for missing data. We assume that in those countries with less missing data, trends would not notably vary. Conversely, in those countries with more missing data, results could have been affected to a certain extent, and should be interpreted carefully.

From the matrices of certified death and resident population, age-standardised mortality rates per 100,000 for each 5-year age group (from 50-54 to 85 and more) and calendar period for men and women were computed, using the direct method and based on the 2013 European Standard Population.

We also conducted an analysis to assess regional mortality trends, distinguishing four European regions: Northern (Denmark, Estonia, Finland, Ireland, Latvia, Lithuania, Sweden, and the United Kingdom), Southern (Croatia, Cyprus, Greece, Italy, Malta, Portugal, Slovenia, and Spain), Eastern (Bulgaria, Czech Republic, Hungary, Poland, Romania, and Slovakia), and Western Europe (Austria, Belgium, France, Germany, Luxembourg, and the Netherlands).

We used the Joinpoint regression software (version 4.2.0.2) provided by the Surveillance Research Program of the USA National Cancer Institute to analyse significant changes in mortality trends. This analysis identifies inflexion points (called “joinpoints”) at which there is a significant change in the linear slope of the trend [8]. The number and location of significant joinpoints for each country were determined using a log-linear model. We computed the estimated annual percent change (APC) and corresponding 95% confidence intervals (95% CIs), which describes the magnitude of change for each of the identified trends. In this model, age-standardised mortality rates were used as the dependent variable, and the year of death as the independent variable. In all analyses, a p value lower than 0.05 was regarded as statistically significant.

Results

Between 1994 and 2013, the number of recorded deaths from AD in the EU increased steadily from 41,255 (13,508 men and 27,747 women) to 86,822 (26,974 men and 59,848 women).

Overall age-standardised mortality rate increased from 28.18 to 45.19 per 100,000. In 1994, the highest rates were found in France (20.58 per 100,000), and the lowest in Lithuania (0.43 per 100,000). In 2013, Finland had the highest mortality rate (278.92 per 100,000), while the lowest were observed in Malta and Latvia (below 5 per 100,000). (Table S1)

According to our findings, during the 2004-2013 period the entire EU showed a 5.6% statistically significant increase, with no identifiable joinpoints. Mortality rates rose over the last two decades in 26 countries throughout the EU. Slovakia and Romania had the biggest increases (APC=26.0% and APC=22.7%, respectively), while Luxembourg (APC=1.2%) and Latvia (APC=2.8%) showed the slightest increases. Only in Malta (APC=-4.1%) and Germany (APC=-0.4%) were declining trends observed.

Trends of mortality from AD by gender

Age-standardised mortality rates for men are presented in Table S2. In 1994, the highest rates were observed in France, Spain and Czech Republic (over 10 per 100,000), and the lowest in Lithuania, Slovakia, Greece and Hungary (below 2 per 100,000). In 2013, Finland had the highest male rates (270.02 per 100,000), while the lowest were found in Malta, Greece and Bulgaria (below 6 per 100,000).

Throughout the EU, men showed a statistically significant increase in mortality (APC=4.7%), with no joinpoints observed. Mortality rates between 1994 and 2013 rose in 25 countries. Slovakia, Romania and Lithuania had the largest increases, while for Poland, Greece and Belgium we observed less pronounced increases. In contrast, only Germany, Malta and Luxembourg showed an overall downward trend. (Table 1)

For eleven countries which had an overall upward trend (Hungary, Lithuania, Romania, Greece, Italy, Sweden, Croatia, Portugal, the United Kingdom, Spain, and

Denmark) APCs peaked, increasing at a lower rate or decreasing thereafter. For three countries (Austria, Slovakia and Czech Republic) we observed fluctuating mortality trends, with non-significant decreases, followed by pronounced increases.

For women, the highest rates in 1994 were recorded in France, Spain and Czech Republic (over 14 per 100,000), and the lowest in Slovakia and Lithuania (below 1 per 100,000). In 2013, we observed in Finland the highest female rate (over 280 per 100,000), and the lowest in Malta, Latvia and Bulgaria (below 7 per 100,000). (Table S3)

Among European women, we recorded a 6.0% steady and statistically significant increase, without identifying any joinpoints. Mortality from AD rose in 26 countries. The most pronounced increases were observed in Slovakia, Romania and Lithuania, while Latvia and Luxembourg showed the smallest increases. In Germany rates levelled off, and only Malta showed a declining trend. (Table 2)

In twelve countries with an overall upward trend (Slovakia, Romania, Hungary, Sweden, Slovenia, Denmark, France, Italy, Poland, Portugal, Spain, and the United Kingdom), APCs peaked and continued increasing at a lower rate. In Latvia and Luxembourg, after the APC peaked we observed a declining trend, and increases thereafter. The Czech Republic, after a decreasing trend, showed the steepest increases in the latter years of the study.

Trends for both men and women are shown graphically in Figure 1. Except for the Czech Republic, Finland, Hungary, Latvia, Lithuania, the Netherlands, and Romania trends were more pronounced in women than in men.

Trends of mortality from AD by region

Results from the regional mortality trends analysis showed the sharpest increase in Northern and Eastern Europe. In Western Europe we observed an overall slight increase,

and in the period 2009-2013 a statistically significant declining trend, during the same period, in Eastern Europe a pronounced increase was recorded. Since the mid 2000s, in Southern countries rates have levelled off. (Table 3)

Discussion

The present updated analysis of mortality from AD in the EU showed overall upward trends in both sexes over the past two decades. The largest increases were found in Slovakia, Romania, and Lithuania. In Finland we observed the highest mortality rates, with a steady increase over the study period. Mortality rates levelled off or declined for only two countries, Germany and Malta.

Most of the countries showed increasing mortality trends for both genders. We compared our findings with previous studies. According to the findings of Desesquelles and colleagues [9], in France mortality has been increasing since 1985, which is consistent with our results. An Italian study also showed evidence of an upward trend in the period 1985-2003 in this country, with the steepest increases in the latter years [10]. We only analysed available data in the 2000s, when we also observed a pronounced increase in mortality rates. In England and Wales, mortality rates experienced an 8-fold increase in men and 12-fold increase in women between 1985 and 2004 [11]. According to our findings, the United Kingdom (which also included Scotland and North Ireland) also showed rising trends for both sexes, especially in women.

Economic development and improvement of social conditions over the last decades have led to an increase in life expectancy [12], which might explain the increasing trends in mortality from age-related diseases, especially in Eastern countries (Slovakia, Lithuania, Slovenia, Romania, Hungary), where we observed the lowest mortality rates in the 1990s.

Several Northern European countries also showed pronounced increasing trends, presumably due not only to the progressive ageing of their population, but also to other factors. Studies have demonstrated evidence that *APOE* $\epsilon 4$ allele frequencies, a well-studied risk factor for AD [13], are higher in Northern countries [14, 15].

Although it might be thought that increasing mortality rates could be attributed to better diagnostics, Hallberg [16] rejected this idea in Sweden, and remarked on the contribution of environmental factors. However, we cannot discard that better diagnostics and increased awareness of the condition by physicians could explain the increase in mortality rates in other countries.

In many countries, the APC peaked in the early years of the study, when most of the countries implemented ICD-10. Previous studies found a 55% increase in AD recorded deaths when classified by ICD-10 instead ICD-9 [17], due to the inclusion of pre-senile dementia and a lax criterion of imputation to any mention of AD [18], which could be the reason why mortality rates rose in this period. Posterior lower increases or declining trends could be attributed to improvements in health services and prevention policies addressing modifiable risk factors. Norton and colleagues [19] showed that in Europe a 10% reduction per decade of the prevalence of seven modifiable risk factors would result in a 9.1% reduction of the prevalence of AD in the future.

In Germany, mortality rates in men declined, while in women they levelled off. Surprisingly, its population is one of the oldest in the entire EU, but this was not reflected in rising mortality trends. Previous studies described decreasing trends in dementia prevalence between 2007 and 2009, suggesting the reason for these trends might be protective factors (better education, economic development) related to the non-war period of the 20th century [20]. We also hypothesised that, due to the characteristics and progress

of the disease, which might lead to other underlying causes of death, mortality from AD has possibly been underreported [21,22].

Cyprus and Malta were the countries with the smallest populations, and we also observed low mortality figures. It must be taken into account that our results, which showed rising and declining trends, respectively, could be affected by the effect of their small populations.

It is worth noting that, because of the low rate of recording dementia as the cause of death, mortality data were not useful in exploring geographical variation and time trends [23,24]. This fact may have contributed to an underestimation of the real AD mortality observed in this study.

Our findings showed pronounced mortality trends for women in most of the countries. Sex differences in AD have been widely studied and attributed to several factors, including genetic, hormonal and social factors, or the longer life expectancy of women [25, 26].

When we assessed the regional mortality trends, we observed the biggest increases in Northern and Eastern Europe. In contrast, in the latter study years in Southern Europe mortality rates levelled off, and in Western Europe a declining trend was observed. We hypothesised these differences may be due to lifestyle factors (as well as the social and genetic factors previously stated), such as a higher adherence to the Mediterranean diet, which has been found as a protecting factor for developing AD [27], and associated with a lower mortality risk [28].

This study has several strengths. To our knowledge, this is the first study analysing AD mortality trends in the whole of the EU. Moreover, mortality data were extracted from official databases. Our study also has limitations. The main limitation is the lack of

data from some countries. These databases are updated with data from national statistical offices, but in some cases data were not provided for several years. We decided not to extrapolate or impute in order to analyse only official data. Another limitation is the reflection of the condition as an underlying cause of death, but not as a contributing cause of death.

Conclusion

In conclusion, we confirm mortality from AD has significantly increased in the EU in the last two decades, especially in Eastern and Northern Europe and the female population. Consequently, in the upcoming years, the EU will face not only health, but also social and economic challenges. Primary prevention policies addressing to preventable risk factors are recommendable. The effect of diagnostics or medical awareness of the condition deserves further analyses.

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Table 1. Joinpoint analysis for Alzheimer's disease mortality trends in men in the European Union, 1994-2013.

	Total study period		Period 1		Period 2		Period 3	
	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)
European Union	2004-2013	4.7* (4.2, 5.3)	-	-	-	-	-	-
Austria	1994-2013	10.0* (7.7, 12.3)	1994-1999	-3.0 (-11.8, 6.8)	1999-2003	34.3* (8.5, 66.3)	2003-2013	3.5* (0.1, 7.0)
Belgium	1998-2013	3.8* (3.1, 4.5)	-	-	-	-	-	-
Bulgaria	2005-2013	10.5* (2.7, 18.8)	2005-2007	48.9 (-15.2, 161.4)	2007-2013	3.3 (-6.1, 13.6)	-	-
Croatia	1995-2013	8.7* (5.8, 11.6)	1995-2000	27.8* (10.4, 47.9)	2000-2013	4.3* (0.8, 8.0)	-	-
Cyprus	2004-2013	4.5 (-1.1, 10.5)	-	-	-	-	-	-
Czech Republic	1994-2013	6.0* (3.0, 9.1)	1994-2006	11.2* (6.9, 15.6)	2006-2009	-26.2 (-62.1, 43.7)	2009-2013	40.3* (13.6, 73.1)
Denmark	1994-2013	10.8* (9.5, 12.1)	1994-2006	13.9* (12.2, 15.6)	2006-2013	4.3* (0.8, 7.9)	-	-
Estonia	1997-2013	6.1* (2.9, 9.4)	-	-	-	-	-	-
Finland	1996-2013	13.7* (12.7, 14.7)	1996-1999	6.6 (-0.9, 14.6)	1999-2007	17.3* (15.0, 19.6)	2007-2013	9.0* (6.3, 11.7)
France	1994-2011	7.4* (5.8, 9.0)	1994-2003	12.8* (11.4, 14.3)	2003-2011	1.3 (-0.2, 2.9)	-	-
Germany	1998-2013	-1.8* (-2.6, -1.0)	1998-2003	1.4 (-0.8, 3.7)	2003-2008	-6.0* (-8.9, -3.0)	2008-2013	2.2 (-0.0, 4.5)
Greece	1994-2013	3.7 (-0.1, 7.7)	1994-2000	35.1* (24.0, 47.1)	2000-2013	-4.9* (-7.4, -2.4)	-	-
Hungary	1994-2013	11.2* (9.4, 13.0)	1994-1996	50.9* (10.3, 106.3)	1996-2013	9.7* (8.5, 10.9)	-	-
Ireland	1997-2013	5.2* (3.2, 7.3)	-	-	-	-	-	-
Italy	2001-2013	4.7* (2.1, 7.4)	2001-2003	33.3* (14.7, 55.0)	2003-2013	1.7* (0.0, 3.3)	-	-
Latvia	1996-2013	8.7* (2.8, 15.0)	-	-	-	-	-	-
Lithuania	1994-2013	23.2* (17.6, 29.1)	1994-1999	81.4* (55.9, 111.2)	1999-2013	12.9* (9.3, 16.5)	-	-
Luxembourg	1998-2013	-1.5 (-5.0, 2.1)	-	-	-	-	-	-
Malta	1995-2013	-5.8* (-10.5, -0.9)	-	-	-	-	-	-
Netherlands	1996-2013	8.7* (7.3, 10.0)	1996-2011	7.4* (6.5, 8.3)	2011-2013	35.8* (11.7, 65.2)	-	-
Poland	1999-2013	3.4* (2.5, 4.3)	-	-	-	-	-	-
Portugal	1994-2013	11.3* (8.3, 14.3)	1994-2003	24.5* (21.4, 27.7)	2003-2013	0.8 (-1.2, 2.8)	-	-
Romania	1999-2013	23.2* (19.6, 26.9)	1999-2004	39.6* (25.7, 55.0)	2004-2013	16.7* (11.8, 21.8)	-	-
Slovakia	1994-2013	23.8* (19.6, 28.2)	1994-1996	-24.8 (-66.0, 65.9)	1996-2001	59.8* (24.4, 105.3)	2001-2013	15.2* (9.9, 20.7)
Slovenia	1995-2013	12.1* (4.7, 20.1)	-	-	-	-	-	-
Spain	1994-2013	6.5* (4.8, 8.3)	1994-1997	8.2 (-1.0, 18.2)	1997-2001	21.5* (11.2, 32.7)	2001-2013	1.6* (0.5, 2.6)
Sweden	1994-2013	11.6* (8.9, 14.3)	1994-2001	27.7* (21.1, 34.6)	2001-2013	4.9* (2.4, 7.3)	-	-
United Kingdom	1994-2013	7.7* (6.3, 9.1)	1994-1999	3.2 (-2.5, 9.2)	1999-2002	23.4 (-4.2, 58.8)	2002-2013	4.3* (2.5, 6.0)

APC: Annual percent change; CI: Confidence intervals

*p<0.05 for change in trend.

Table 2. Joinpoint analysis for Alzheimer's disease mortality trends in women in the European Union, 1994-2013.

	Total study period		Period 1		Period 2		Period 3	
	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)
European Union	2004-2013	6.0* (5.3, 6.7)	-	-	-	-	-	-
Austria	1994-2013	11.4* (9.2, 13.7)	1994-1999	-4.6 (-10.4, 1.7)	1999-2003	37.6* (19.4, 58.6)	2003-2013	5.4* (3.0, 7.7)
Belgium	1998-2013	4.6* (3.7, 5.5)	-	-	-	-	-	-
Bulgaria	2005-2013	11.4* (5.7, 17.3)	-	-	-	-	-	-
Croatia	1995-2013	10.3* (7.2, 13.4)	1995-1997	-10.0 (-43.5, 43.2)	1997-2001	41.4* (12.1, 78.4)	2001-2013	3.4* (0.6, 6.3)
Cyprus	2004-2013	7.7* (1.1, 14.7)	-	-	-	-	-	-
Czech Republic	1994-2013	4.0* (1.1, 6.9)	1994-2005	10.4* (6.3, 14.5)	2005-2009	-21.1 (-40.1, 3.9)	2009-2013	37.3* (15.4, 63.4)
Denmark	1994-2013	12.5* (10.8, 14.2)	1994-2004	18.2* (15.7, 20.8)	2004-2013	6.1* (3.4, 8.8)	-	-
Estonia	1997-2013	8.5* (5.5, 11.6)	-	-	-	-	-	-
Finland	1996-2013	13.0* (12.3, 13.7)	1996-2000	8.2* (2.8, 13.7)	2000-2013	13.9* (13.0, 14.9)	-	-
France	1994-2011	8.8* (7.2, 10.5)	1994-2003	14.5* (13.0, 16.0)	2003-2011	2.5* (1.0, 4.1)	-	-
Germany	1998-2013	0.2 (-0.4, 0.9)	1998-2002	3.6 (-0.7, 8.2)	2002-2010	-1.6 (-3.3, 0.2)	2010-2013	5.4 (-1.5, 12.8)
Greece	1994-2013	6.1* (2.6, 9.7)	1994-2000	34.0* (24.4, 44.5)	2000-2013	-1.8 (-4.0, 0.5)	-	-
Hungary	1994-2013	9.5* (7.8, 11.3)	1994-1996	61.0* (26.2, 105.3)	1996-2013	7.7* (6.8, 8.6)	-	-
Ireland	1997-2013	6.2* (4.7, 7.6)	-	-	-	-	-	-
Italy	2001-2013	5.6* (3.0, 8.2)	2001-2003	32.2* (10.9, 57.5)	2003-2013	2.7* (0.7, 4.6)	-	-
Latvia	1996-2013	1.6 (-1.9, 5.2)	1996-2001	31.5* (11.5, 54.9)	2001-2004	-23.4 (-63.2, 59.8)	2004-2013	3.4 (-3.3, 10.6)
Lithuania	1994-2013	20.4* (16.2, 24.8)	-	-	-	-	-	-
Luxembourg	1998-2013	2.8* (1.2, 4.4)	1998-2000	32.2* (4.3, 67.5)	2000-2007	-1.6 (-5.5, 2.4)	2007-2013	5.6* (1.4, 9.9)
Malta	1995-2013	-3.2 (-7.7, 1.5)	-	-	-	-	-	-
Netherlands	1996-2013	7.3* (5.8, 8.9)	1996-2000	-0.2 (-7.2, 7.3)	2000-2011	7.4* (5.5, 9.3)	2011-2013	32.8* (5.7, 66.9)
Poland	1999-2013	4.4* (3.6, 5.3)	1999-2005	7.2* (5.3, 9.1)	2005-2013	2.7* (1.5, 3.9)	-	-
Portugal	1994-2013	12.1* (9.1, 15.1)	1994-2003	25.3* (22.8, 27.8)	2003-2013	1.6* (0.0, 3.2)	-	-
Romania	1999-2013	22.3* (19.2, 25.5)	1999-2004	37.0* (26.3, 48.5)	2004-2013	16.4* (12.7, 20.4)	-	-
Slovakia	1994-2013	28.6* (22.6, 34.9)	1994-1999	87.2* (49.3, 134.8)	1999-2013	18.1* (12.6, 23.9)	-	-
Slovenia	1995-2013	15.1* (9.4, 21.1)	1995-1999	82.3* (30.4, 154.9)	1999-2013	6.8* (1.6, 12.2)	-	-
Spain	1994-2013	8.0* (5.9, 10.0)	1994-2002	18.4* (15.9, 21.1)	2002-2013	1.8* (0.4, 3.2)	-	-
Sweden	1994-2013	13.5* (9.9, 17.3)	1994-1999	49.6* (33.7, 67.4)	1999-2013	6.7* (4.2, 9.2)	-	-
United Kingdom	1994-2013	8.6* (7.2, 10.0)	1994-1999	6.0* (0.7, 11.6)	1999-2002	22.5 (-2.7, 54.2)	2002-2013	5.1* (3.5, 6.7)

APC: Annual percent change; CI: Confidence intervals

*p<0.05 for change in trend

Table 3. Joinpoint analysis for Alzheimer's disease mortality trends by European regions.

	Total study period		Period 1		Period 2		Period 3	
	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)
Northern Europe	1994-2013	10.2* (9.0, 11.3)	1994-2002	15.0* (12.1, 18.0)	2002-2013	7.2* (5.5, 8.9)	-	-
Eastern Europe	1994-2013	7.4* (6.4, 8.4)	1994-2005	9.5* (7.5, 11.5)	2005-2009	-0.8 (-13.2, 13.4)	2009-2013	15.0* (5.7, 25.2)
Southern Europe	1994-2013	7.0* (5.2, 8.9)	1994-2004	13.5* (10.8, 16.3)	2004-2013	0.0 (-2.9, 2.9)	-	-
Western Europe	1994-2013	3.4* (1.9, 5.0)	1994-2009	5.8* (4.7, 7.0)	2009-2013	-11.6* (-18.4, -4.2)	-	-

APC: Annual percent change; CI: Confidence intervals

*p<0.05 for change in trend

Figure 1. Trends in mortality from Alzheimer's disease in the European Union, 1994-2013

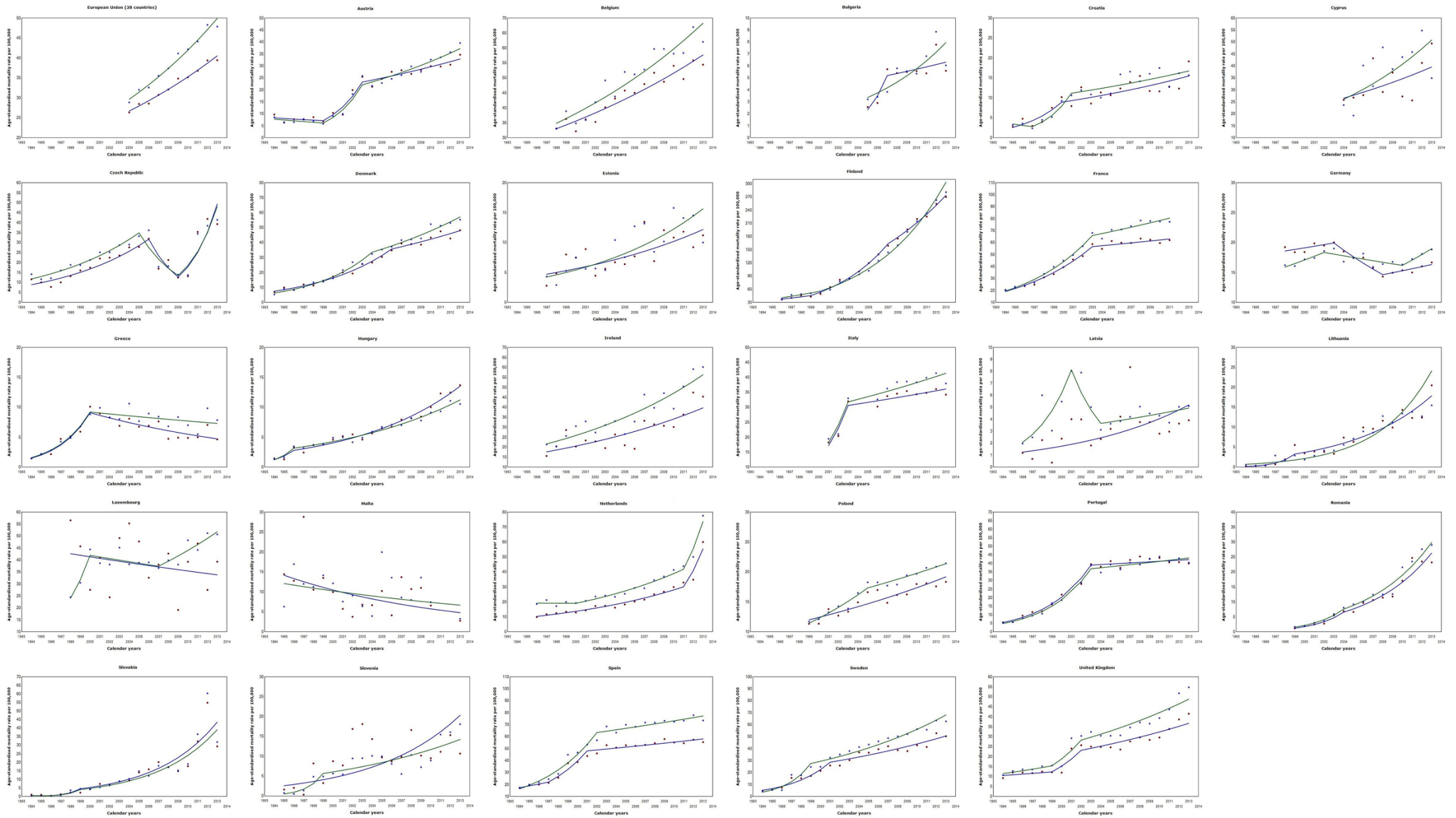


Figure 1 legend

Blue line: men

Green line: women

Red circle: men (age-standardised mortality rates)

Blue cross: women (age-standardised mortality rates)

Supplemental table 1. Overall age-standardised mortality rates in the European Union, 1994-2013.

Countries	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
European Union	-	-	-	-	-	-	-	-	-	-	28.18	31.01	31.41	34.10	35.78	39.20	40.03	41.86	45.45	45.19
Austria	8.91	6.47	6.91	7.53	7.46	6.12	9.57	9.74	18.67	25.88	21.66	23.52	25.60	26.85	28.59	28.36	31.78	32.73	34.22	37.95
Belgium	-	-	-	-	33.18	38.14	34.13	36.02	39.90	46.74	44.09	50.54	49.25	51.23	57.22	56.15	57.15	55.55	63.38	59.42
Bulgaria	-	-	-	-	-	-	-	-	-	-	-	2.93	3.23	4.56	5.67	5.52	5.38	6.30	8.42	5.86
Croatia	-	3.06	3.91	2.55	4.25	5.89	9.47	9.86	12.13	10.01	10.26	11.10	14.77	16.13	14.48	14.65	15.69	12.79	15.06	16.65
Cyprus	-	-	-	-	-	-	-	-	-	-	24.99	22.55	34.72	36.62	40.07	38.19	36.77	37.35	49.27	41.27
Czech Republic	13.30	11.14	10.82	14.16	17.23	18.02	20.05	23.98	24.21	27.23	28.61	31.59	34.86	17.72	19.20	13.53	13.53	34.75	39.64	40.63
Denmark	5.98	9.33	8.19	10.63	12.79	14.25	16.38	21.09	24.16	25.69	30.52	33.72	36.37	40.93	40.93	41.36	49.17	50.05	49.40	53.35
Estonia	-	-	-	3.72	3.16	6.49	6.79	6.37	5.24	5.64	9.33	7.28	11.68	12.79	7.98	10.47	13.97	12.90	13.22	10.02
Finland	-	-	37.75	45.42	48.31	48.53	52.26	60.51	78.25	84.37	96.43	108.23	129.76	149.05	165.35	192.87	218.10	233.03	260.96	278.92
France	20.58	23.06	24.17	26.12	33.09	37.96	43.40	48.71	54.53	65.41	61.03	68.18	67.77	69.54	73.81	73.26	72.06	72.73	-	-
Germany	-	-	-	-	17.15	16.85	17.69	18.27	18.97	19.43	17.53	17.68	18.16	16.11	15.88	16.37	16.20	16.75	17.56	18.32
Greece	1.45	2.20	2.55	4.45	4.98	6.40	9.39	9.59	8.29	7.57	9.57	7.30	8.13	8.11	5.99	6.97	6.17	5.30	8.65	6.54
Hungary	1.36	1.46	3.37	2.91	3.69	3.84	4.76	5.11	4.61	4.80	5.82	6.65	6.93	7.21	8.16	7.96	9.44	10.15	11.51	11.46
Ireland	-	-	-	19.60	20.50	27.34	27.27	29.68	25.57	27.21	30.81	24.70	28.40	42.00	37.34	41.41	36.51	45.34	55.01	54.63
Italy	-	-	-	-	-	-	-	19.07	20.83	32.74	-	-	31.97	35.46	37.21	37.71	37.18	38.25	39.77	36.90
Latvia	-	-	1.78	1.93	4.91	2.22	4.69	7.12	6.87	4.05	2.87	3.63	3.85	4.96	4.85	4.17	3.93	3.61	4.57	4.72
Lithuania	0.43	0.35	0.50	2.13	1.80	3.68	2.45	3.17	4.07	3.91	5.94	6.97	9.15	8.96	12.32	10.92	13.85	13.32	12.50	16.90
Luxembourg	-	-	-	-	35.39	35.93	39.94	39.48	34.79	46.15	42.51	42.03	36.50	37.15	40.95	31.39	45.96	46.26	44.88	47.37
Malta	-	9.12	15.52	17.68	10.44	14.33	11.66	7.19	7.06	6.86	4.90	16.20	10.25	10.56	9.20	12.59	7.31	7.85	-	2.85
Netherlands	-	-	15.94	18.50	15.96	18.16	17.47	18.74	21.74	22.17	21.40	23.35	26.36	26.84	31.68	33.88	37.84	40.42	45.24	72.06
Poland	-	-	-	-	-	11.61	11.88	13.46	13.76	13.75	15.87	17.76	17.88	16.81	17.26	18.39	19.08	19.86	19.81	20.41
Portugal	5.39	5.88	8.55	10.37	11.20	16.56	19.86	-	28.70	39.06	36.16	40.32	36.91	41.29	41.23	42.96	43.94	41.34	42.41	40.49
Romania	-	-	-	-	-	1.48	1.99	2.86	3.29	5.85	7.70	8.29	9.97	11.85	12.16	12.39	20.03	23.95	26.20	27.07
Slovakia	0.58	0.62	0.42	0.84	3.00	3.75	4.32	6.04	7.09	8.71	10.29	14.63	13.31	18.67	17.29	15.16	18.49	35.15	58.80	31.13
Slovenia	-	1.10	1.01	1.11	5.93	4.33	6.48	6.28	11.77	11.79	11.43	10.17	8.73	6.67	12.05	8.33	9.50	14.80	16.02	16.24
Spain	17.35	19.94	21.19	23.48	27.85	42.57	44.10	50.16	53.22	63.42	59.26	64.35	63.06	65.66	66.07	68.30	66.58	67.08	70.96	67.47
Sweden	4.47	5.64	6.17	17.11	16.66	21.90	23.45	30.21	31.76	35.12	39.77	40.95	43.79	46.50	46.19	46.78	51.46	50.56	59.47	58.17
United Kingdom	10.20	12.56	13.09	12.97	14.42	14.49	14.11	27.52	29.00	29.95	28.63	28.52	28.33	32.21	34.61	33.62	35.94	40.15	46.99	49.84

Supplemental table 2. Age-standardised mortality rates in men in the European Union, 1994-2013.

Countries	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
European Union	-	-	-	-	-	-	-	-	-	-	26.36	28.48	28.57	30.77	32.10	34.84	35.18	36.80	39.40	39.45
Austria	9.74	6.36	7.70	7.80	8.61	6.89	10.41	9.69	19.95	25.47	21.33	24.60	27.56	28.25	26.71	28.35	29.95	29.79	30.53	34.69
Belgium	-	-	-	-	33.09	36.30	32.18	36.16	35.31	40.19	43.13	45.79	45.03	47.96	51.73	48.74	54.07	49.63	55.87	54.43
Bulgaria	-	-	-	-	-	-	-	-	-	-	-	2.57	2.91	5.73	5.41	5.50	5.57	5.39	7.78	5.60
Croatia	-	2.73	4.78	2.98	3.97	7.52	10.18	7.95	12.67	8.59	11.37	10.69	12.37	13.98	15.49	11.72	11.64	12.76	12.35	19.15
Cyprus	-	-	-	-	-	-	-	-	-	-	25.86	26.78	27.82	43.21	29.13	37.24	27.28	25.61	41.27	49.40
Czech Republic	11.61	10.09	7.79	10.07	13.17	16.08	17.46	22.04	22.47	23.57	27.65	27.85	31.97	16.95	21.28	12.51	13.18	35.39	41.89	39.31
Denmark	7.09	10.03	8.41	12.09	11.35	14.55	17.34	20.08	19.35	25.67	26.67	30.47	34.81	39.44	39.05	38.65	43.40	47.56	42.79	48.29
Estonia	-	-	-	2.80	4.87	8.02	7.48	8.92	4.48	5.63	6.72	6.40	7.72	13.47	6.91	12.09	10.85	11.83	9.24	11.22
Finland	-	-	36.56	40.57	45.93	43.20	49.42	64.82	81.65	84.24	100.46	119.54	139.32	159.14	175.22	196.00	219.90	225.24	254.24	270.02
France	20.42	22.54	23.74	24.87	30.97	33.69	39.46	45.91	48.76	58.72	54.80	61.33	59.94	59.72	63.41	62.38	59.65	62.07	-	-
Germany	-	-	-	-	19.25	18.41	18.43	19.87	19.51	20.04	18.52	17.42	17.50	15.77	14.33	14.96	15.38	15.01	16.04	16.68
Greece	1.46	2.19	2.17	4.73	5.17	5.93	10.10	8.96	8.29	6.91	8.10	6.75	6.93	7.64	4.74	4.92	4.89	5.00	7.05	4.64
Hungary	1.47	1.30	3.31	2.44	3.71	3.77	4.58	5.18	5.48	4.61	5.64	6.48	6.75	7.96	8.17	8.44	10.02	12.31	12.47	13.70
Ireland	-	-	-	15.61	20.38	28.61	20.30	23.38	22.91	19.55	26.38	20.99	19.20	33.26	31.46	30.75	30.11	36.38	47.41	45.36
Italy	-	-	-	-	-	-	-	18.27	20.40	31.99	-	-	30.26	33.75	34.57	35.44	34.36	34.82	36.10	34.23
Latvia	-	-	1.19	0.69	2.26	0.38	2.38	4.01	3.99	1.81	2.35	3.20	4.22	8.36	3.77	3.76	2.80	2.97	3.64	3.92
Lithuania	0.19	0.38	0.40	0.71	1.96	5.56	3.50	3.93	3.82	3.34	7.42	6.35	9.96	9.62	11.64	9.94	14.37	12.34	12.42	20.51
Luxembourg	-	-	-	-	56.59	45.73	27.55	40.96	24.45	49.18	55.29	47.76	32.61	38.06	42.70	19.16	39.27	46.92	27.50	39.30
Malta	-	14.45	12.80	28.82	10.55	13.51	9.96	5.77	3.77	6.80	6.68	10.24	4.14	13.71	10.73	11.02	6.59	-	-	2.77
Netherlands	-	-	9.88	11.75	12.51	13.47	12.87	14.33	17.30	17.41	16.19	18.30	20.27	21.52	25.10	26.81	29.96	32.98	34.86	60.04
Poland	-	-	-	-	-	11.34	11.36	13.81	12.71	13.37	14.93	16.63	16.99	14.85	16.16	16.25	17.99	18.11	17.60	18.36
Portugal	5.60	5.78	9.48	11.58	11.97	16.03	21.79	-	28.03	39.58	38.09	41.35	37.41	42.06	44.06	42.65	43.24	40.69	40.75	39.99
Romania	-	-	-	-	-	1.16	1.96	2.47	2.76	5.52	6.93	6.66	9.67	10.66	11.43	11.81	17.06	24.70	23.50	23.22
Slovakia	1.08	1.01	0.45	1.33	2.27	2.27	4.26	7.37	6.62	8.80	9.37	14.11	15.89	20.13	17.14	14.83	17.74	32.25	54.88	29.32
Slovenia	-	1.62	2.05	0.35	8.20	3.25	8.75	7.70	16.86	18.09	14.34	9.72	8.70	9.89	16.60	10.17	9.50	11.13	15.32	10.68
Spain	17.08	19.72	19.97	21.38	25.69	37.81	38.76	43.85	46.03	52.87	50.85	52.82	52.34	53.18	54.62	58.07	55.17	54.58	57.49	55.45
Sweden	4.87	5.96	7.41	15.58	15.31	17.19	21.43	25.93	25.89	30.39	36.87	36.67	39.54	42.00	38.73	37.97	42.85	41.41	52.89	50.35
United Kingdom	9.23	12.04	12.06	11.73	12.50	12.20	12.01	24.07	25.73	25.06	24.85	24.67	23.58	27.65	29.67	28.41	29.60	33.84	38.65	41.52

Supplemental table 3. Age-standardised mortality rates in women in the European Union, 1994-2013.

Countries	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
European Union	-	-	-	-	-	-	-	-	-	-	28.87	32.03	32.61	35.55	37.42	41.13	42.19	44.14	48.31	47.88
Austria	8.61	6.52	6.51	7.55	6.94	5.81	9.05	9.97	18.26	25.86	21.75	22.88	24.63	26.16	29.83	27.59	32.64	33.61	35.78	39.60
Belgium	-	-	-	-	33.03	38.89	34.86	35.91	41.91	49.18	43.80	52.01	51.20	52.85	59.70	59.72	58.11	58.35	67.00	62.06
Bulgaria	-	-	-	-	-	-	-	-	-	-	-	3.21	3.42	3.84	5.80	5.56	5.36	6.82	8.86	6.05
Croatia	-	3.22	3.57	2.37	4.48	5.18	9.24	10.63	11.93	10.87	10.07	11.13	15.91	16.58	14.15	16.05	17.49	12.86	16.18	15.68
Cyprus	-	-	-	-	-	-	-	-	-	-	23.67	19.30	40.22	31.53	47.78	38.72	43.74	45.83	54.80	34.92
Czech Republic	14.17	11.67	12.18	16.05	18.86	18.75	21.32	25.14	25.17	28.74	29.03	33.23	36.21	17.93	18.19	13.96	13.74	34.40	38.50	41.43
Denmark	5.36	9.19	8.32	10.06	13.43	13.83	16.09	21.67	26.89	25.86	32.41	35.38	37.28	41.70	42.14	42.84	52.34	51.30	53.17	55.38
Estonia	-	-	-	4.32	2.91	5.28	7.53	5.62	5.68	5.40	10.43	7.57	12.73	13.20	8.48	10.19	15.80	14.12	14.55	10.02
Finland	-	-	38.23	47.41	49.18	51.05	53.22	58.92	77.39	83.96	93.81	102.03	125.07	143.93	160.05	190.37	214.47	233.36	262.78	280.82
France	20.52	23.12	24.28	26.48	33.91	39.85	45.01	49.60	57.02	68.12	63.37	70.67	71.01	73.83	78.49	78.11	77.64	77.40	-	-
Germany	-	-	-	-	16.23	16.09	17.21	17.43	18.60	19.02	16.83	17.52	18.16	15.95	16.42	16.79	16.33	17.26	18.11	18.85
Greece	1.48	2.22	2.85	4.27	4.89	6.80	8.83	9.92	8.30	8.03	10.62	7.69	8.96	8.44	6.83	8.37	7.01	5.51	9.84	7.86
Hungary	1.35	1.62	3.47	3.20	3.68	3.91	4.92	4.99	4.17	4.92	5.94	6.74	7.10	7.02	8.21	7.79	9.13	9.33	11.09	10.55
Ireland	-	-	-	21.37	20.39	25.66	30.54	32.95	27.38	31.06	33.07	26.58	32.88	46.38	39.77	47.11	39.32	50.47	59.13	60.19
Italy	-	-	-	-	-	-	-	19.48	21.03	33.03	-	-	32.66	36.28	38.43	38.61	38.38	39.90	41.41	37.98
Latvia	-	-	1.98	2.49	6.01	3.05	5.48	8.04	7.90	5.02	3.12	3.63	3.84	4.20	5.06	4.49	4.30	3.72	5.04	5.11
Lithuania	0.60	0.30	0.51	2.92	1.73	2.92	1.89	2.87	4.17	4.17	5.60	7.16	8.96	8.67	12.80	11.20	13.45	13.85	12.75	15.50
Luxembourg	-	-	-	-	24.51	30.50	44.44	38.69	38.12	45.17	38.21	38.92	39.04	36.63	39.84	38.12	48.27	44.23	51.21	50.72
Malta	-	6.32	16.97	12.02	11.29	14.16	12.17	7.59	9.10	6.40	3.96	19.98	13.59	8.61	8.01	13.59	7.43	-	-	3.28
Netherlands	-	-	18.57	21.27	17.18	19.99	19.21	20.71	23.62	24.19	23.44	25.45	29.31	29.14	34.59	37.00	41.39	43.87	50.09	77.67
Poland	-	-	-	-	-	11.70	12.11	13.25	14.28	13.89	16.48	18.28	18.27	17.73	17.90	19.44	19.69	20.71	20.89	21.45
Portugal	5.18	5.65	7.89	9.44	10.62	16.83	18.60	-	28.82	38.81	34.72	39.36	36.49	40.44	39.36	42.81	44.03	41.28	43.05	40.55
Romania	-	-	-	-	-	1.67	2.02	3.06	3.62	5.97	8.08	9.22	10.10	12.46	12.51	12.63	21.57	23.51	27.64	29.02
Slovakia	0.25	0.38	0.39	0.65	3.64	4.55	4.34	5.39	7.05	8.98	10.39	14.83	12.11	17.97	17.28	15.28	19.05	36.45	60.36	31.86
Slovenia	-	0.78	0.53	1.39	4.87	4.90	5.65	5.44	9.47	9.51	10.11	9.99	8.11	5.54	10.31	7.25	8.93	15.46	16.04	18.07
Spain	17.45	19.98	21.80	24.53	28.90	44.97	46.73	53.36	57.01	68.55	63.40	69.99	68.31	71.82	71.75	73.31	72.46	73.39	77.97	73.57
Sweden	4.17	5.44	5.33	18.11	17.65	24.68	24.86	32.50	35.15	38.00	41.32	43.41	46.11	48.78	50.32	52.11	56.31	55.83	63.57	62.84
United Kingdom	10.69	12.80	13.59	13.56	15.17	15.51	15.18	29.23	30.37	32.38	30.47	30.48	30.65	34.62	37.17	36.53	39.33	43.65	51.75	54.78