Editor's Choice – Trends in Lower Extremity Amputation Incidence in European Union 15+ Countries 1990–2017

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WHAT THIS PAPER ADDS

This is an observational analysis of lower limb amputation incidence in European Union (EU) 15+ countries between 1990 and 2017, using data obtained from the Global Burden of Disease (GBD) Study 2017. The hypothesis was that reducing incidence trends would be identified, given previous work from the present study group using the GBD Study, which identified reducing incidence of peripheral arterial disease over the same time period in EU15+ countries. However, the present study identifies variable trends in lower limb amputation incidence across EU15+ countries between 1990 and 2017. The potential contributors to the observed results are discussed.

Objective: Lower extremity amputation (LEA) carries significant mortality, morbidity, and health economic burden. In the Western world, it most commonly results from complications of peripheral arterial occlusive disease (PAOD) or diabetic foot disease. The incidence of PAOD has declined in Europe, the United States, and parts of Australasia. The present study aimed to assess trends in LEA incidence in European Union (EU15+) countries for the years 1990–2017.

Methods: This was an observational study using data obtained from the 2017 Global Burden of Disease (GBD) Study. Age standardised incidence rates (ASIRs) for LEA (stratified into toe amputation, and LEA proximal to toes) were extracted from the GBD Results Tool (http://ghdx.healthdata.org/gbd-results-tool) for EU15+ countries for each of the years 1990–2017. Trends were analysed using Joinpoint regression analysis.

Results: Between 1990 and 2017, variable trends in the incidence of LEA were observed in EU15+ countries. For LEAs proximal to toes, increasing trends were observed in six of 19 countries and decreasing trends in nine of 19 countries, with four countries showing varying trends between sexes. For toe amputation, increasing trends were observed in eight of 19 countries and decreasing trends in eight of 19 countries for both sexes, with three countries showing varying trends between sexes. Australia had the highest ASIRs for both sexes in all LEAs at all time points, with steadily increasing trends. The USA observed the greatest reduction in all LEAs in both sexes over the time period analysed (LEAs proximal to toes: female patients −22.93%, male patients −29.76%; toe amputation: female patients −29.93%, male patients −32.67%). The greatest overall increase in incidence was observed in Australia.

Conclusion: Variable trends in LEA incidence were observed across EU15+ countries. These trends do not reflect previously observed reductions in incidence of PAOD over the same time period.

Keywords: Amputation, Epidemiology, Incidence, Peripheral arterial disease
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INTRODUCTION

Lower extremity amputation (LEA) represents a significant burden on global health systems. Significant morbidity and mortality accompanies both traumatic and non-traumatic amputations.[1,2] One year mortality rates vary by country, age, gender, and anatomical level of amputation, but are estimated at between 12% and 58%.[3] In a retrospective cohort of 18 463 patients who underwent major peripheral

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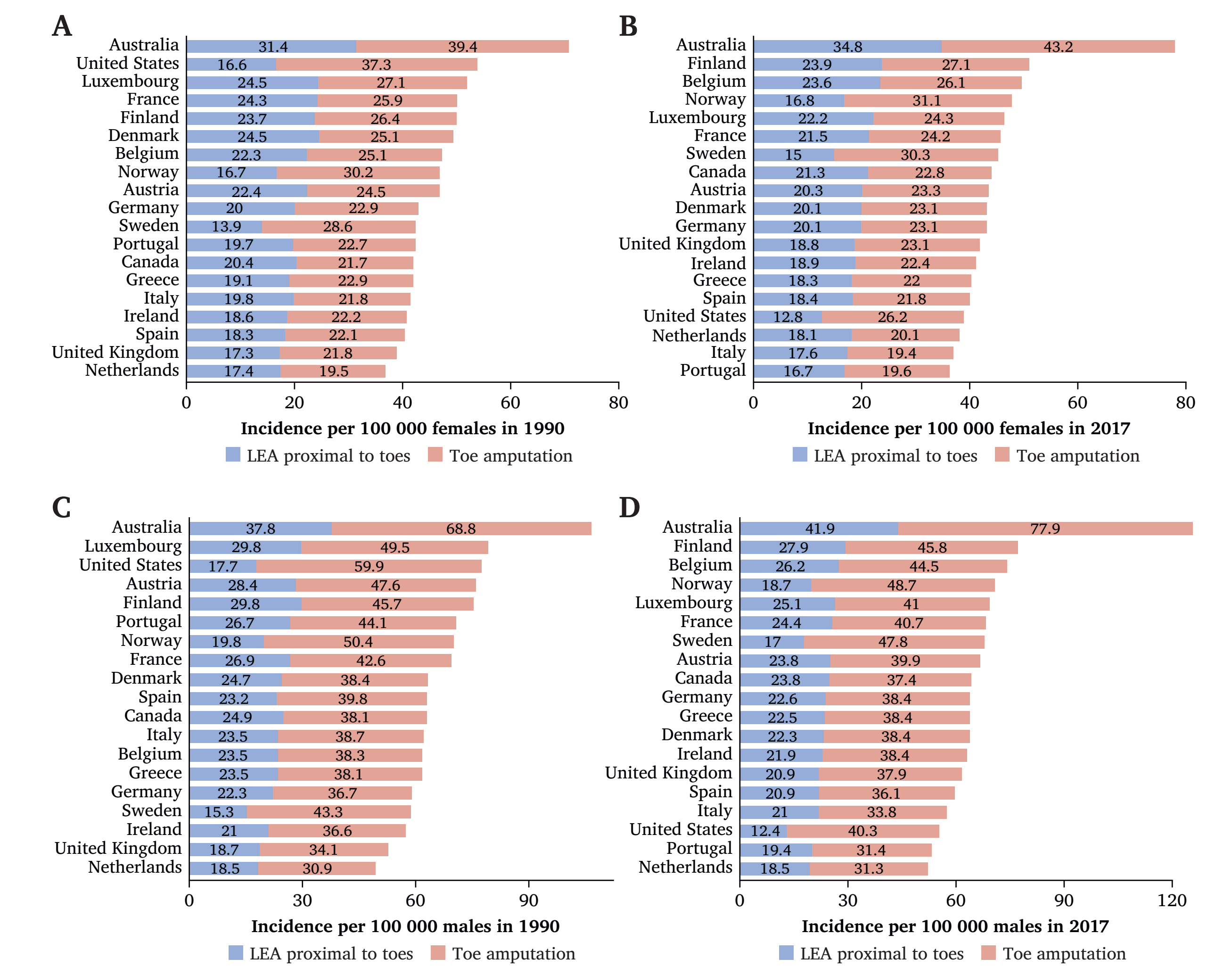

Figure 1. Age standardised incidence rates (ASIRs) per 100 000 for lower extremity amputation (LEA) in the European Union (EU) 15+ countries in 1990 (female patients, A, male patients, C) and 2017 (female patients, B, male patients D).

arterial occlusive disease (PAOD) related amputation in the United States between 2003 and 2010, the mean cost of inpatient care in the year before amputation, including the amputation itself, was $22,405.[4] There are several indications for LEA, including an injured or malperfused limb not amenable to salvage (or where attempts at salvage have failed), and an injured limb wherein mortality is a risk from infection, or malignancy.[5,6] In developed countries, LEA results primarily from failure of limb conserving interventions in the management of diabetes and/or PAOD.[7]

The present study group has previously used data obtained from the Global Burden of Disease (GBD) Study to demonstrate decreasing trends in PAOD incidence across European Union (EU) 15+ countries,[8] a group of countries that have previously been demonstrated to be comparable in terms of their health expenditure.[9,10] Decreasing PAOD incidence rates in Western European populations have also been reported elsewhere.[11] Conversely, data pertaining to diabetes incidence, a known risk factor for PAOD, demonstrate increasing worldwide trends.[12]

Country specific data for trends in LEA incidence have been published;[13—17] however only a few studies have investigated intercountry incidence over a period of time.[18,19] Furthermore, to the present authors' knowledge, no study has used the GBD database[20,21] to compare trends in age standardised incidence rates (ASIRs) of LEA in EU15+ countries.

The primary objective of this observational analysis was to compare LEA incidence rates across EU15+ countries between 1990 and 2017. Given the reduction in PAOD incidence rates observed in previous analysis,[8] it was hypothesised that similar temporal reductions would be observed for LEA incidence across these countries.

METHODS

Data source

Data collected for the GBD study was used for this observational analysis of LEA incidence. GBD combines multiple data sources to provide results related to specific diseases: deaths/death rates, years of life lost (YLLs) because of premature death, prevalence, and incidence. The GBD methodology has been published previously.[20,21] For estimations of disease incidence within a population, the GBD study combines multiple sources of information for a disease (including [but not limited to] systematic reviews, claims data, inpatient hospital admissions data, and outpatient encounter data [based on International Classification of Disease {ICD} coding]) using a Bayesian meta-regression tool DisMod-MR 2.1.[20] The DisMod-MR tool evaluates and pools available data, adjusted for systematic bias associated with methods that varied from the reference, and produces estimates by population with corresponding uncertainty intervals using Bayesian statistical methods.[20] The results are then made publicly available online via the GBD Results Tool http://ghdx.healthdata.org/gbd-results-tool. Age standardised incidence rates were extracted for LEA for EU15+ countries between 1990 and 2017 from the GBD Results Tool. The EU15+ countries are as follows: Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, United Kingdom, and United States. Age standardised incidence data were extracted for both toe amputation and LEA proximal to toes.

Data handling

Age standardised incidence rates per 100 000 population (ASIRs) were extracted from the GBD Results Tool for each of the years 1990–2017 inclusive for each EU15+ country per sex. For all ASIRs, GBD uses a standard population calculated as the non-weighted average across all countries of the percentage of the population in each five year age group for the years 2010–2035 from the United Nations Population Division's World Population Prospects (2012 revision).[22] Put simply, using age standardised rates accounts for differences in the age structure of different populations and improves the comparability between countries. Absolute and relative changes in ASIRs over the observation period were calculated between the start and end for each sex in each country by computing the difference between the start and end age standardised incidence rates for male patients and female patients independently. The GBD data were analysed for LEAs, which were further stratified into toe amputation and LEA proximal to toes (unilateral and bilateral combined).

Statistical analysis

Trends in LEAs were analysed by gross percentage change from 1990 to 2017, and using Joinpoint regression analysis (Joinpoint software [Joinpoint Command Line Version 4.5.0.1] provided by the United States National Cancer Institute Surveillance Research Program[23]). Joinpoint regression software analyses trends in data over time and uses a logarithmic scale to connect different line segments in the simplest possible model. Starting with the minimum number of Joinpoints (zero Joinpoints represents a straight line), the addition of more Joinpoints is tested for statistical significance using a Monte Carlo permutation method and, if significant, that Joinpoint is added to the model. Additionally, the software computes estimated annual percent changes (EAPC) for each line segment (with corresponding 95% confidence intervals). EAPCs are evaluated to establish whether there is a difference from the null hypothesis of no change. Therefore, for the final model, each Joinpoint represents a statistically significant change in trend (increase or decrease) and each trend is described by the EAPC with confidence estimates. By estimating the annual percentage change, one is able to assess trend changes at a constant per cent per year.

RESULTS

1990–2017 lower extremity amputation incidence

Figure 1 demonstrates LEA ASIRs per country in 1990 and 2017 for male and female patients. In 1990, Sweden had the lowest incidence of LEA proximal to toes in both male and female patients (15.3 and 13.9 per 100 000, respectively). In 2017, the USA had the lowest incidence of LEA proximal to toes for both sexes (male patients: 12.4 per 100 000; female patients: 12.8 per 100 000). In 1990, the highest incidence of LEA proximal to toes in both sexes was observed in Australia (male patients: 37.8 per 100 000; female patients: 31.4 per 100 000). The highest incidences in 2017 were also seen in Australia, increasing to 41.9 per 100 000 for male patients and 34.8 per 100 000 for female patients.

In 1990, the lowest incidences for toe amputation among female patients were observed in the Netherlands (19.5 per 100 000). For male patients in 1990, Ireland had the lowest incidences (26.6 per 100 000). In 2017, Italian female patients had the lowest ASIR (19.4 per 100 000). The lowest incidence for male patients in 2017 was observed in the Netherlands (31.2 per 100 000). Australia saw the highest toe amputation ASIRs among both sexes in both 1990 and 2017.

Trends in lower extremity amputation incidence

LEA proximal to toes ASIRs per 100 000 increased between 1990 and 2017 for both sexes in Australia, Belgium, Germany, Ireland, Sweden, and the UK. In female patients, the greatest overall percentage increase was seen in Australia (+11.02%), followed by the UK (+8.52%) and Sweden (+8.35%). In male patients, the greatest percentage increase occurred in the UK (+11.93%), followed by Belgium, Sweden, and Australia (+11.45%, +11.10%, and +11%, respectively). Decreasing rates in LEA proximal to toes were seen in both sexes in Austria, Denmark, France, Greece, Italy, Luxembourg, Portugal, Spain, and the USA. The USA showed the greatest overall percentage reduction in both male and female patients (−29.76% and −22.93%, respectively). Considerable percentage reductions were seen in Portugal and Luxembourg in male patients (−27.34% and −16.42%, respectively), and Denmark and Portugal in female patients (−18.16% and −15.25%, respectively). Canada, Finland, the Netherlands, and Norway all showed $<$ 5% increase in incidence in female patients, but reductions in incidence in male patients for LEAs proximal to toes.

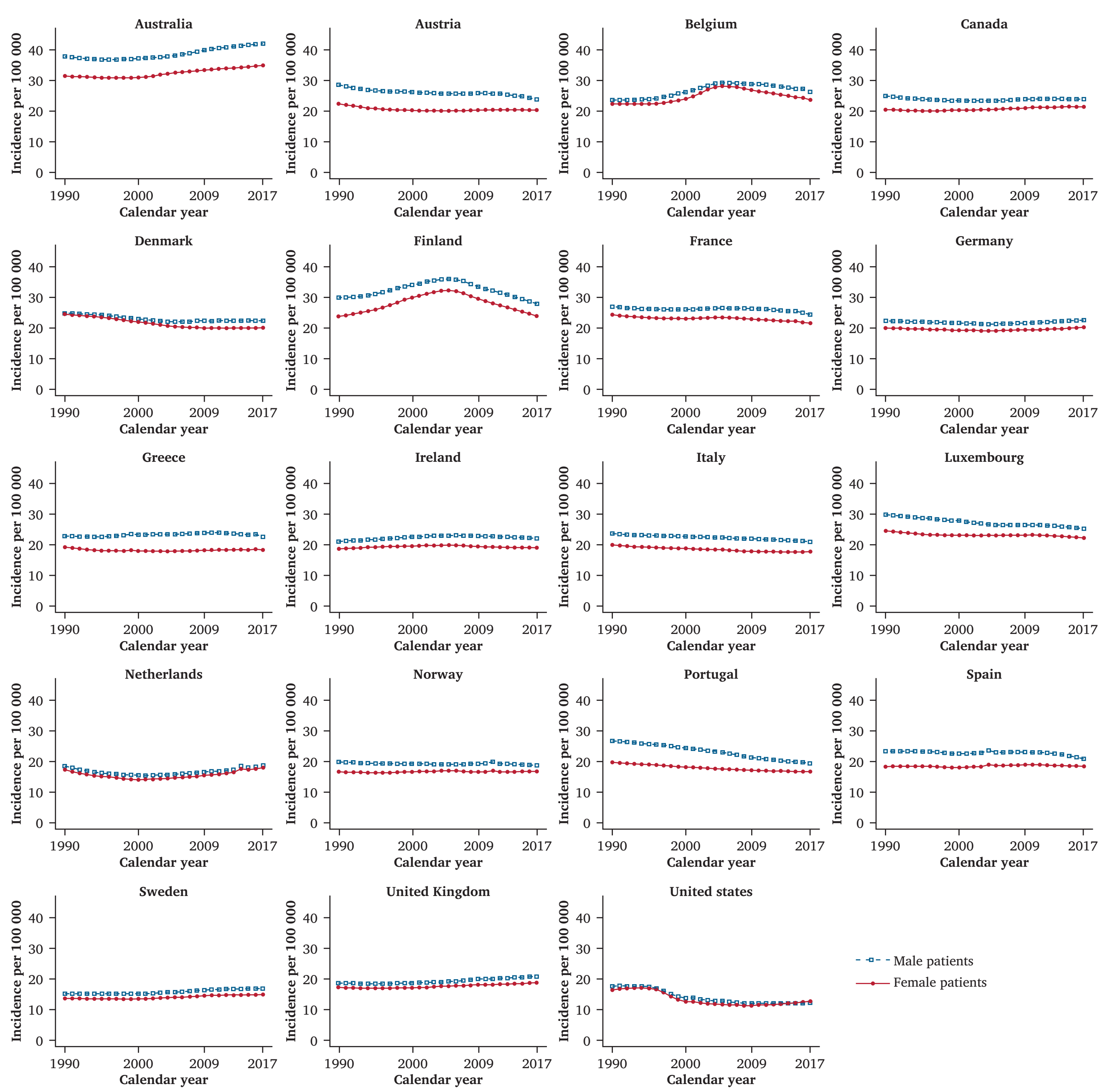

Figure 2. Trends in age standardised incidence rates (ASIRs) per 100 000 for lower extremity amputation (LEA) proximal to toes in European Union (EU) 15+ countries between 1990 and 2017. Open squares (blue) indicate male patients; and filled circles (red) indicate female patients.

Toe amputation ASIRs increased between 1990 and 2017 for both sexes in Australia, Belgium, Finland, Germany, Ireland, the Netherlands, Sweden, and the UK. In female patients, the greatest overall percentage increase was seen in Australia (+9.66%), followed by the UK (+6.27%) and Sweden (+6.11%), mirroring the changes seen in LEAs proximal to toes. In male patients, this greatest percentage increase occurred in Belgium (+16.02%), followed by Australia and the UK (+13.29% and +11.04%, respectively). Decreasing ASIRs in toe amputation were seen in both sexes in Austria, Denmark, France, Italy, Luxembourg, Portugal, Spain, and the USA, mirroring LEA proximal to toes except for Greece. The USA showed the greatest overall percentage reduction in both male and female patients (−32.67% and −29.93%, respectively). Considerable percentage reductions were seen in Portugal and Luxembourg in male patients (−28.8% and −17.20%, respectively), and in Portugal and Italy in female patients (−13.60% and −11.31%, respectively). Canada and Norway observed percentage increases in female, but decreases in male patients, with Greece demonstrating decreases in female, but increases in male patients; however, all changes were less than ± 5% for these countries.

Joinpoint analysis for lower extremity amputation incidence

Figures 2 and 3, and Tables 1—4 present the results of the Joinpoint regression analysis for the trends in all LEA ASIRs between 1990 and 2017 in female and male patients. EAPC in incidence rates for periods covered by each trend are demonstrated. Significant trend changes in ASIRs are reported.

For LEAs proximal to the toes, trends in ASIR were variable. Across the included countries, over half of all the observed trends were negative for both male and female patients. The greatest single reduction was observed in the USA for both male and female patients (−6.3% for both sexes). The most consistently positive trends were observed in the UK, Canada, and Belgium in female patients, and in the UK and Australia for male patients.

Trends were also variable across countries for toe amputation. Just under half of all trends were negative for female patients; however, in male patients over half of the trends were negative. In both sexes the greatest single reduction was observed in the USA (−8.1% for male patients and −8.2% for female patients). The most consistently positive trends were observed in the UK and Canada in female patients, and in Sweden and Australia for male patients.

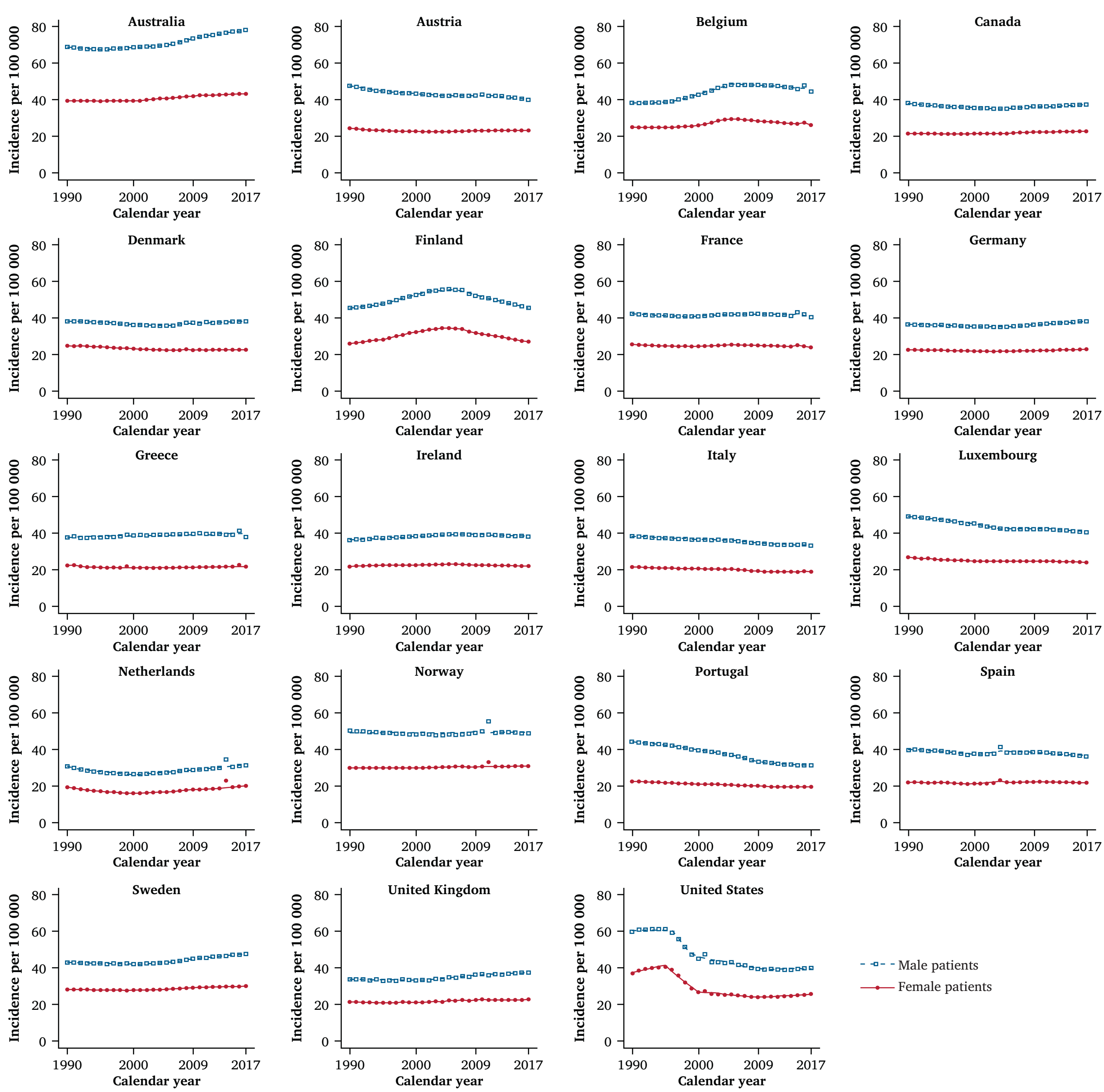

Figure 3. Trends in age standardised incidence rates (ASIRs) per 100 000 for toe amputation in European Union (EU) 15+ countries between 1990 and 2017. Open squares (blue) indicate male patients; and filled circles (red) indicate female patients.

Table 1. Joinpoint analysis for age standardised incidence rates (ASIRs) for lower extremity amputation (LEA) proximal to toes in European Union (EU) 15+ countries for years 1990–2017 in female patients

Country	Trend 1			Trend 2			Trend 3			Trend 4		
	Years	EAPC (95% CI)	*p*	Years	EAPC (95% CI)	*p*	Years	EAPC (95% CI)	*p*	Years	EAPC (95% CI)	*p*
Australia	1990–1995	−0.3 (−0.3−−0.2)	<.001	1995–2000	−0.1 (−0.1−0)	.10	2000–2005	+1.1 (+1.0 − +1.1)	<.001	2005–2017	+0.6 (+0.6 − +0.6)	<.001
Austria	1990–1994	−1.7 (−1.7−−1.9)	<.001	1994–2001	−0.6 (−0.8−−0.5)	<.001	2001–2013	+0.2 (+0.1 − +0.2)	<.001	2013–2017	−0.2 (−0.4 − +0.1)	.10
Belgium	1990–1996	+0.1 (−0.1 − +0.2)	.40	1996–1999	+1.5 (+0.6 − +2.4)	<.001	1999–2005	+3.4 (+3.2 − +3.6)	<.001	2005–2017	−1.5 (−1.6−−1.5)	<.001
Canada	1990–1995	−0.4 (−0.4−−0.4)	<.001	1995–2005	+0.3 (+0.2 − +0.3)	<.001	2005–2010	+0.6 (+0.6 − +0.7)	<.001	2010–2017	+0.2 (+0.1 − +0.2)	<.001
Denmark	1990–1995	−0.8 (−0.9−−0.6)	<.001	1995–2005	−1.4 (−1.5−−1.4)	<.001	2005–2010	−0.5 (−0.7−−0.4)	<.001	2010–2017	0.1 (0 − +0.1)	.10
Finland	1990–1995	+1.9 (+1.7 − +2.0)	<.001	1995–2000	+2.9 (+2.7 − +3.2)	<.001	2000–2005	+1.7 (+1.5 − +2.0)	<.001	2005–2017	−2.5 (−2.6−−2.5)	<.001
France	1990–1994	−0.9 (−1.2−−0.7)	<.001	1994–2000	−0.3 (−0.5−−0.1)	<.001	2000–2005	+0.5 (+0.2 − +0.7)	<.001	2005–2017	−0.7 (−0.7−−0.6)	<.001
Germany	1990–2001	−0.4 (−0.4−−0.4)	<.001	2001–2006	0 (−0.1 − +0.0)	.20	2006–2013	+0.4 (+0.3 − +0.4)	<.001	2013–2017	+0.6 (+0.6 − +0.7)	<.001
Greece	1990–1994	−1.4 (−1.8−−10)	<.001	1994–2003	−0.2 (−0.3 − +0)	<.001	2003–2017	+0.2 (+0.2 − +0.3)	<.001			
Ireland	1990–1994	+0.7 (+0.6 − +0.8)	<.001	1994–2005	+0.3 (+0.3 − +0.4)	<.001	2005–2011	−0.6 (−0.7−−0.6)	<.001	2011–2017	−0.2 (−0.2−−0.1)	<.001
Italy	1990–1995	−0.7 (−0.8−−0.6)	<.001	1995–2005	−0.5 (−0.5−−0.4)	<.001	2005–2010	−0.6 (−0.7−−0.5)	<.001	2010–2017	0 (−0.1 − +0)	.70
Luxembourg	1990–1995	−0.9 (−1−−0.8)	<.001	1995–1999	−0.4 (−0.6−−0.2)	<.001	1999–2012	0 (0−0)	.40	2012–2017	−0.7 (−0.7−−0.6)	<.001
Netherlands	1990–1994	−3.1 (−4−−2.2)	<.001	1994–2000	−1.5 (−2.1−−0.8)	<.001	2000–2008	+0.9 (+0.5 − +1.3)	<.001	2008–2017	+2.0 (+1.8 − +2.3)	<.001
Norway	1990–1995	−0.4 (−0.8−−0.1)	<.001	1995–2005	+0.5 (+0.3 − +0.6)	<.001	2005–2009	−0.7 (−1.5 − +0.1)	.10	2009–2017	+0.1 (+0 − +0.3)	.10
Portugal	1990–1996	−0.7 (−0.8−−0.7)	<.001	1996–1999	−1.0 (−1.3−−0.7)	<.001	1999–2009	−0.7 (−0.7−−0.7)	<.001	2009–2017	−0.3 (−0.3−−0.3)	<.001
Spain	1990–2001	−0.2 (−0.3−−0.1)	<.001	2001–2004	+1.1 (−0.1 − +2.4)	.10	2004–2011	+0.2 (0 − +0.4)	.10	2011–2017	−0.4 (−0.6−−0.2)	<.001
Sweden	1990–1996	−0.3 (−0.4−−0.3)	<.001	1996–2001	+0.2 (+0.1 − +0.3)	<.001	2001–2011	+0.8 (+0.8 − +0.8)	<.001	2001–2017	+0.2 (+0.2 − +0.3)	<.001
United Kingdom	1990–1995	−0.2 (−0.3−−0.1)	<.001	1995–2005	+0.2 (0 − +0.3)	<.001	2000–2007	+0.6 (+0.5 − +0.7)	<.001	2007–2017	+0.4 (+0.4 − +0.4)	<.001
United States	1990–1995	+1.1 (+0.5 − +1.6)	<.001	1995–2000	−6.3 (−7−−5.6)	<.001	2000–2008	−1.4 (−1.7−−1.1)	<.001	2008–2017	+1.2 (+1 − +1.4)	<.001

Data presented as Estimated Annual Percentage Change (EAPC %), with 95% confidence intervals (CI) in brackets. *p* values deemed significant if < .050.

DISCUSSION

In this 28 year observational study of lower extremity amputation incidence in EU15+ countries, significant variability is identified in amputation incidence both geographically and temporally. For both sexes, Australia has consistently observed the highest incidences of LEAs across the period studied, as well as the greatest percentage increase in ASIRs. Meanwhile, the incidence of LEA was consistently low in the Netherlands and the USA, with the greatest percentage reduction in incidence observed in the USA.

The primary objective of this analysis was to compare amputation incidence across the EU15+ countries. Based on previous analyses of LEA incidence[18,19] and the decreasing incidence of PAOD over the same time period presented elsewhere,[8,11] the hypothesis was that amputation incidence would decrease over the studied period. This would match data observed for PAOD and its risk factors.[8,24] The findings from this study do not directly support this hypothesis, with variability in trends differing from the uniformly downward trends observed in the aforementioned previous studies. Several potential reasons for this are discussed.

The latest figures from the International Diabetes Federation (IDF) suggest that the global incidence of diabetes has increased from 151 million in 2000, to 425 million in 2017, and is projected to increase further.[25] Harding *et al.*[26] recently reviewed trends in LEA incidence among global diabetic populations from 1988 to 2011. Despite the rising incidence of diabetes, consistent reductions in LEA in a diverse and global population were identified. While the body of evidence is significant, the difficulties in drawing direct comparisons have been highlighted previously,[7] and include the use of different denominators (proportion of diabetic *vs.* whole population), healthcare expenditure, population sizes, and data gathered from specialised vascular centres *vs.* district general hospitals or equivalent. It should be noted that there is a significant lack of data from countries outside North America, Europe, and the high income Asia Pacific countries.

Traumatic amputations in Western countries and countries not affected by conflict are now rare, with amputation occurring in only 1% of trauma patients in the USA.[1] Instead, declining PAOD incidence may be partly responsible for the results of this study. The present study group

Table 2. Joinpoint analysis for age standardised incidence rates (ASIRs) for lower extremity amputation (LEA) proximal to toes in European Union (EU) 15+ countries for years 1990–2017 in male patients

Country	Trend 1			Trend 2			Trend 3			Trend 4		
	Years	EAPC (95% CI)	*p*	Years	EAPC (95% CI)	*p*	Years	EAPC (95% CI)	*p*	Years	EAPC (95% CI)	*p*
Australia	1990–1996	−0.5 (−0.5−−0.4)	<.001	1996–2005	+0.4 (+0.4 − +0.4)	<.001	2005–2010	+1.2 (+1.1 − +1.3)	<.001	2010–2017	+0.6 (+0.6 − +0.6)	<.001
Austria	1990–1994	+1.5 (−1.7–1.3)	<.001	1994–2004	−0.4 (−0.5−−0.4)	<.001	2004–2012	0 (−0.1 − +0.1)	.40	2012–2017	−1.4 (−1.6−−1.3)	<.001
Belgium	1990–1996	+0.4 (+0.2 − +0.7)	<.001	1996–2005	+2.3 (+2.1 − +2.4)	<.001	2005–2012	−0.5 (−0.7−−0.2)	<.001	2012–2017	−1.4 (−1.7−−1.1)	<.001
Canada	1990–1995	−1.0 (−1.0−−0.9)	<.001	1995–2004	−0.2 (−0.3−−0.2)	<.001	2004–2010	+0.5 (+0.4 − +0.6)	<.001	2010–2017	−0.1 (−0.1−0)	<.001
Denmark	1990–1994	−0.3 (−0.5−−0.1)	<.001	1994–2005	−1.0 (−1.0−−0.9)	<.001	2005–2008	+0.7 (+0.1 − +1.2)	<.001	2008–2017	0 (0 − +0.1)	.40
Finland	1990–1994	+0.7 (+0.4 − +1.0)	<.001	1994–2003	+1.7 (+1.6 − +1.8)	<.001	2003–2006	0.2 (−0.8 − +1.2)	.60	2006–2017	−2.2 (−2.3−−2.2)	<.001
France	1990–1998	−0.4 (−0.5−−0.3)	<.001	1998–2007	+0.3 (+0.2 − +0.4)	<.001	2007–2015	−0.5 (−0.7−−0.4)	<.001	2015–2017	−2.0 (−2.9−−1.2)	<.001
Germany	1990–2005	−0.3 (−0.4−−0.3)	<.001	2005–2013	+0.5 (+0.5 − +0.5)	<.001	2013–2017	+0.6 (+0.5 − +0.7)	<.001			
Greece	1990–1993	−0.4 (−1.3 − +0.5)	.40	1993–2011	+0.3 (+0.3 − +0.4)	<.001	2011–2017	−0.8 (−1.1−−0.5)	<.001			
Ireland	1990–2003	+0.7 (+0.6 − +0.7)	<.001	2003–2006	+0.2 (−0.3 − +0.7)	.50	2006–2012	−0.3 (−0.4−−0.2)	<.001	2012–2017	−0.6 (−0.7−−0.5)	<.001
Italy	1990–1995	−0.5 (−0.6−−0.4)	<.001	1995–2000	−0.2 (−0.3−−0.1)	<.001	2000–2013	−0.4 (−0.5−−0.4)	<.001	2013–2017	−0.6 (−0.7−−0.5)	<.001
Luxembourg	1990–2000	−0.7 (−0.7−−0.7)	<.001	2000–2004	−1.1 (−1.3−−0.9)	<.001	2004–2012	−0.1 (−0.2−−0.1)	<.001	2012–2017	−0.8 (−0.9−−0.8)	<.001
Netherlands	1990–1997	−2.3 (−2.7−−1.8)	<.001	1997–2005	0 (−0.4 − +0.5)	.90	2005–2017	+1.4 (+1.2 − +1.6)	<.001			
Norway	1990–2006	−0.2 (−0.3−−0.2)	<.001	2006–2011	+0.7 (+0.3 − +1.0)	<.001	2011–2017	−0.8 (−0.9−−0.6)	<.001			
Portugal	1990–1997	−0.8 (−0.8−−0.8)	<.001	1997–2005	−1.2 (−1.2−−1.1)	<.001	2005–2009	−1.9 (−2.0−−1.8)	<.001	2009–2017	−1.1 (−1.2−−1.1)	<.001
Spain	1990–2001	−0.4 (−0.5−−0.3)	<.001	2001–2004	+1.0 (−0.4 − +2.4)	.20	2004–2012	−0.1 (−0.3−0)	.10	2012–2017	−1.8 (−2.1−−1.5)	<.001
Sweden	1990–1998	−0.1 (−0.1−0)	<.001	1998–2003	+0.4 (+0.2 − +0.5)	<.001	2003–2011	+0.9 (+0.9 − +1.0)	<.001	2011–2017	+0.3 (+0.3 − +0.4)	<.001
United Kingdom	1990–1996	−0.1 (−0.1−0)	<.001	1996–2004	+0.3 (+0.3 − +0.4)	<.001	2004–2010	+0.9 (+0.8 − +1.0)	<.001	2010–2017	+0.5 (+0.5 − +0.6)	<.001
United States	1990–1996	−0.6 (−0.9−−0.2)	<.001	1996–1999	−6.3 (−8.3−−4.2)	<.001	1999–2009	−1.7 (−1.9−−1.5)	<.001	2009–2017	+0.3 (+0.1 − +0.6)	<.001

Data presented as Estimated Annual Percentage Change (EAPC %), with 95% confidence intervals (CI) in brackets. *p* values deemed significant if < .050.

has previously used the GBD Study to demonstrate reducing incidence of PAOD across the EU15+ countries,[8] despite concomitant increases in mortality from PAOD over the 27 year period. Evidence suggests that many patients suffering with symptomatic PAOD are not receiving the recommended secondary preventive medications.[27–29]

Failure of PAOD treatment can ultimately manifest as LEA; however, the level of amputation is important. Below, through, or above knee amputations result from failure of conservative treatment. Toe or forefoot amputations are often used as an adjunct to conservative measures in treating limb threatening disease, aiming to prevent the need for more proximal amputation.[7] Previous research from VASCUNET identified reductions in major amputations (defined in the VASCUNET Report as a level above the ankle) in 11 of 12 countries over a four year period, with corresponding increases in minor amputations (defined by VASCUNET as below ankle level).[18] While this differs from the results presented in this analysis, it is important to note the length of the analysed period. In countries such as Finland and Belgium, there are increasing amputation incidence rates from 1996 to 2006 (before the VASCUNET study), which then start to decrease from 2010 to 2017 (the time of the VASCUNET study).

Goodney *et al.*[30] analysed amputation data in the USA using Medicare and Medicaid databases. They found a 45% reduction in amputation incidence over a 15 year period (1996–2011), with a concomitant increase in the number of angiographic revascularisation procedures performed. This reduction corresponds with the dramatic reduction in all LEAs observed in this analysis over a similar time period. It is important to note that amputation rates vary with socioeconomic status and healthcare expenditure, with more affluent, insured, non-African American patients reported as benefiting from earlier limb revascularisation therapies.[31,32]

The greatest incidences for all LEAs were observed in Australia in both sexes. Australia also saw the greatest increase in incidence over time for both amputation levels. The IDF data do not suggest that there is a significantly higher prevalence of diabetes in Australia. Previous research has established that nearly half of all amputees in Australia are affected by diabetes.[33] Work using the GBD data identified Australia as having the lowest incidence of PAOD, with

Table 3. **Joinpoint analysis for age standardised incidence rates (ASIRs) for toe amputation in European Union (EU) 15+ countries for years 1990–2017 in female patients**

Country	Trend 1			Trend 2			Trend 3			Trend 4		
	Years	EAPC	*p*	Years	EAPC (95% CI)	*p*	Years	EAPC (95% CI)	*p*	Years	EAPC (95% CI)	*p*
Australia	1990–2000	0 (0–0)	.10	2000–2010	+0.7 (+0.7 − +0.8)	<.001	2010–2017	+0.3 (+0.3 − +0.3)	<.001			
Austria	1990–1994	+1.3 (−1.6 − −1)	<.001	1994–2001	−0.4 (−0.6–−0.2)	<.001	2001–2013	+0.3 (+0.2 − +0.3)	<.001	2013–2017	0 (−0.3 − +0.3)	.70
Belgium	1990–1998	+0.1 (−0.2 − +0.4)	.60	1998–2005	+2.4 (+1.9 − +2.8)	<.001	2005–2017	−0.9 (−1.1–−0.8)	<.001			
Canada	1990–1995	−0.3 (−0.4–−0.2)	<.001	1995–2005	+0.1 (+0.1 − +0.2)	<.001	2005–2008	+1 (+0.5 − +1.4)	<.001	2008–2017	+0.3 (+0.2 − +0.3)	<.001
Denmark	1990–2005	−0.7 (−0.8–−0.7)	<.001	2005–2017	+0.2 (+0.1 − +0.2)	<.001						
Finlan	1990–1994	+1.6 (+1.2 − +2)	<.001	1994–2002	+2.5 (+2.3 − +2.6)	<.001	2002–2006	+0.3 (−0.3 − +0.9)	.30	2006–2017	−2.1 (−2.2–−2.1)	<.001
France	1990–1998	−0.6 (−0.8–−0.3)	<.001	1998–2005	+0.6 (+0.2 − +0.9)	<.001	2005–2017	−0.3 (−0.4–−0.2)	<.001			
Germany	1990–2000	−0.3 (−0.4–−0.3)	<.001	2000–2005	−0.1 (−0.2–0)	.40	2005–2017	+0.4 (+0.4 − +0.4)	<.001			
Greece	1990–1996	−1.1 (−1.9–−0.4)	<.001	1996–2017	+0.2 (+0.1 − +0.3)	<.001						
Ireland	1990–1994	+0.6 (+0.4 − +0.9)	<.001	1994–1999	0 (−0.2 − +0.3)	.80	1999–2005	+0.3 (+0.1 − +0.5)	<.001	2005–2017	−0.4 (−0.4–−0.3)	<.001
Italy	1990–1995	−0.6 (−0.9–−0.3)	<.001	1995–2005	−0.3 (−0.4–−0.2)	<.001	2005–2011	−1.2 (−1.5–−0.9)	<.001	2011–2017	+0.2 (0 − +0.4)	<.001
Luxembourg	1990–1999	−0.8 (−0.9–−0.8)	<.001	1999–2012	0 (−0.1–0)	.70	2012–2017	−0.6 (−0.8–−0.4)	<.001			
Netherlands	1990–2000	−1.9 (−2.7–−1.1)	<.001	2000–2017	−1.6 (+1.2 − +1.9)	<.001						
Norway	1990–2017	+0.2 (+0.1 − +0.2)	<.001									
Portugal	1990–2000	−0.7 (−0.7–−0.6)	<.001	2000–2005	−0.5 (−0.7–−0.3)	<.001	2005–2011	−0.8 (−0.9–−0.6)	<.001	2011–2017	−0.1 (−0.2–0)	<.001
Spain	1990–2001	−0.4 (−0.5–−0.2)	<.001	2001–2004	+1.9 (−0.2 − +3.9)	.10	2004–2017	−0.2 (−0.3–−0.1)	<.001			
Sweden	1990–2000	−0.2 (−0.2–−0.2)	<.001	2000–2005	+0.3 (+0.2 − +0.5)	<.001	2005–2010	+0.8 (+0.7 − +0.9)	<.001	2010–2017	+0.3 (+0.3 − +0.4)	<.001
United Kingdom	1990–1995	−0.3 (−0.6–−0.1)	<.001	1995–2001	+0.2 (−0.1 − +0.4)	.10	2001–2009	+0.7 (+0.6 − +0.9)	<.001	2009–2017	+0.1 (0 − +0.2)	.10
United States	1990–1995	+2.1 (+1.2 − +2.9)	<.001	1995–2000	−8.2 (−9.2–−7.1)	<.001	2000–2009	−1.3 (−1.7–−0.9)	<.001	2009–2017	+0.8 (+0.4 − +1.2)	<.001

Data presented as Estimated Annual Percentage Change (EAPC %), with 95% confidence intervals (CI) in brackets. *p* values deemed significant if $< .050$.

the highest PAOD related mortality.[8] These data suggest an opportunity for improvement in the management of PAOD and an at risk diabetic population. The large landmass and variable population density could present a challenge in managing at risk limbs, with patients having to travel significant distances for specialist care. Such travel times and the related expenses could result in patients presenting later with more significant disease requiring amputation.[34] In addition to this, recent data (adjusted for socio-economic status) from New Zealand suggests that the considerable fourfold variation in LEA incidence seen within regions of the same country may be in part caused by variation in quality and availability of diabetic foot management services.[35]

Limitations

One of the main limitations specific to the present study relates to the definition of the level of amputation. Previous studies have described "minor" amputations as those occurring below the ankle, with "major" comprising an amputation at ankle level and above. The GBD does not categorise amputation into the "major" and "minor" categories that have been described in previous studies (including the VASCUNET Report[18]), and instead categorises amputation into "Toes", "Lower Limb Unilateral", or "Lower Limb Bilateral". The definition of the level of toe amputation is omitted from the GBD methodology, therefore it is not possible to accurately ascertain in which category forefoot amputations (i.e. those in which part or all of metatarsals are amputated) should be included. Furthermore, whether bilateral relates to a first presentation requiring two amputations, or a pre-existing unilateral amputee requiring a second amputation of the contralateral limb is unclear. The incidence rate of bilateral limb amputation is, however, largely negligible in comparison with the unilateral rate. For simplicity and comparability, unilateral and bilateral LEAs were therefore combined in this analysis to assimilate LEAs proximal to toes. It has not been possible to establish the exact International Classification of Disease (ICD) 10th revision codes that were used. There are several additional limitations that need consideration when interpreting the data from the GBD Study. These have been discussed previously,[8] and include the following important limitations:

Table 4. Joinpoint analysis for age standardised incidence rates (ASIRs) for toe amputation in European Union (EU) 15+ countries for years 1990–2017 in male patients

Country	Trend 1			Trend 2			Trend 3			Trend 4		
	Years	EAPC (95% CI)	*p*	Years	EAPC (95% CI)	*p*	Years	EAPC (95% CI)	*p*	Years	EAPC (95% CI)	*p*
Australia	1990–1995	−0.4 (−0.5−−0.4)	<.001	1995–2005	+0.4 (+0.3 − +0.4)	<.001	2005–2010	+1.3 (+1.2 − +1.4)	<.001	2010–2017	+0.7 (+0.7 − +0.8)	<.001
Austria	1990–1994	−1.5 (−2−−1.1)	<.001	1994–2004	−0.6 (−0.7−−0.5)	<.001	2004–2012	0 (−0.2 − +0.2)	.80	2012–2017	−1.1 (−1.4−−0.8)	<.001
Belgium	1990–1996	+0.3 (−0.3 − +0.9)	.30	1996–2005	+2.5 (+2.1 − +2.9)	<.001	2005–2017	−0.4 (−0.7−−0.2)	<.001			
Canada	1990–1995	−0.8 (−1−−0.7)	<.001	1995–2004	−0.5 (−0.5−−0.4)	<.001	2004–2008	+0.8 (+0.4 − +1.2)	<.001	2008–2017	+0.4 (+0.3- +0.4)	<.001
Denmark	1990–2005	−0.5 (−0.6−−0.5)	<.001	2005–2008	+1.4 (+0.1 − +2.6)	<.001	2008–2017	+0.3 (+0.2 − +0.4)	<.001			
Finland	1990–1994	+0.9 (+0.4 − +1.3)	<.001	1994–2002	+1.9 (+1.7 − +2.1)	<.001	2002–2006	+0.4 (−0.3 − +1.2)	.20	2006–2017	−1.8 (−1.9−−1.7)	<.001
France	1990–1998	−0.5 (−0.6−−0.4)	<.001	1998–2005	+0.5 (+0.3 − +0.6)	<.001	2005–2015	0 (−0.1 − +0.1)	.40	2015–2017	−1.8 (−2.8−−0.7)	<.001
Germany	1990–2001	−0.3 (−0.3−−0.3)	<.001	2001–2005	−0.1 (−0.3 − +0.2)	.70	2005–2017	+0.7 (+0.7 − +0.7)	<.001			
Greece	1990–2017	+0.2 (+0.2 − +0.3)	<.001									
Ireland	1990–2006	+0.5 (+0.5 − +0.5)	<.001	2006–217	−0.3 (−0.3−−0.2)	<.001						
Italy	1990–1995	−0.6 (−0.8−−0.4)	<.001	1995–2005	−0.3 (−0.4−−0.2)	<.001	2005–2011	−1 (−1.1−−0.8)	<.001	2011–2017	−0.2 (−0.3−−0.1)	<.001
Luxembourg	1990–2000	−0.9 (−0.9−−0.8)	<.001	2000–2004	−1.5 (−1.9−−1.2)	<.001	2004–2012	−0.1 (0.2–0)	.10	2012–2017	−0.7 (−0.8−−0.5)	<.001
Netherlands	1990–2000	−1.4 (−2−−0.8)	<.001	2000–2017	+1.2 (+0.9 − +1.4)	<.001						
Norway	1990–2017	0 (−0.1 − +0.1)	.90									
Portugal	1990–1995	−0.8 (−0.9−−0.7)	<.001	1995–2005	−1.4 (−1.4−−1.3)	<.001	2005–2010	−2.5 (−2.6−−2.3)	<.001	2010–2017	−0.6 (−0.7−−0.6)	<.001
Spain	1990–2001	−0.7 (−0.9−−0.5)	<.001	2001–2004	+1.9 (−1.3 − +5.1)	.20	2004–2017	−0.5 (−0.7−−0.4)	<.001			
Sweden	1990–2001	−0.2 (−0.2−−0.1)	<.001	2001–2006	+0.6 (+0.4 − +0.8)	<.001	2006–2010	+1.2 (+0.9 − +1.5)	<.001	2010–2017	+0.7 (+0.6 − +0.8)	<.001
United Kingdom	1990–2001	−0.1 (−0.2–0)	.10	2001–2009	+1 (+0.8 − +1.3)	<.001	2009–2017	+0.5 (+0.3 − +0.7)	<.001			
United States	1990–1996	0 (−0.8 − +0.8)	1.0	1996–1999	−8.1 (−12.4−−3.6)	<.001	1999–2010	−1.6 (−2−−1.3)	<.001	2010–2017	+0.2 (−0.4 − +0.9)	.40

Data presented as Estimated Annual Percentage Change (EAPC %), with 95% confidence intervals in brackets. p values deemed significant if < 0.05.

firstly, the present analysis presents trends in LEA in EU15+ countries between 1990 and 2017; however, causal statements cannot be made about these data. The observational nature of the study means that numerous confounding factors not discussed in the manuscript will be differentially contributory to the observed trends. To reduce the effects of confounding on the results presented, age standardised, sex specific incidence rates were used, and it was chosen to compare countries with relatively similar health expenditure/economies. Secondly, the accuracy of death certification may differ across EU15+ countries. Deaths are under registered globally: Only 38% were registered in 2012;[36] however, Europe, Australasia, and North America had the best performing systems for civil registration and vital statistics, which supports the reliability of the GBD Study data from EU15+ countries presented in this study. Furthermore, the GBD study methodology includes corrections for under registration and "garbage" code redistribution algorithms (a "garbage" code is a death assigned to either a condition that cannot be the underlying cause of death or a poorly defined diagnosis). Finally, differences and changes in data coding practices within the EU15+ countries across the time period may compromise data robustness: of note, a transition from ICD-9 to ICD-10 occurred over the study period.

CONCLUSIONS

There are variable international trends in the incidence of lower limb amputation among the EU15+ countries over the 28 year study period. These changes do not mirror the decreasing incidence trends observed over the same time period for PAOD.[8]

CONFLICTS OF INTEREST

None.

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COUP D'OEIL

Continued Haemorrhage due to Type II Endoleak After EVAR for Ruptured Abdominal Aortic Aneurysm Necessitating Open Conversion

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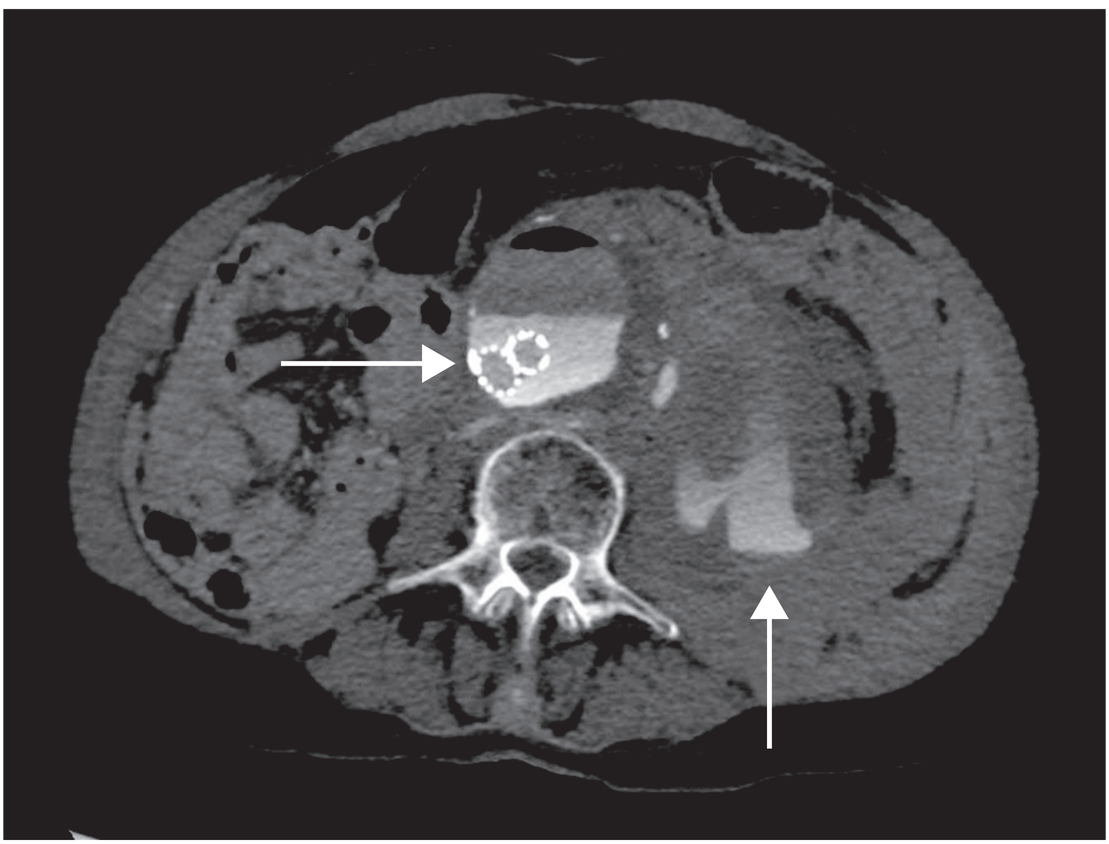

A 74 year old female with coronary heart disease presented with left lower quadrant abdominal pain. Computed tomography angiography (CTA) revealed a 6.5 cm ruptured abdominal aortic aneurysm (RAAA). Endovascular aneurysm repair with an Endurant stent graft (Medtronic, Santa Rosa, CA, USA) was performed. She remained clinically unstable with hypotension and falling haemoglobin levels. A new CTA showed contrast in the RAAA lumen (horizontal arrow) and the left abdominal haematoma (vertical arrow). The stent graft was removed. Four large lumbar arteries were oversewn. A 16 mm straight tube polyester prosthesis was sewn in. The type II endoleak was contained and the patient stabilised in the intensive care unit.

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