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Stroke Alliance For Europe
THE STROKE PATIENT VOICE IN EUROPE

UNIVERSITY OF OXFORD

AT WHAT COST

THE ECONOMIC IMPACT OF STROKE IN EUROPE

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FOREWARD

Since the research contained in this report was carried out, the world has been transformed by the COVID-19 pandemic. Across Europe it has impacted on every aspect of life and has, understandably diverted attention from other pressing health issues, such as stroke.

At the height of the pandemic all attention was focussed on preventing the spread of the virus and treating those infected. A recent World Health Organization survey[1] highlighted the impact of the pandemic on the disruption of services and predicted an increase in mortality and morbidity from causes other that COVID-19.

> *COVID-19 should be a lesson to all countries that health is not an 'either or' equation. We must better prepare for emergencies but also keep investing in health systems that fully respond to people's needs throughout the life course."*
>
> *Dr Tedros Adhanom Ghebreyesus*

Hanne Christensen of the University of Copenhagen and Francesca Romana Pezzella of the San Camillo Forlanini Hospital in Rome, wrote in the European Stroke Organisation's blog [2] at the end of March 2020,

> *Before the pandemic, during and after, stroke remains. Stroke is a serious sometimes lethal, sometimes 'just' life-changing condition, which can be prevented and treated. Stroke is an old threat that we have always lived with – but what is new is that we have the means to fight it."*

Many stroke support organisations throughout Europe have reported that an immediate impact of the pandemic was a reluctance of people to report their stroke symptoms, or to attend already over-burdened hospitals. Some reported that dedicated stroke units were used to treat other patients at the height of the pandemic, that stroke patients were discharged early, without appropriate support and that outpatient visits and much rehabilitation were halted. In some places stroke audits were halted and stroke clinicians were concerned that both the momentum to improve stroke care and its priority, may be permanently diminished.

1 https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS_continuity-survey-2020.1

2 https://eso-stroke.org/stroke-still-matters/

At the time of writing, it is not clear what the causes of non-COVID-19 excess deaths are, but it seems likely that stroke mortality rates have been affected.

It is vital that the urgent need to improve stroke prevention and care is not forgotten as in addition to the impact on stroke care, it appears from several research papers that COVID-19 is associated with an increased risk of stroke[3].

In 2017, the European Stroke Organisation and SAFE collaborated to produce the Stroke Action Plan for Europe 2018-2030[4], and, together, launched SAFE's Burden of Stroke in Europe report[5]. With the addition of this report, we now have a comprehensive understanding of the extent and impact of stroke across Europe and, crucially, a blueprint to transform stroke service provision.

So it is vital that this important groundwork is not undermined by the COVID-19 crisis.

The projections in this report of the future cost of stroke should be a wake-up call to health planners and officials across Europe. And the research into the benefits and costs of new treatments demonstrates that actively pursuing the latest, sometimes seemingly expensive interventions, can improve outcomes and, in some instances, save substantial amounts of money.

The response to the pandemic has shown that very rapid system change and adaptation is possible across a variety of different health systems. This should hearten all of us who work to transform stroke care – and this report provides more evidence for why it is now time to do so.

Jon Barrick
SAFE President,

3 Risk of Ischemic Stroke in Patients with Coronavirus Disease 2019 (COVID-19) vs Patients With Influenza. JAMA Neurol. Published online July 2, 2020. DOI:10.1001/jamaneurol.2020.2730, Large-Vessel Stroke as a Presenting Feature of Covid-19 in the Young. New England Journal of Medicine April 28, 2020. N Engl J Med 2020; 382:e60, DOI: 10.1056/NEJMc2009787).

4 Stroke Action Plan for Europe 2018-2030, https://www.safestroke.eu/stroke-action-plan

5 The Burden of Stroke in Europe report, May 2017 https://www.safestroke.eu/burden-of-stroke

INTRODUCTION

In 2017, SAFE published the Burden of Stroke in Europe report[6] which revealed the extent of stroke across the continent and the disparities in provision for stroke between regions and countries. In this report we build on that research, to provide, for the first time, a picture of the economic burden of stroke in 2017, and also over the next 20 years. We then look at three interventions which are in the latest stroke guidelines from the European Stroke Organisation. We estimate the impact they have on the costs of stroke and on the number of years of life in good health that they save.

The research provides details on the costs of different parts of the stroke care pathway, the costs of informal care and the productivity losses due to disability or death from stroke for all of the countries of the European Union (EU), plus Iceland, Israel, Norway, Switzerland and the United Kingdom (UK). A lack of comparable data prevented us from including other European countries.

To the best of our knowledge, this is the first study to quantify the current and future projected costs of stroke and identify the impact of investing in promising cost-effective interventions to prevent, treat and help stroke patients in their rehabilitation across 32 European countries. We believe that our study will be of use to policy makers when assessing whether to make substantial cost commitments in stroke care.

The total cost of stroke in these 32 countries was €60 billion in 2017:

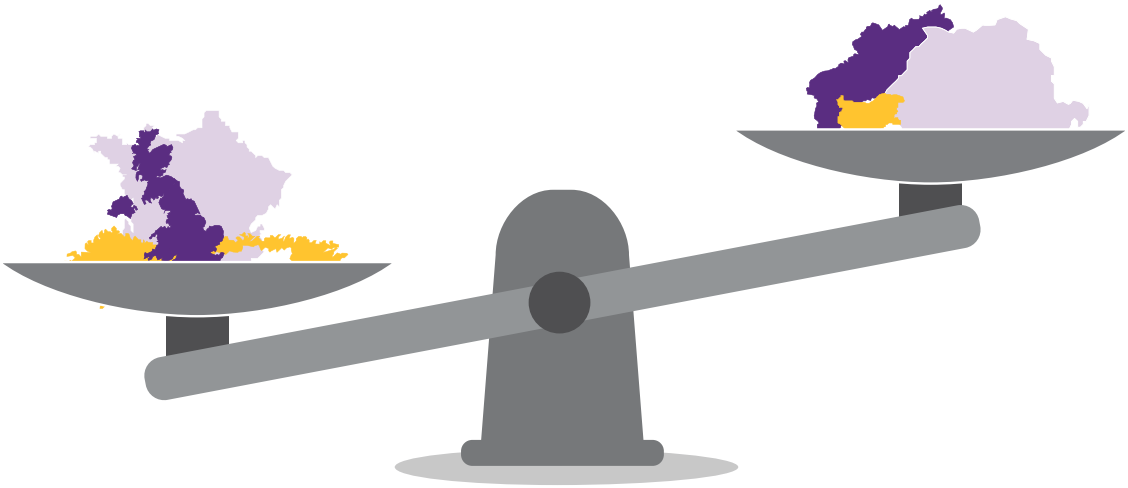
€27 BILLION	on **healthcare**
€5 BILLION	on **social care** (nursing or residential care)
€16 BILLION	on the **informal, unpaid care** provided to millions of stroke survivors by loved ones across Europe
€12 BILLION	are attributed to **lost productivity due to deaths and disability from stroke** of people of working age

6 The Burden of Stroke in Europe report, May 2017 https://www.safestroke.eu/burden-of-stroke

These figures are almost certainly an underestimate. For example, we did not include social care costs such as wheels on meal provisions, social work support, or adaptations and home help costs because this data is simply not available.

The research reveals big disparities in costs between countries. For instance, while the European average costs of hospital care were 60% of the total healthcare costs – it made up 86% of Switzerland's stroke related healthcare costs but just 11% of Cyprus's. This disparity, which mirrors the findings about stroke care from the Burden of Stroke in Europe report, has implications for planning and developing improved stroke services over the coming years and decades. The priorities for investing in improved stroke prevention and care may be different for each country.

Our research shows marked differences between the wealthy and less wealthy countries of Europe. Just five countries (Germany, the UK, France, Italy and Spain - the top five in terms of population) accounted for 71% of all stroke-related health care expenditure in Europe. Yet the less wealthy countries spent, on average, a much bigger proportion of their healthcare budgets on stroke. As a proportion of the countries' overall health expenditure, the European average was 1.7%. However, less wealthier countries such as Hungary spent 3.42% and Estonia spent 4.34%. This contrasts with the wealthier countries - Denmark spends 0.58% of its health budget on stroke and Switzerland spends 0.75%.



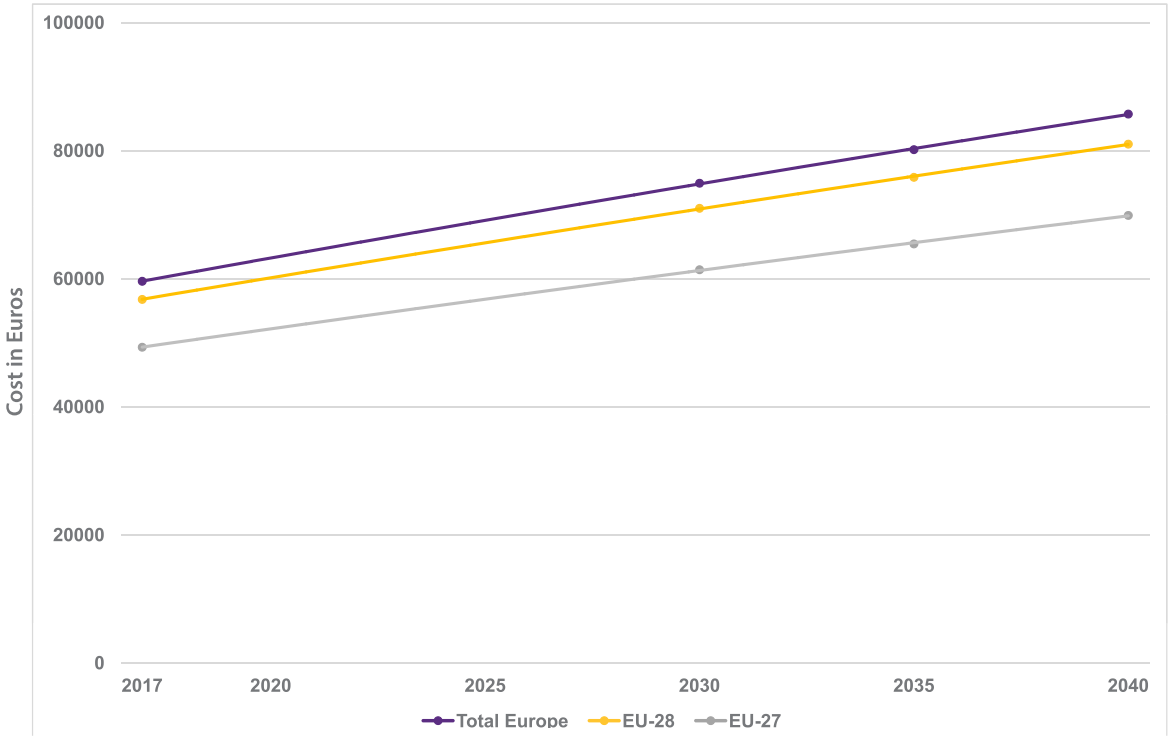
Across Europe, we will see decreasing birth rates, an ageing population, and, for many countries, a reduction in the total population, particularly of working age. Therefore, the number of people having, living with and dying from stroke will be very likely to increase, and with it, the economic costs associated with stroke.

The number of people of working age is projected to fall between 2017 and 2040. As a result, the costs of lost productivity due to deaths and disability are set to go down by €200,000 by 2040 – a 4% reduction due to deaths and 1% reduction due to disability.

Nevertheless, the number of people aged 65 or over is projected to increase by 45% and the number age 85 or over by 89%. As a result, the projected number of people living with stroke will increase by 35% (from nine million in 2017 to 12 million in 2040).

We estimate the costs of stroke will increase from €60 billion in 2017 to €75 billion in 2030, €80 billion in 2035 and €86 billion in 2040. This means that, in just 13 years, the costs of stroke are projected to increase by 26%, and by 44% in 23 years' time.

The graph below shows the increases in total stroke costs between 2017 and 2040 across Europe.



The rising costs of stroke will put strain on already stretched health and social care budgets. **European countries need to invest in stroke interventions that are cost-effective not just to improve outcomes for people who have a stroke, but also to halt this increase in costs and overall burden.**

Our study evaluated investments in three different interventions across the stroke pathway:

- prevention - to reduce the likelihood of people suffering a stroke in the first place;
- acute treatment in order to minimise stroke damage to the brain and reduce the likelihood of disability;
- rehabilitation to improve the quality of life of stroke survivors.

We looked at:

- routinely treating people who have atrial fibrillation (an uneven heartbeat) with either warfarin or new anticoagulant therapies;
- using mechanical thrombectomy (removing blood clots from the brain) to acutely treat people with ischaemic stroke;
- providing rehabilitation in a community setting once stroke patients were discharged from hospital.

All three interventions were shown to be cost effective and very good value for money at the European level. All of them would increase the number of extra years of good health across the population (known as the quality-adjusted life expectancy). And treating atrial fibrillation with warfarin, having mechanical thrombectomy routinely available, and providing community-based rehabilitation would all make cost savings. The new oral anticoagulants increase quality-adjusted life expectancy and are cost effective, but they are also more expensive.

The costs of stroke in the 32 countries we studied will by 44% between 2017 and 2040, with some countries seeing rises in stroke-related costs of nearly 100%. Policy makers and health planners need to act. Health and social care systems need to be improved and the increasing burden on informal carers (who will have to take even greater responsibility for the care of stroke survivors), needs to be acknowledged and acted upon. European countries need to put interventions and policies in place to try and mitigate these cost increases, whilst also maximising the health outcomes and quality of life for stroke survivors.

RECOMMENDATIONS

SAFE believes that all countries studied in this report should urgently recognise the increasing economic burden that stroke will have on their health and social care budgets and services over the next twenty years. We urge all countries to take immediate steps to reduce this burden. We also feel strongly that the EU must use these findings to prioritise stroke.

This report provides evidence that cost savings can be made by providing better treatment and care for stroke patients. The Organisation for Economic Co-operation and Development (OECD) and the European Commission recently published Health at a Glance: Europe"[7] which presents comparative analyses of the health status of EU citizens and the performance of the health systems of the 28 EU member states, five candidate countries and three European Trade Association countries. It highlighted that reducing wasteful spending and make health systems more effective and resilient is a key priority.

In addition, in 2019, the European Commission published its proposals for country specific recommendations as part of the EU's yearly European semester cycle, which monitors the EU member states' economic and fiscal progress. Seventeen countries were tasked with making improvements, including investing in their healthcare systems and making their healthcare system **more** cost-effective**.**

We call upon all individual countries to take the following actions:

- Adopt and implement a national stroke plan, including the recommendations of the Stroke Action Plan for Europe[8], and clear cost-effectiveness framework so that they can properly evaluate their expenditure decisions thus making stroke a national political priority with aligned ambitions and countries pledging themselves to commonly agreed goals

- Invest in stroke prevention, service provision and research in line with the recommendations in the Stroke Action Plan for Europe[8]. In addition, the evidence in this report demonstrated that the three investigated interventions are at the least cost effective and in most cases would save money.

7 OECD/EU (2018), Health at a Glance: Europe 2018: State of Health in the EU Cycle, OECD Publishing, Paris.https://doi.org/10.1787/health_glance_eur-2018-en

8 Stroke Action Plan for Europe 2018-2030, https://www.safestroke.eu/stroke-action-plan

- We call on all of the countries studied to:
  - routinely treat patients with known atrial fibrillation with warfarin or the new anticoagulant therapies;
  - acutely treat non-minor ischaemic stroke patients with mechanical thrombectomy;
  - provide rehabilitation in a community setting once stroke patients are discharged from hospital.

- Accurately collect comparable, data in order to help in understanding the impact of public health interventions, social care and provision for people living with stroke.

In addition, as an Alliance, we call for:

- members of the European Parliament to adopt a Resolution calling on Member states to implement the recommendations of the Stroke Action Plan for Europe[8] and, together with the European Commission, should approve a pilot project to support the international implementation of the Stroke Action Plan for Europe, as outlined by the Stroke Alliance for Europe and European Stroke Organisation in 2018.

- DG SANTE should support the creation of a stroke-specific subgroup in the Steering Group on Health Promotion, Disease Prevention and Management of non-communicable diseases, and help facilitate discussions about creating national plans for stroke, encompassing the entire chain of care from primary prevention through to life after stroke, in order to better manage and reduce the societal and economic burden of stroke in Europe.

- The European Commission must include research into stroke as a key priority in Horizon Europe, the research and innovation programme which will succeed Horizon 2020.

SAFE also commits to seek funding to carry out further research so that we have a better understanding of the reasons for the differences in the costs of stroke between countries and to provide further evidence to why, across Europe we need to increase disease prevention and improve access to care.

HOW MUCH DOES STROKE COST NOW?

The research in this report covers the 27 countries in the EU plus Iceland, Israel, Norway, Switzerland and the UK and provides the costs of stroke for the year 2017.

Where did we get the data and what did we measure?

We started by looking at the data on:

- the number of strokes and the number of people who die as a result of their stroke;
- hospital admissions for stroke;
- disease related costs;
- other health related indicators.

Among the sources consulted were the World Health Organization (WHO), the OECD, the Statistical Office of the European Communities (EUROSTAT), the World Bank Group, national ministries of health, national statistical institutes, and large cohort studies. Where there was little data on a particular country, projections based on similar countries (including health care costs, life expectancy and geography) were used. The framework used was based upon similar work carried out on cardiovascular diseases (CVD), cancer, blood disorders and dementia.

We looked at the health costs and the costs to society per year in following categories:

- Health costs: primary care, accident and emergency (A&E) care, hospital inpatient care (including day cases), outpatient care and medications;
- Social care costs: nursing and residential care homes but not things like home care, provision of meals, and social carer visits because of the lack of data about these areas of provision;
- The costs of “informal” care (most often provided by loved ones): the informal care costs of people who were severely affected by stroke or who were terminally ill, using country-specific data from the Global Burden of Disease[1] and data from the Survey of

Health, Ageing and Retirement in Europe (SHARE)[2] to assess the informal care needs of stroke patients;

- The impact of stroke on productivity: the costs of stroke survivors having to take sickness leave from work; being too disabled to get employment; or dying from their stroke at an employable age.

OUR METHODOLOGY IN DETAIL

A cost of illness analysis involves the identification, measurement and valuing of all resources related to a specific illness. The perspective of the analysis is fundamental in determining which resources should be considered, and how they should be measured and valued. A health service perspective, for instance, would only consider costs imposed on hospitals and other healthcare providers. A societal perspective enables a wider analysis, in which all costs are considered, irrespective of who bears them or where they are incurred. Such a perspective not only includes healthcare costs but also those costs falling outside the healthcare sector, such as social care, the opportunity costs associated with unpaid (i.e. informal) care to stroke patients, or productivity losses associated with premature death or morbidity. **For this analysis, a societal perspective was adopted.**

All costs due to stroke within the most recent year for which data were available were measured, regardless of the time of disease onset. We have used 2017 prices, and if necessary adjusted using the health consumer price indices of each country.[3] Where applicable, all national currencies were converted to Euros using 2017 exchange rates.[3]

A top down approach was employed to calculate the total expenditure due to stroke across 32 European countries. This approach used aggregate data on morbidity, mortality, hospital admissions, disease related costs, and other health-related indicators. An advantage of using this approach was the readily availability of international and national aggregate data.

A variety of international and national sources of epidemiological and healthcare utilisation data on and stroke were used including the WHO, the OECD, EUROSTAT, the World Bank Group, national ministries of health, national statistical institutes and large cohort studies. International data were used in preference to national data whenever available, as the former enable cross-country comparisons and are less prone to potential methodological biases. When relevant data could not be obtained from national or international sources, peer-reviewed articles or national reports from governmental or professional bodies were consulted. If no data were found for a particular country, extrapolations of resource use and unit costs were performed from similar countries. A country was judged to be similar if it had similar healthcare expenditure per person, life expectancy and geographical location.

The framework used to estimate healthcare and non-healthcare costs was similar to the approach by Leal et al. (2006),[4] Luengo-Fernandez (2011),[5] Luengo-Fernandez (2013),[6] Leal et al. (2016),[7] and Burns et al.(2016)[8] to estimate the economic burden of CVD, cancer and dementia in the EU.

HEALTHCARE COSTS

Stroke healthcare included:

- primary care;
- accident and emergency care;
- hospital inpatient care (including day cases);
- outpatient care;
- medications.

Other categories of health provision (such as school/community-based prevention and health education activities, and out-of-pocket expenses incurred by patients in purchasing over the counter medications, aids, home modifications) were not included in the study due to the difficulties of identifying them in the majority of countries. They are likely to represent a small proportion of the total costs identified.

To account for private spending on healthcare, in countries where only public resource use was found, cost estimates were inflated using the total proportion of private spending on healthcare.[3]

Primary care activities consisted of stroke-related visits to or from general practitioners (GPs). Outpatient care comprised specialist consultations taking place in outpatient wards, clinics, or patients' homes due to stroke. A&E consisted of all stroke-related hospital emergency visits.

To work out the amount of expenditure related to stroke we started with country specific visits (Table 1). In four countries (Iceland, Israel, Luxembourg, Slovenia) we found no data on A&E activity. As a result, we used the total per capita A&E visits from similar countries.

Therefore, for:

1. Iceland we used estimates from Denmark;[9]
2. Israel we used estimates from Greece;[10]
3. Luxembourg we used estimates from Belgium;[11]
4. Slovenia we used estimates from Croatia.[12]

Table 1. Sources of healthcare resource use by category and country*

	PRIMARY CARE	OUTPATIENT CARE	A&E	INPATIENT CARE
AUSTRIA	3	3	13	3
BELGIUM	14	11	11	3
BULGARIA	3	3	15	3
CROATIA	12	12	12	3
CYPRUS	16	16	16	3
CZECH REPUBLIC	17	18	19	3
DENMARK	20	21	9	3
ESTONIA	22	22	22	3
FINLAND	23	23	23	3
FRANCE	24	24	25	3
GERMANY	3	3	10	3
GREECE	26	26	10	3
HUNGARY	27	28	29	3
ICELAND	30	31	9	3
IRELAND	3	3	32	3
ISRAEL	33	33	10	34

	PRIMARY CARE	OUTPATIENT CARE	A&E	INPATIENT CARE
ITALY	3	3	35	3
LATVIA	36	36	37	3
LITHUANIA	38	38	39	3
LUXEMBOURG	40	40	11	3
MALTA	41	41	41	3
NETHERLANDS	42	42	43	3
NORWAY	44	45	46	3
POLAND	47	47	47	3
PORTUGAL	3	48	48	3
ROMANIA	49	49	50	3
SLOVAKIA	51	51	51	3
SLOVENIA	52	52	12	3
SPAIN	53	54	54	3
SWEDEN	55	55	56	3
SWITZERLAND	57	57	58 59	3
UK	60 61	62-65	62 66-68	3

**For this and following tables, source numbers refer to References given at the end of this report*

We needed to divide the overall population by age because one of the most important sources of data, SHARE, is about people over 50.[2] So we determined the proportion of these visits for people over 50 using, where possible, the country specific data already obtained or EUROSTAT,[3] which contained self-reported number of primary and outpatient care visits by age. For A&E, when visits were not reported by age group, we used the proportion of all hospital discharges for those aged over 50 years or more.[3]

To obtain the proportion of primary, outpatient and A&E visits due to stroke in those under the age of 50, we estimated for that age group the proportion of overall hospital discharges due to stroke,[3] and applied it to the total number of visits for those under the age of 50.

SHARE is a multidisciplinary and cross-national panel database of micro data on health, socio-economic status and social and family networks, freely available to researchers, in which all data are collected via face-to-face, computer-aided personal interviews, supplemented by self-completion paper and pencil questionnaires (Table 2). The SHARE target population consists of all persons aged 50 years and over who have their regular domicile in the respective SHARE country.

We used data collected in Wave 2, Wave 4 and Wave 6 which included over 30,000 respondents resident in 21 European countries (Austria, Belgium, Croatia, the Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Israel, Luxembourg, the Netherlands, Poland, Portugal, Slovenia, Spain, Sweden and Switzerland). Residents from Ireland and Hungary were only included in Waves 2 and 4 respectively, and the data collected in these two waves were combined with Wave 6 data on the remaining 19 countries. For countries not in SHARE, we combined data from similar countries that were in SHARE to obtain estimates for the 11 remaining countries. Therefore, for Bulgaria, Latvia, Lithuania, Romania, and Slovakia we used combined data from the Czech Republic, Estonia, Hungary, Poland and Slovenia. For Iceland, Finland and Norway we used combined data from Denmark and Sweden. For Cyprus and Malta, we used combined data from Greece, Italy, Israel, Portugal and Spain. Finally, for the UK we used combined data from Austria, Belgium, France, Germany, Ireland, Luxembourg, and the Netherlands.

Table 2. Waves and Field time available in SHARE survey

WAVE	FIELD TIME
1	2004-2006
2	2006-2007
3	2008-2010
4	2010-2012
5	2013
6	2015
7	2017

Participants in SHARE were asked amongst other things the number of times they had visited a primary healthcare physician, a specialist in an outpatient setting or attended A&E over the last 12 months. Using three Poisson multivariate regressions, one for each type of resource use, we estimated the country-specific number of visits given the patient had a history of stroke, after adjusting for presence of dementia and/or other health conditions and country of residence. This expected number of visits was then multiplied with the number of people with stroke in each country in SHARE, and divided by the total number of visits in that country (i.e. number of people responding in SHARE multiplied by the mean number of visit), in order to obtain the proportion of primary, outpatient, and A&E visits due to stroke in each country (Table 3).

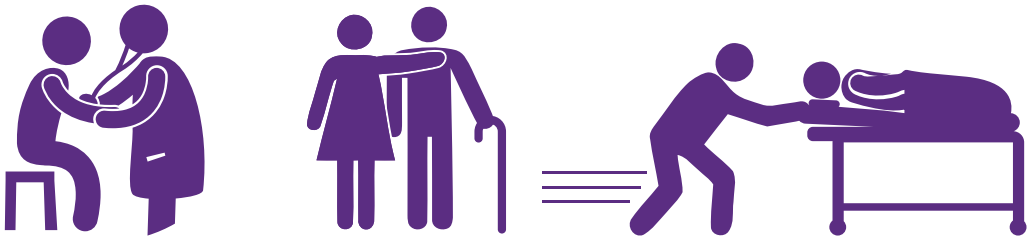


Table 3. Proportion of primary, outpatient and A&E care visits due to stroke

	PRIMARY CARE		OUTPATIENT CARE		A&E CARE	
	<50 YEARS	≥50 YEARS	<50 YEARS	≥50 YEARS	<50 YEARS	≥50 YEARS
AUSTRIA	2.28%	7.38%	2.28%	7.39%	2.28%	6.63%
BELGIUM	1.22%	4.36%	1.22%	4.37%	1.22%	3.94%
BULGARIA	2.92%	6.79%	2.92%	6.73%	2.92%	6.76%
CROATIA	2.26%	4.91%	2.26%	4.97%	2.26%	4.19%
CYPRUS	1.96%	4.95%	1.96%	4.89%	1.96%	4.98%
CZECH REPUBLIC	3.66%	5.03%	3.66%	5.05%	3.66%	4.86%
DENMARK	1.89%	4.59%	1.89%	4.52%	1.89%	5.37%
ESTONIA	5.16%	6.20%	5.16%	6.15%	5.16%	7.27%
FINLAND	3.06%	6.24%	3.06%	6.13%	3.06%	6.69%
FRANCE	0.91%	4.55%	0.91%	4.52%	0.91%	7.69%
GERMANY	2.97%	4.51%	2.97%	4.52%	2.97%	4.15%
GREECE	1.96%	4.71%	1.96%	4.58%	1.96%	6.96%
HUNGARY	5.66%	7.73%	5.66%	10.32%	5.66%	6.47%
ICELAND	2.35%	6.24%	2.35%	6.13%	2.35%	6.69%
IRELAND	0.65%	4.97%	0.65%	5.01%	0.65%	6.67%
ISRAEL	1.96%	6.48%	1.96%	6.48%	1.96%	6.47%
ITALY	3.89%	3.83%	3.89%	3.83%	3.89%	3.42%
LATVIA	5.16%	6.79%	5.16%	6.73%	5.16%	6.76%
LITHUANIA	5.31%	6.79%	5.31%	6.73%	5.31%	6.76%
LUXEMBOURG	1.79%	2.79%	1.79%	2.80%	3.66%	4.86%
MALTA	1.18%	4.95%	1.18%	4.89%	1.18%	4.98%
NETHERLANDS	1.83%	3.91%	1.83%	3.87%	1.83%	4.27%
NORWAY	2.32%	6.24%	2.32%	6.13%	2.32%	6.69%
POLAND	2.58%	5.35%	2.58%	5.36%	2.58%	5.90%
PORTUGAL	1.84%	6.79%	1.84%	6.69%	1.84%	7.17%
ROMANIA	2.92%	6.79%	2.92%	6.73%	2.92%	6.76%
SLOVAKIA	4.16%	6.79%	4.16%	6.73%	4.16%	6.76%
SLOVENIA	2.20%	5.75%	2.20%	5.69%	2.20%	6.89%
SPAIN	1.80%	3.21%	1.80%	3.16%	1.80%	3.80%
SWEDEN	3.32%	6.21%	3.32%	6.14%	3.32%	6.42%
SWITZERLAND	2.61%	2.67%	2.61%	2.64%	2.61%	3.07%
UK	1.13%	5.16%	1.13%	5.11%	1.13%	5.05%

Inpatient care was estimated from the number of stroke-related days in hospital, including day case admissions. The number of days in hospital, which included day cases, was obtained for all countries by primary diagnosis stroke. Except for Israel, where data was derived from the OECD,34 all stroke-related days in hospital and day cases were obtained from EUROSTAT.3

For all countries, healthcare resource use was valued using country-specific unit costs, which were derived from published studies, reports, and national fee schedules.

Sources of unit costs per country and resource use category are reported in Table 4. Unit costs are reported in Table 5. For some countries, unit costs were derived from the predictions of linear regression analyses of the unit costs of countries with available data.[6 7]

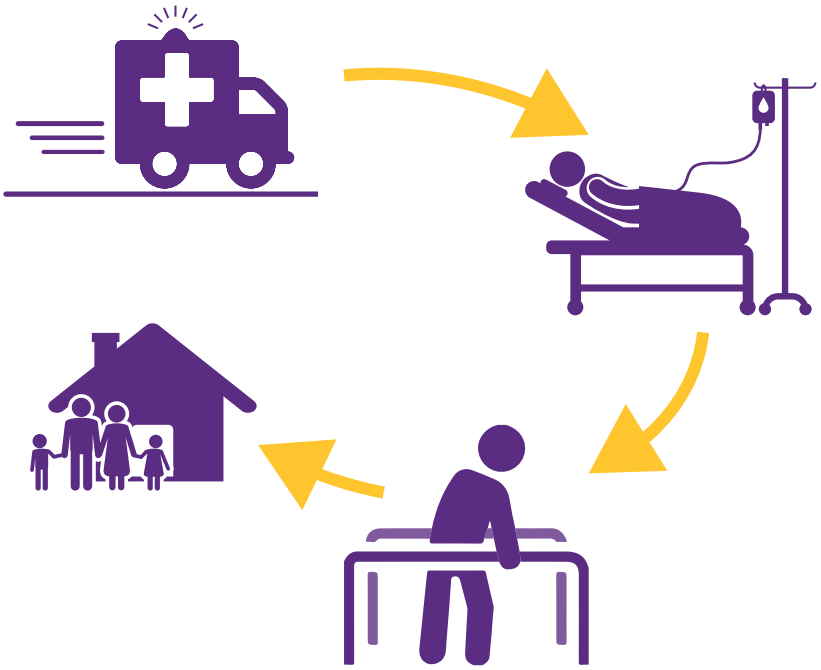


Table 4. Sources of unit costs by country and healthcare utilisation category

	PRIMARY CARE	OUTPATIENT CARE	A&E	INPATIENT CARE
AUSTRIA	13	13	69	3
BELGIUM	70	70	70	71
BULGARIA	3	3	Regression*	3
CROATIA	72	72	72	72
CYPRUS	73	73	74	75
CZECH REPUBLIC	18	18	Regression*	18
DENMARK	76	76	77	3
ESTONIA	22	22	22	22
FINLAND	78	78	78	79
FRANCE	24	24	80	3
GERMANY	81	82	81	83
GREECE	84	85	84	84
HUNGARY	28	28	29	29
ICELAND	86	86	87	86
IRELAND	88	88	88	89
ISRAEL	90	90	90	90
ITALY	81	81	81	3
LATVIA	36	36	Regression	3
LITHUANIA	91	91	81	3
LUXEMBOURG	92	92	92	3
MALTA	41	Regression	93	93
NETHERLANDS	93	93	94	93
NORWAY	95	95	95	96
POLAND	97	98	98	3
PORTUGAL	99	100	100	100
ROMANIA	101	101	Regression	3
SLOVAKIA	101	101	Regression	3
SLOVENIA	101	101	93	3
SPAIN	102	102	102	103
SWEDEN	104	56	56	56
SWITZERLAND	97	97	105	97
UK	106	107	107	107

Table 5. Unit costs (€)

	VISITS					HOURLY EARNINGS		YEARLY EARNINGS		
	GP	OUTPATIENT	A&E	DAY IN HOSPITAL	DAY IN NURSING HOME	EMPLOYED	NON-EMPLOYED	MALE	FEMALE	DAILY EARNINGS
AUSTRIA	55	69	160	588	136	24	10	50,443	38,703	195
BELGIUM	28	58	91	966	74	26	9	49,717	45,237	207
BULGARIA	6	24	31	93	13	4	1	8,117	6,758	33
CROATIA	17	15	261	110	16	8	3	14,992	13,737	63
CYPRUS	15	30	51	148	70	14	7	28,508	23,155	113
CZECH REPUBLIC	12	16	83	261	34	8	3	16,380	12,271	63
DENMARK	21	86	139	1,540	245	35	22	71,550	56,239	280
ESTONIA	16	53	57	269	29	8	3	18,219	12,586	67
FINLAND	153	377	423	778	196	24	14	50,407	39,176	196
FRANCE	39	146	91	717	82	21	10	41,687	34,469	166
GERMANY	53	78	96	868	131	29	9	52,774	52,774	229
GREECE	20	50	72	476	53	12	4	24,769	20,527	100
HUNGARY	5	7	121	168	19	7	2	13,260	10,922	53
ICELAND	84	141	300	1,311	227	27	19	52,962	44,998	214
IRELAND	51	137	272	671	147	27	9	54,479	45,724	219
ISRAEL	12	69	200	501	112	16	7	34,456	22,548	125
ITALY	23	88	235	654	132	20	10	38,697	32,266	156
LATVIA	11	40	39	93	14	7	2	14,199	11,069	55
LITHUANIA	11	27	22	123	9	6	2	12,056	9,638	47
LUXEMBOURG	46	65	81	1,175	205	33	12	62,491	58,530	264
MALTA	39	58	97	413	176	13	4	26,211	21,937	107
NETHERLANDS	32	134	167	1,446	196	27	9	53,790	44,018	214
NORWAY	70	156	152	1,364	387	30	23	59,440	51,206	241
POLAND	6	54	24	197	99	7	3	14,430	12,032	58
PORTUGAL	31	68	96	312	31	10	4	20,418	17,025	82
ROMANIA	9	14	70	96	14	5	2	9,745	9,165	41
SLOVAKIA	22	33	41	198	31	8	3	15,693	12,159	61
SLOVENIA	26	37	98	333	61	13	5	25,596	23,413	107
SPAIN	39	130	185	714	92	16	5	31,161	27,022	127
SWEDEN	162	428	394	922	211	27	13	52,580	45,557	214
SWITZERLAND	49	49	142	1,219	229	38	18	73,725	64,884	303
UNITED KINGDOM	34	137	169	665	136	23	9	48,109	35,491	183

PHARMACEUTICAL EXPENDITURE

The costs related to consumption of stroke-related medication were included in the analysis.

OECD health data provided the total CVD-related pharmaceutical expenditure, defined as those medications coded under the Anatomical Therapeutic Chemical (ATC) Classification Code C (Cardiovascular System), for Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Luxembourg, the Netherlands, Norway, Portugal, Slovakia, Slovenia, Spain, Sweden, Switzerland and the UK.[34] CVD-related expenditure on medication was obtained from other sources for: Bulgaria,[3 108] Croatia,[109] Cyprus,[3 110] Latvia,[111] and Poland.[3 112] For Israel, Malta and Romania no data on CVD-related pharmaceutical expenditure was identified. Therefore, for: 1) Israel we used estimates from Italy, 2) Malta we used the average from Cyprus, Italy, Portugal, and Spain; and 3) Romania we used estimates from Bulgaria.

As only France,[113] Germany[83] and the Netherlands[114] provided data on the proportion of CVD-related pharmaceutical expenditure on stroke, the proportion of pharmaceutical expenditure due to stroke was averaged across the three countries and applied to the total CVD sales in the remaining countries.

NURSING HOME AND RESIDENTIAL CARE COSTS

Social care costs included in the study were those related to nursing and residential care home institutionalisation for which there is data across the 32 countries. As a result, other social care resource use categories like home care, provision of meals, and social carer visits were not included.

Nursing and residential care was measured as the number of stroke-related days spent in care homes. There are two types of care homes, nursing and residential homes. A residential home provides care for people who are not able to manage everyday tasks or maintain an independent home of their own while a nursing home provides 24-hour nursing care. Given the data available, we conservatively assumed that only those aged 65 years of age or more, would be institutionalised in a nursing/residential care home.

Data on the number of people aged 65 years or over living in a nursing or residential home care was obtained from the OECD for: Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Israel, Luxembourg, the Netherlands, Norway, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and Switzerland.[34] For seven other countries this information was derived from country-specific reports drawn up by the European Commission: Bulgaria,[115] Cyprus,[116] Italy,[117] Latvia,[118] Lithuania,[119] Malta,[120] and Poland.[121] For the remaining four countries, this information was derived from a number of different sources: Austria,[122] Croatia,[12] Greece,[123] and the UK.[124]

Participants in SHARE were asked whether they lived in a nursing or residential home. Using logistic regression analysis, we estimated the country-specific probability of a respondent being institutionalised in a nursing/residential care home due to stroke, adjusting by age, presence of stroke, dementia and/or other health conditions and country of residence. This proportion was then applied to the total number of institutionalised people and multiplied by 365.25 to obtain the annual number of days institutionalised in a nursing/residential home due to stroke.

In addition, participants in SHARE were asked whether a relative or friend they cared for had died within the last 12 months. As part of these questions, participants were asked, the age and gender of the deceased, the place of death (which could include nursing or residential care home) and the main cause of death (which could include stroke). We, therefore, evaluated the number of people who died within the last 12 months in a nursing/residential care home due to stroke. This was undertaken by adding the age and sex-specific products of: the number of stroke-related deaths.[3 34]; and the probability of having been institutionalised before a stroke-related death and

assessed using a logistic regression, adjusting for stroke death, country of residence, age and gender.

As these people would not have been institutionalised for the full year, we assumed that all patients died halfway through the year. Therefore, the total number of people who died as a result of stroke in a nursing/residential care home was multiplied by 183 days. This estimate was then added to the number of institutionalised days for people living with stroke to obtain the annual number of days institutionalised in a nursing/residential home due to stroke.

A day in a nursing home was then valued using a number of different country-specific sources. For 10 countries, this information was obtained from long-term care institutionalisation expenditure estimates compiled in country-specific reports authored by the European Commission: Bulgaria,[115] Cyprus,[116] Greece,[125] Hungary,[126] Italy,[117] Latvia,[118] Lithuania,[119] Malta,[120] Poland[121] and Slovenia.[127] For the remaining countries, unit costs were obtained from a wide range of sources: Austria,[128] Belgium,[129] Croatia,[130] Czech Republic,[131] Denmark,[132] Estonia,[133] Finland,[134] France,[135] Germany,[135] Iceland,[136] Ireland,[137] Israel,[138] Luxembourg,[40] the Netherlands,[139] Norway,[140] Portugal,[141] Romania,[142] Slovakia,[142] Spain,[143] Sweden,[144] Switzerland,[145] and the UK (Table 5).[106]

INFORMAL CARE COSTS

Informal care costs were based upon the conservative assumption that only patients severely limited in daily activities or who were terminally ill would receive informal care. We used country-specific data from to estimate the number of people with stroke using prevalence estimates from the Global Burden of Disease1 and then used data from SHARE to assess the informal care needs of stroke patients.[2]

We then assessed the:

- prevalence of stroke in the population, which was obtained from prevalence estimates for stroke from the GBD study;[1]
- probability of being severely limited in daily activities due to stroke. Using data from SHARE, we undertook logistic regressions adjusting for age, gender, presence of stroke, dementia and of other health conditions, and country of residence. As a result, we obtained country-specific estimates of the probability of being severely limited in daily activities due to stroke;

- probability of receiving informal care due to stroke. Using data from SHARE, we evaluated the probability that stroke patients received informal care. We performed two logistic regressions (one for care from inside household and another for care outside the household) after adjusting for age, gender, presence of stroke, dementia and other health conditions, limitations in daily living and country of residence;

- hours of informal care received due to stroke.

Using data from SHARE, we performed an ordered logistic regression to assess the amount of informal care time (almost daily, almost weekly, almost every month or less often) that patients with stroke received after adjusting for age, gender, presence of stroke, dementia and other health conditions, limitations in daily living, and country of residence. These were converted into hours using the information from SHARE on the number of unpaid care hours (either daily, weekly, monthly or annually) patients with stroke received.

The hours of informal care for terminally ill stroke patients were estimated by adding the age and sex-specific products of:

- Number of stroke deaths. Age and gender-stratified cancer deaths were derived from EUROSTAT (WHO in the case of Israel).[3 146]

- Probability of receiving informal care in the year before dying from stroke. Using the end-of-life questionnaire, participants in SHARE were asked to report whether they had provided unpaid care for anyone who had died in the last year, including the age of the person to whom care was provided and the health conditions from which that person was suffering. The probability of providing informal care for a stroke patient was estimated using a logistic regression analysis after adjusting for age, gender and country.

- Hours of informal care received due to stroke. Using data from the end-of-life questionnaire in SHARE, we performed an ordered logistic regression to assess the amount of informal care time (almost daily, almost weekly, almost every month or less often) that caregivers provided to a stroke patient after adjusting for age, gender, and country of residence. These were converted into hours using the information from SHARE on the number of unpaid care hours (either daily, weekly, monthly or annually) that caregivers provided to stroke patients.

Participants in SHARE were asked about the relationship between carer and person being cared for (for example spouse, sibling, offspring, parent friend). We assumed that spouses, siblings and friends providing the care would be of similar age to the patient. Therefore carers of patients aged 65 years or more were assumed to be retired, and those carers of patients

aged less than 65 years were assumed to be of working-age. If care was being provided by either the patients' children or their children's spouses, then it was assumed that these informal carers would be under 65 years of age. Using gender-specific economic activity and unemployment rates for each country,[3 147] we then determined the proportion of these carers who were employed or unemployed/economically inactive.

The mean net hourly wage rate was applied to informal care provided by those carers in working age and who were economically active and in employment. Annual earnings were adjusted to hourly wage rates, assuming there were 230 working days each year, and each day consisted of eight hours of work. For those carers in retirement, unemployed, or economically inactive, the national hourly minimum wage was applied.[3 148] For those countries with no official minimum wage rate (Cyprus, Denmark, Finland, Germany, Italy and Sweden), the worst paid sector in the economy was proxied as a minimum wage.

PRODUCTIVITY COSTS

The costs associated with lost productivity due to morbidity (that is, disability caused by stroke) were the costs associated with absence of work due to stroke. Morbidity losses could occur due to: individuals taking absence from leave for a defined period of time; or due to individuals being declared incapacitated or long-term disabled due to their condition, and therefore leaving the labour market. Table 6 details all the sources used to obtain temporary and permanent absence from work due to stroke.

Country-specific overall annual days of sickness leave due to all conditions was obtained for all countries, except for Cyprus (Table 6). As a result, we used the total per employed person days of work due to temporary sickness in Greece and multiplied this by the number of employed people in Cyprus.[3 149]

Table 6. Sources used to obtain morbidity losses

	TEMPORARY ABSENCE FROM WORK	PERMANENT ABSENCE FROM WORK
AUSTRIA	13 124	124
BELGIUM	150 151	151
BULGARIA	152 153	153 154
CROATIA	12 52	12 52
CYPRUS	149 155	149 156
CZECH REPUBLIC	157	17 157

	TEMPORARY ABSENCE FROM WORK	PERMANENT ABSENCE FROM WORK
DENMARK	158 159	159 160
ESTONIA	22	22 161
FINLAND	162 163	163
FRANCE	34 164	165
GERMANY	166 167	168 169
GREECE	149 155	149 156
HUNGARY	153 170	153 171
ICELAND	86 159	159 172
IRELAND	173 174	175 176
ISRAEL	34 177	178 179
ITALY	177 180	179 181
LATVIA	22 182	22 183
LITHUANIA	22 38	22 184
LUXEMBOURG	185 186	40 186
MALTA	41 177	41 179
NETHERLANDS	187 188	188 189
NORWAY	34 190	190 191
POLAND	153	47 153
PORTUGAL	155 192	156 193
ROMANIA	153 154	153 154
SLOVAKIA	157 194	157 194
SLOVENIA	52	52 195
SPAIN	34 155	156 196
SWEDEN	159 197	159 197
SWITZERLAND	167 198	169 199
UK	174	176

To the total number of days of work due to sickness we applied the proportion of absence that was attributable to stroke using the following:

- in the Czech Republic,[157] France,[164] Germany,[167] and the UK[174] published data were available on the proportion of temporary absence from work due to stroke;

- in Austria,[13] Belgium,[200], Estonia,[22] Italy,[177] Luxembourg,[186] the Netherlands,[188] Norway,[190] Poland,[153] Slovenia,[52] and Spain[155] published data were available on the proportion of temporary

absence from work due to CVD. To evaluate the proportion of temporary absence from work due to stroke, we obtained the proportion of CVD-related hospital inpatient days in the working age population due to stroke,[3] and applied it to the total number of CVD-related days of temporary work absence;

- in Finland[163] and Sweden[159] we obtained data on the proportion of overall permanent absence from work (in the form of disability pensions for the working age population) due to CVD in the working age population, and assumed this would be the same as the proportion for temporary absence from work. To evaluate the proportion of temporary absence from work due to stroke, we obtained the proportion of CVD-related hospital inpatient days in the working age population due to stroke,[3] and applied it to the total number of CVD-related days of temporary work absence;

- we obtained no information on the proportion of absence from work due to stroke or CVD for 16 countries:

    - for Slovakia, we used estimates from the Czech Republic;[157]

    - for Switzerland, we used estimates from Germany;[167]

    - for Bulgaria, Hungary, and Romania, we used estimates from Poland;[153]

    - for Croatia, we used estimates from Slovenia;[52]

    - for Cyprus, Greece and Portugal, we used estimates from Spain;[155]

    - for Denmark and Iceland, we used estimates from Sweden;[159]

    - for Ireland, estimates from the UK were used;[174]

    - for Israel and Malta, estimates from Italy were used;[177]

    - For Latvia and Lithuania, estimates from Estonia were used.[22]

To evaluate the proportion of temporary absence from work due to stroke, we obtained the proportion of CVD-related hospital inpatient days in the working age population due to stroke,[3] and applied it to the total number of CVD-related days of temporary work absence.

To calculate permanent absence from work due to sickness, country-specific information on the numbers of working-age individuals receiving incapacity or disability benefits and not being able to work due to all conditions was obtained for all countries except for Bulgaria and Cyprus (Table 6). We used the per capita number of people receiving disability benefits in the working age population in Romania[154] and Greece[149] and multiplied this by the working age population in Bulgaria[3] and Cyprus,[3] respectively.

To the total number of people receiving disability benefits we applied the proportion of permanent absence that was attributable to stroke using the following:

- in Austria,[124] France,[165] Germany[169] and the UK[176] published data were available on the proportion of permanent absence from work due to stroke;

- in Belgium,[151] Finland,[163] Italy,[179] Luxembourg,[186] Norway,[190] Spain[156] and Sweden[159] published data were available on the proportion of permanent absence from work due to CVD. To evaluate the proportion of permanent absence from work due to stroke, we obtained the proportion of CVD-related hospital inpatient days in the working age population due to stroke,[3] and applied it to the total number of CVD-related number of people receiving disability/incapacity benefits;

- in the Czech Republic[157] we obtained data on the proportion of temporary absence from work (in the form of sickness days) due to stroke, and assumed this would be the same as the proportion for permanent absence from work;

- in Estonia,[22] the Netherlands,[188] Poland,[153] and Slovenia[52] we obtained data on the proportion of overall temporary absence from work (in the form of sickness days) due to CVD, and assumed this would be the same as the proportion for permanent absence from work. To evaluate the proportion of permanent absence from work due to stroke, we obtained the proportion of CVD-related hospital inpatient days in the working age population due to stroke,[3] and applied it to the total number of CVD-related number of people receiving disability/incapacity benefits.

We obtained no information on the proportion of absence from work due to stroke or CVD for 16 countries.

We used the proportion of permanent absence from work due to stroke for:

- Ireland,[176] where estimates from the UK were used;
- Switzerland,[169] where estimates from Germany were used;
- For Slovakia we used the proportion of temporary absence from work due to stroke from the Czech Republic.[157]

For seven countries, we used the proportion of permanent absence from work due to CVD for:

- Cyprus, Greece and Portugal, where estimates from Spain were used;[156]
- Denmark and Iceland, where estimates from Sweden were used;[159]
- Israel and Malta were estimates from Italy were used;[179]

For the remaining six countries, we used the proportion of temporary absence from work due to CVD for:

- Bulgaria, Hungary and Romania, where estimates from Poland were used;[153]
- Croatia, where estimates from Slovenia were used;[52]
- Latvia and Lithuania, were estimates from Estonia[22] were used.

To evaluate the proportion of permanent absence from work due to stroke, we obtained the proportion of CVD-related hospital inpatient days in the working age population due to stroke,[3] and applied it to the total number of CVD-related number of people receiving disability/incapacity benefits.

To put a value on the absence from work, the mean annual earnings were converted to mean daily earnings.[3 148] The product of working days lost and mean daily earnings provided the productivity losses associated with stroke. Furthermore, we used the friction period approach as absent workers are likely to be replaced, whereby only the first 90 days of work absence were counted.[201]

To assess the mortality losses, for all countries we assumed an initial working age of 15. Age and gender specific deaths due to stroke were obtained for all countries.[3 146] The number of potential working years lost was then estimated as the difference between the age at death and maximum age of retirement (which we set at 79 years of age).

However, this estimate would overestimate the total working years lost as not everyone will be economically active (i.e. either working or actively searching for work) or employed. Therefore, age and gender-specific unemployment and activity rates,[3 147] for each of the 32 countries were applied to the potential foregone earnings due to premature mortality. The total number of working years lost was then multiplied by gender-specific average annual earnings.[3 148] Future earnings lost due to mortality were discounted to present values using a 3.5% annual rate,[202] i.e. the value society attaches to present as opposed to future costs.

Finally, we used statistical analysis to investigate variations in stroke related healthcare expenditure between countries. We undertook a series of ordinary least squares univariate regression analyses, using national income, overall health expenditure, stroke incidence, stroke mortality, case fatality (mortality divided by incidence), stroke prevalence, and stroke specific disability adjusted lifeyears (DALYs /the number of years of healthy life lost to stroke)as explanatory variables. We did diagnostic tests for omitted variables (RESET test and link test) and heteroskedasticity (BreuschPagan test). We deemed an explanatory variable to be significant if its p value was less than 0·05. All regression analyses were done in Stata (version 15.1).

We also did a sensitivity analysis to measure what effect changes in different categories of resource use would have in terms of total costs of stroke. The aim was to identify which categories were most sensitive. Therefore, we examined the effects of a 20% increase or decrease in health and social care costs and earnings for men and women. We also assessed the effect of discounting productivity costs using rates of 0% and 5%, and of not using a friction-period (i.e. using a human capital approach) when estimating morbidity losses.

RESULTS

In 2017, nearly 1.5 million people suffered a stroke in the 32 European countries under study, nine million Europeans lived with stroke, and 438,000 died due to a stroke.

Table 7 shows, for each of the countries studied:

- the number of new strokes (incidence);
- the number of people who have had a stroke (prevalence);
- the number of people who died from a stroke (deaths);
- the number of years of healthy life lost to stroke (DALYs).

Table 7. Non-economic stroke burden

	INCIDENCE	PREVALENCE	DEATHS	DALYS
AUSTRIA	23,698	154,877	5,246	68,833
BELGIUM	28,085	192,320	6,943	116,340
BULGARIA	38,368	205,683	21,513	327,622
CROATIA	20,469	98,358	7,487	118,848
CYPRUS	1,573	11,079	374	7,522
CZECH REPUBLIC	38,959	216,547	9,630	165,197
DENMARK	12,540	92,553	3,392	60,016
ESTONIA	4,610	32,633	853	23,179
FINLAND	17,429	133,952	4,300	75,047
FRANCE	131,416	942,293	32,271	548,745
GERMANY	242,497	1,685,144	57,082	926,146
GREECE	34,149	212,536	14,445	200,543
HUNGARY	40,003	237,789	12,500	232,778
IRELAND	7,462	56,931	1,920	31,653
ITALY	166,015	778,199	61,783	641,405
LATVIA	12,188	68,840	5,117	73,098
LITHUANIA	15,035	83,143	5,680	77,217
LUXEMBOURG	1,074	8,273	234	4,966
MALTA	892	6,646	287	4,105
NETHERLANDS	35,385	254,094	9,679	162,107
POLAND	124,540	690,591	30,475	653,330

	INCIDENCE	PREVALENCE	DEATHS	DALYS
PORTUGAL	27,447	191,120	11,776	187,018
ROMANIA	103,102	489,826	44,251	776,798
SLOVAKIA	20,560	103,365	5,488	95,249
SLOVENIA	6,204	38,875	1,983	27,499
SPAIN	101,845	550,941	28,434	389,291
SWEDEN	24,807	166,065	6,154	103,126
TOTAL EU-27	1,280,353	7,702,671	389,297	6,097,675
UK	134,979	992,413	40,054	667,392
TOTAL EU-28	1,415,332	8,695,085	429,351	6,765,066
ICELAND	603	4,167	154	2,342
ISRAEL	11,390	82,396	2,454	45,122
NORWAY	12,254	81,671	2,623	43,207
SWITZERLAND	19,766	135,329	3,642	63,410
TOTAL EUROPE	1,459,345	8,998,648	438,224	6,919,147

THE COSTS TO THE HEALTHCARE SYSTEM

The next table (Table 8) shows the number (in thousands) of stroke patients treated at different stages of the health system:

- visits to the GP (primary care);
- visits to a clinic at the hospital (outpatient visits);
- emergency care incidents;
- days in hospital;
- and days in nursing homes.

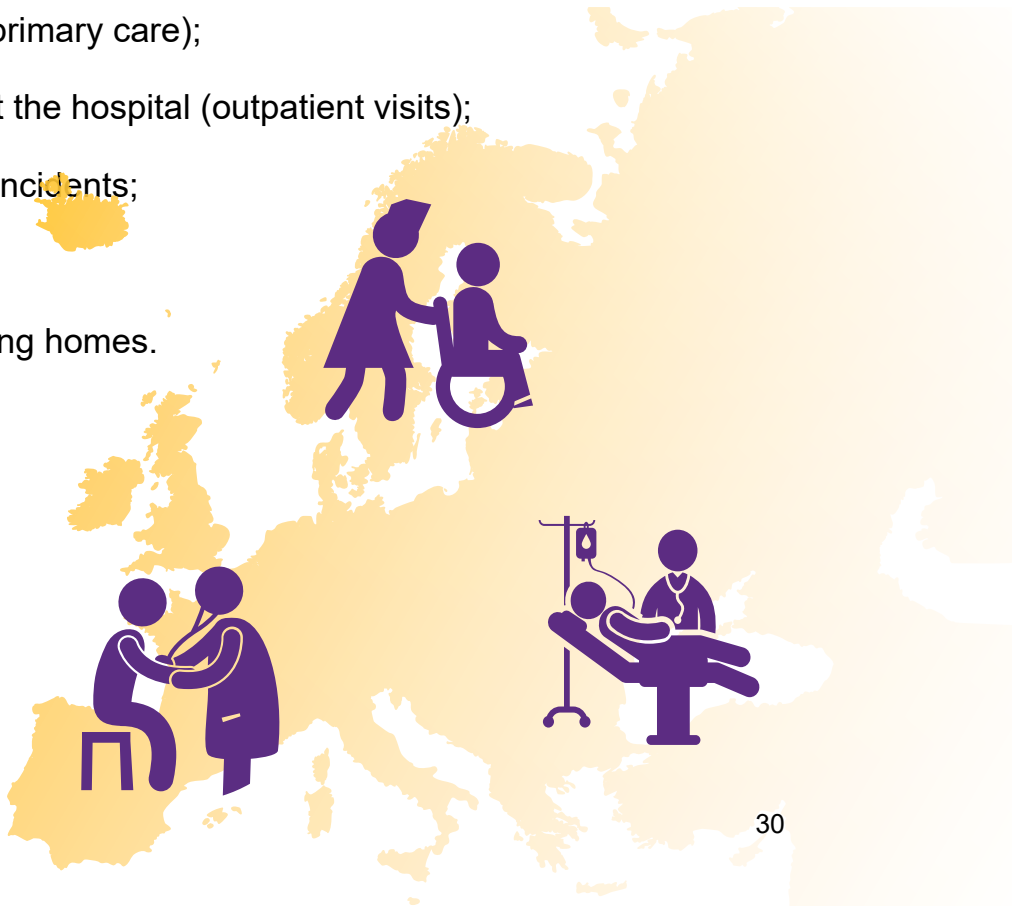


Table 8. Health and social care resource use

	NUMBER OF GP VISITS	NUMBER OF OUTPATIENT VISITS	NUMBER OF EMERGENCY CARE VISITS	DAYS IN HOSPITAL	DAYS IN NURSING HOME
AUSTRIA	2,841	1,830	188	858	784
BELGIUM	1,367	647	75	425	4,439
BULGARIA	1,791	486	55	329	658
CROATIA	572	411	30	196	118
CYPRUS	36	207	39	8	26
CZECH REPUBLIC	2,015	3,899	37	1,071	708
DENMARK	943	224	43	74	634
ESTONIA	537	289	43	123	104
FINLAND	123	427	69	542	677
FRANCE	7,548	2,747	954	1,624	7,674
GERMANY	21,745	17,403	252	7,381	6,606
GREECE	277	227	241	438	680
HUNGARY	3,829	5,414	49	1,164	711
IRELAND	529	189	84	123	119
ITALY	11,118	4,743	799	3,303	2,841
LATVIA	392	209	27	141	208
LITHUANIA	1,140	528	42	262	545
LUXEMBOURG	40	71	6	18	93
MALTA	23	17	5	18	14
NETHERLANDS	2,578	1,623	75	312	1,071
POLAND	7,082	4,799	358	1,285	905
PORTUGAL	1,188	894	458	292	493
ROMANIA	2,040	4,413	51	920	2,340
SLOVAKIA	1,451	2,358	85	280	346
SLOVENIA	392	200	20	76	139
SPAIN	10,860	2,584	960	797	1,449
SWEDEN	748	674	139	338	1,095
TOTAL EU-27	**83,206**	**57,510**	**5,185**	**22,397**	**35,476**
UK	11,666	3,773	728	2,459	5,651
TOTAL EU-28	**94,872**	**61,283**	**5,912**	**24,855**	**41,128**
ICELAND	90	46	4	8	28
ISRAEL	1,644	719	181	167	192

	NUMBER OF GP VISITS	NUMBER OF OUTPATIENT VISITS	NUMBER OF EMERGENCY CARE VISITS	DAYS IN HOSPITAL	DAYS IN NURSING HOME
NORWAY	607	298	50	154	481
SWITZERLAND	461	261	55	395	1,339
TOTAL EUROPE	**97,674**	**62,606**	**6,202**	**25,581**	**43,168**

Table 9 shows the costs (in millions) for 2017 of the six areas of health and social care:

PRIMARY CARE

With over 98 million visits to the GP due to stroke in the 32 countries the overall cost was €3.3 billion. About half of this amount is accounted for by just two countries – Germany and Spain.

OUTPATIENT CARE

The 63 million visits to outpatient consultants cost the healthcare systems of the 32 countries €4.7 billion. Germany (€1.4 billion), the UK (€0.5 billion) and Italy (€0.4 billion) accounted for approximately half of outpatient care costs in Europe.

EMERGENCY CARE

6.2 million visits to A&E departments across Europe cost €919 million overall. Italy (€188 million). Spain and the UK accounted for 53% of emergency care costs in Europe.

HOSPITAL CARE

Across Europe the 26 million days spent in hospital due to stroke in 2017 resulted in a total cost €16.4 billion for the 32 countries. Countries spending the most in terms of inpatient care for stroke included: Germany (€6.4 billion); Italy (€2.2 billion); the UK (€1.6 billion) and France (€1.2 billion), with these 4 countries accounting for approximately 70% of European healthcare spend on inpatient care for stroke patients.

PHARMACEUTICALS

In 2017, the European spend on pharmaceuticals used to prevent and treat stroke was €1.3 billion. The highest spend on stroke medications was in France (€199 million), followed by Spain (€175 million), the Netherlands (€169 million), Germany (€143 million) and Italy (€115 million). These five countries accounted for 61% of total European pharmaceutical expenditure on stroke medications.

NURSING HOME/RESIDENTIAL CARE

There were 43 million days spent in nursing/residential care homes by stroke survivors in 2017. This resulted in a total cost for European social care systems of €4.7 billion and €4.2 billion for the EU. Countries spending the most in terms of social care for stroke included: Germany (€866 million); the UK (€767 million), France (€630 million), Italy (€375 million) and Belgium (€328 billion).

Table 9. Health and social care costs (€ millions)

	PRIMARY CARE	OUTPATIENT CARE	EMERGENCY CARE	HOSPITAL CARE	PHARMA	TOTAL HEALTHCARE	SOCIAL CARE
AUSTRIA	155	127	30	504	29	845	106
BELGIUM	39	38	7	411	31	524	328
BULGARIA	11	12	2	31	15	70	8
CROATIA	10	6	8	22	5	50	2
CYPRUS	1	6	2	1	1	11	2
CZECH REPUBLIC	25	64	3	280	18	390	24
DENMARK	20	19	6	114	7	166	155
ESTONIA	9	15	2	33	1	61	3
FINLAND	19	161	29	421	10	640	133
FRANCE	292	401	87	1,165	199	2,143	630
GERMANY	1,155	1,359	24	6,408	143	9,089	866
GREECE	6	11	17	209	41	284	36
HUNGARY	20	37	6	196	28	286	13
IRELAND	27	26	23	83	14	172	17
ITALY	250	418	188	2,160	115	3,131	375
LATVIA	4	8	1	13	3	30	3
LITHUANIA	13	14	1	32	2	62	5
LUXEMBOURG	2	5	0	21	2	29	19
MALTA	1	1	0	7	1	10	2
NETHERLANDS	83	217	12	450	169	932	210
POLAND	45	261	9	253	67	636	89
PORTUGAL	37	60	44	91	24	257	15
ROMANIA	19	61	4	88	26	198	33
SLOVAKIA	32	78	3	55	8	177	11
SLOVENIA	10	8	2	25	4	48	9
SPAIN	427	336	178	569	175	1,685	133

	PRIMARY CARE	OUTPATIENT CARE	EMERGENCY CARE	HOSPITAL CARE	PHARMA	TOTAL HEALTHCARE	SOCIAL CARE
SWEDEN	121	289	55	311	12	788	231
TOTAL EU-27	**2,832**	**4,038**	**743**	**13,955**	**1,146**	**22,715**	**3,459**
UK	399	516	123	1,636	101	2,775	767
TOTAL EU-28	**3,231**	**4,554**	**866**	**15,590**	**1,247**	**25,489**	**4,226**
ICELAND	8	6	1	11	1	27	6
ISRAEL	20	49	36	84	12	201	22
NORWAY	43	46	8	211	8	316	186
SWITZERLAND	23	13	8	482	33	558	307
TOTAL EUROPE	**3,324**	**4,669**	**919**	**16,378**	**1,301**	**26,592**	**4,748**

TOTAL HEALTH CARE EXPENDITURE

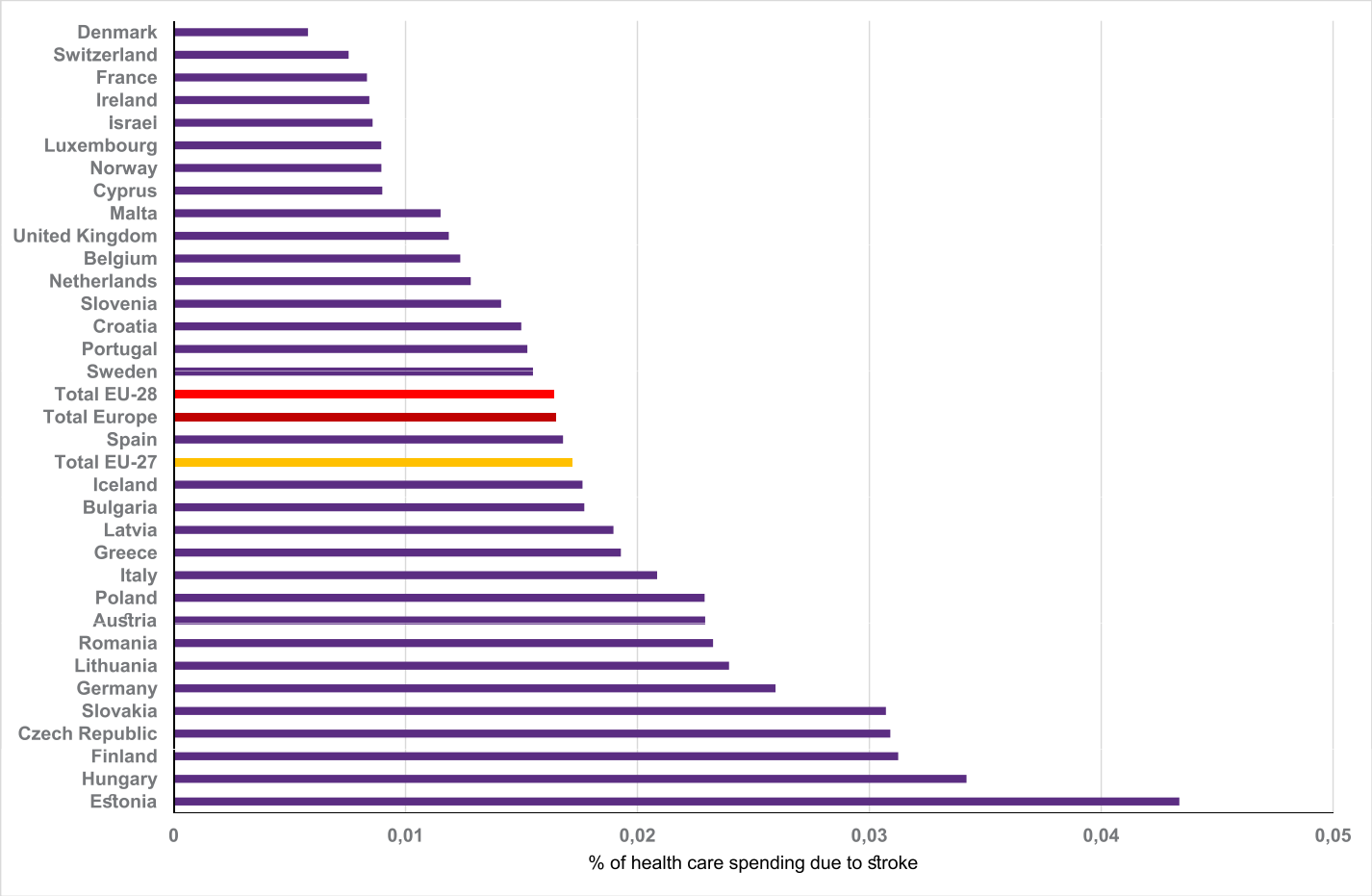
In total, in 2017 stroke cost the healthcare systems of the 32 countries under study €27 billion. Of this, €16 billion (62%) was due to inpatient hospital care, followed by outpatient care (€4.7 billion, 18%), primary care (€3.3 billion, 13%), pharmaceuticals (€1.3 billion, 5%) and emergency care (€919 million, 3%).

The top five countries with the highest healthcare expenditure due to stroke also have the biggest populations. Germany (€9.1 billion), Italy (€3.1 billion), the UK (€2.8 billion), France (€2.1 billion) and Spain (€1.7 billion). Health expenditure due to stroke in these five countries accounted for 71% of all stroke-related healthcare expenditure in Europe.

The average cost of stroke as a proportion of the countries' overall health expenditure was 1.7%. But there was a very wide variation between countries, with less wealthier countries such as Hungary spending 3.42% and Estonia spending 4.34%. This contrasts with the wealthier countries, for example, Denmark spends 0.58% of its health budget on stroke and Switzerland spends 0.75%.

The graph (Figure 1) below shows the proportion of health expenditure on stroke for each of the countries studied.

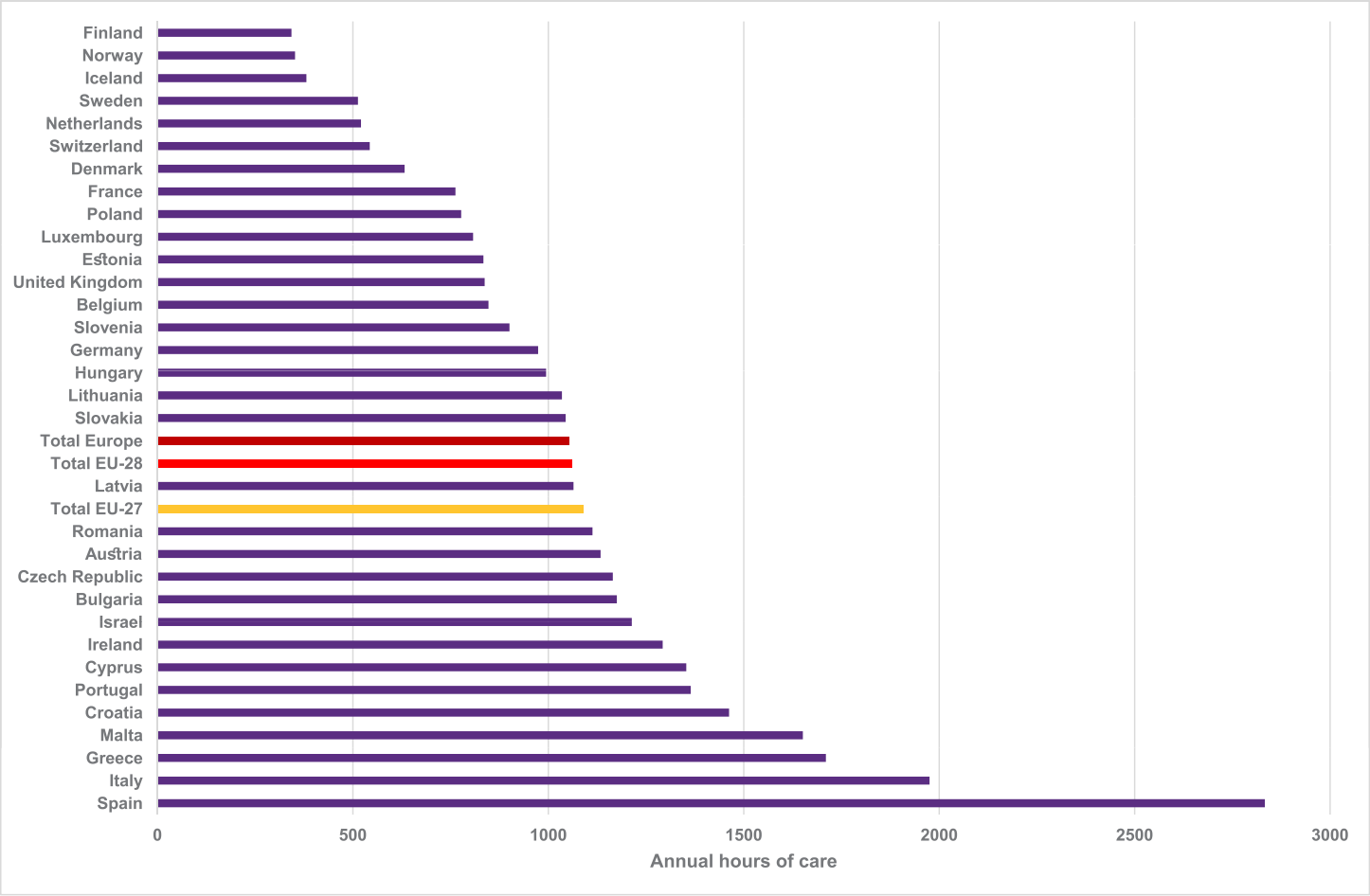
Figure 1. Proportion of healthcare spending due to stroke



THE COSTS OF INFORMAL CARE

On average, in 2017, friends and family provided 1,052 hours of informal care for each person with stroke who was severely limited in activities of daily living. This varied widely across Europe from 343 hours in Finland to 2,833 hours in Spain. Scandinavian countries tended to provide the least hours of informal care, whereas Southern European countries provided the most. The graph below (Figure 2) shows the average number of hours per year of informal care that stroke survivors receive.

Figure 2. Annual hours of informal care per stroke survivor



The next table (Table 10) shows the amount of informal care in the 32 countries studies in 2017. Of the nine million people with stroke, 1.2 million were severely hampered in their activities of daily living. They received 1.3 billion hours of care from friends and family. The most care took place in Germany with 271 million hours of care provided (21% of the total), followed by Italy with 170 million hours (13%) and Spain with 110 million hours (8%).

These 1.3 billion hours of informal care provided across Europe were valued at €16 billion for the year 2017 (Table 11). As with the total number of hours of care, Germany had the highest informal care costs across Europe of €5 billion (32%), followed by Italy with costs of €2 billion (15%) and France of €1 billion (8%).

Table 10. Informal care and work time lost (thousands) due to stroke

	HOURS OF INFORMAL CARE	DEATHS	WORKING YEARS LOST DUE TO DEATH	WORKING DAYS LOST DUE TO ILLNESS
AUSTRIA	22,215	5	3	920
BELGIUM	21,128	7	3	770
BULGARIA	40,133	22	15	193
CROATIA	21,541	7	3	421
CYPRUS	1,255	0.4	0.3	54
CZECH REPUBLIC	35,784	10	7	507
DENMARK	5,099	3	3	297
ESTONIA	5,837	1	1	362
FINLAND	4,743	4	2	832
FRANCE	86,846	32	19	7,648
GERMANY	270,850	57	39	5,191
GREECE	21,982	14	5	889
HUNGARY	38,342	13	9	224
IRELAND	4,726	2	2	507
ITALY	169,878	62	21	3,199
LATVIA	12,571	5	4	299
LITHUANIA	14,738	6	6	620
LUXEMBOURG	828	0.2	0.1	16
MALTA	895	0.3	0.2	50
NETHERLANDS	27,764	10	7	548
POLAND	90,924	30	33	604
PORTUGAL	44,808	12	9	905
ROMANIA	90,407	44	33	405
SLOVAKIA	17,075	5	5	359
SLOVENIA	5,071	2	1	111
SPAIN	110,152	28	13	2,804
SWEDEN	9,301	6	3	568
TOTAL EU-27	**1,174,893**	**389**	**245**	**29,303**
UK	116,847	40	34	5,705
TOTAL EU-28	**1,291,740**	**429**	**279**	**35,008**
ICELAND	158	0.2	0.2	22
ISRAEL	10,272	2	3	1,551

	HOURS OF INFORMAL CARE	DEATHS	WORKING YEARS LOST DUE TO DEATH	WORKING DAYS LOST DUE TO ILLNESS
NORWAY	2,922	3	2	1,149
SWITZERLAND	6,157	4	3	267
TOTAL EUROPE	**1,311,249**	**438**	**286**	**37,997**

THE COSTS OF LOST PRODUCTIVITY DUE TO DEATH AND DISABILITY

In 2017, there were a total of 438,000 deaths due to stroke in the 32 European countries under analysis, amounting to 286,000 potential years of work lost. After discounting future losses (i.e. those losses incurred after the first year of death), premature mortality cost the 32 European countries under study a total of €6.2 billion. Germany, with productivity losses of €1.5 billion due to premature death, accounted for nearly a quarter of total mortality costs.

A total of 38 million working days were lost due to permanent and temporary absence from work across Europe due to stroke. These losses were valued at €6.3 billion. In total productivity losses due to stroke amounted to €12.5 billion.

THE TOTAL COST OF STROKE

Stroke cost the 32 European economies under study a total of €60 billion in 2017. For the EU-28 this was €57 billion, and without including the UK the costs of stroke to the EU would be just under €50 billion. Of that total, healthcare cost €27 billion, 45% of total costs; informal care cost €16 billion and loss of productivity due to disability and death about €12 billion. Nursing home and residential care, costing €5 billion, made up 8% of the total cost.

However, these proportions of spending varied widely between countries. For example, in Luxembourg social care accounted for 25% (€19 million) of total costs of stroke, whereas in Croatia these costs accounted for less than 1% (€2 million) of total costs.

As a proportion of total costs, productivity losses due to premature mortality were highest in Bulgaria, accounting for 31% (€88 million) of total costs, and lowest in Norway, where they accounted for 7% (€68 million) of total costs.

The table below (Table 11) shows all of the different areas of cost discussed above to provide the overall cost (in millions €) of stroke across the 32 countries.

Table 11. Total costs of stroke in Europe (€ millions)

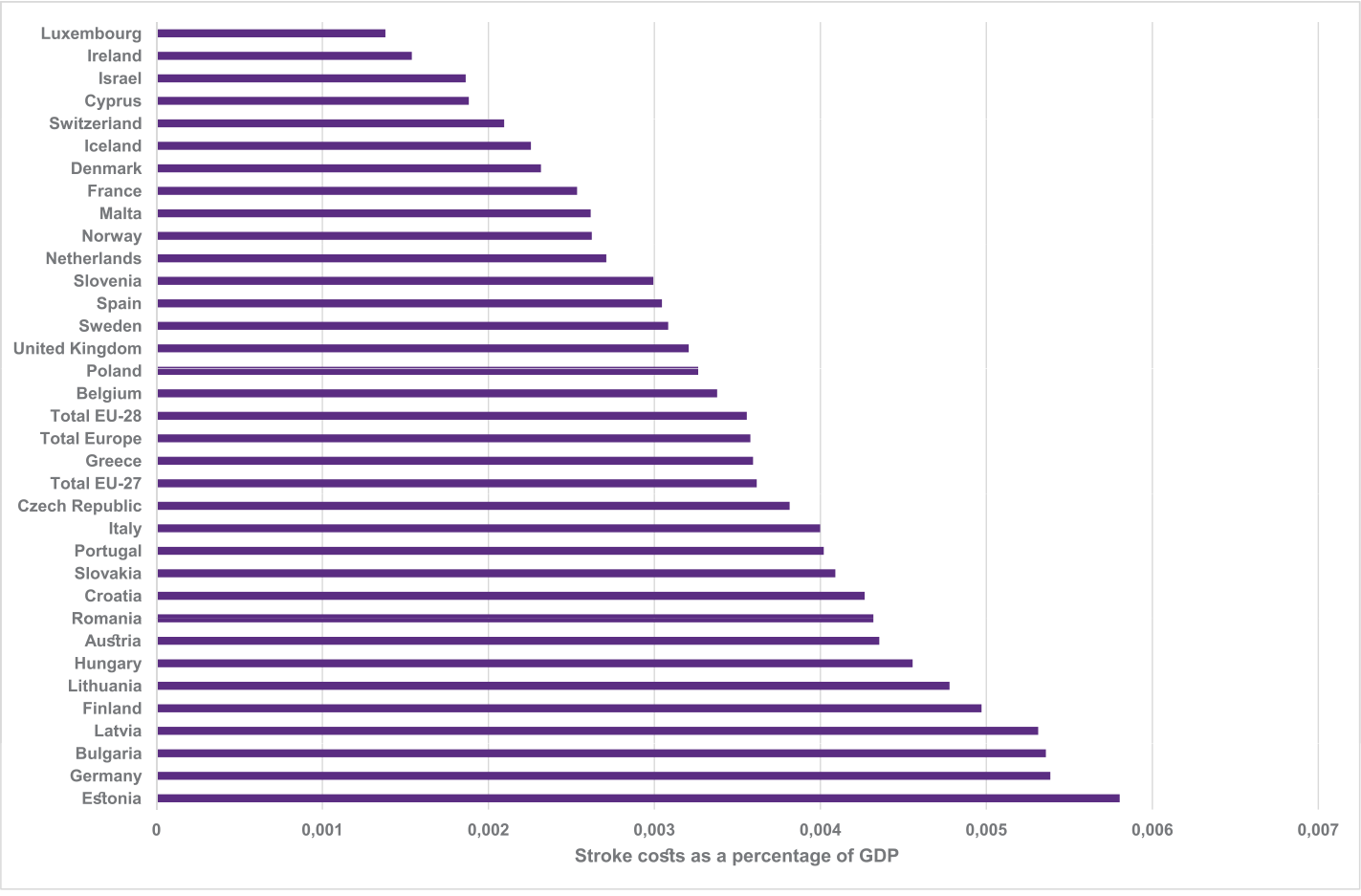
	HEALTH AND SOCIAL CARE	INFORMAL CARE	MORTALITY LOSSES	MORBIDITY LOSSES	TOTAL
AUSTRIA	952	383	94	180	1,608
BELGIUM	853	354	118	159	1,484
BULGARIA	78	106	87	6	278
CROATIA	52	101	31	26	211
CYPRUS	13	13	5	6	37
CZECH REPUBLIC	414	206	79	32	730
DENMARK	322	148	124	83	677
ESTONIA	64	35	14	24	137
FINLAND	773	92	83	163	1,111
FRANCE	2,773	1,260	519	1,271	5,823
GERMANY	9,954	4,971	1,483	1,191	17,600
GREECE	320	160	82	89	650
HUNGARY	300	168	87	12	567
IRELAND	189	83	67	111	451
ITALY	3,507	2,355	543	501	6,905
LATVIA	32	59	36	16	144
LITHUANIA	67	59	47	29	203
LUXEMBOURG	48	17	6	4	75
MALTA	13	8	3	5	29
NETHERLANDS	1,142	484	247	117	1,991
POLAND	725	421	331	35	1,512
PORTUGAL	272	304	133	74	783
ROMANIA	231	333	234	17	815
SLOVAKIA	188	83	54	22	347
SLOVENIA	57	45	15	12	129
SPAIN	1,818	1,109	274	357	3,557
SWEDEN	1,019	193	122	122	1,455

	HEALTH AND SOCIAL CARE	INFORMAL CARE	MORTALITY LOSSES	MORBIDITY LOSSES	TOTAL
TOTAL EU-27	**26,174**	**13,549**	**4,920**	**4,665**	**49,308**
UK	3,542	1,838	1,044	1,046	7,470
TOTAL EU-28	**29,716**	**15,387**	**5,964**	**5,711**	**56,778**
ICELAND	33	4	7	5	48
ISRAEL	223	123	57	195	597
NORWAY	501	78	68	277	926
SWITZERLAND	866	170	139	81	1,256
TOTAL EUROPE	**31,339**	**15,762**	**6,235**	**6,269**	**59,605**

The total gross domestic product (GDP) of the 32 countries was €16,658 billion in 2017. **Stroke accounted for 0.36% of total GDP**. The country with the highest share of GDP lost due to stroke was Estonia at 0.58% followed by Bulgaria and Germany, both at 0.54%. The countries with the lowest share of GDP lost due to stroke were Luxembourg (0.14%), Ireland (0.15%) and Israel (0.19%).

The graph below (Figure 3) shows the overall cost of stroke as a proportion of GDP.

Figure 3. Proportion of GDP lost due to stroke



WHAT ARE THE FUTURE COSTS OF STROKE?

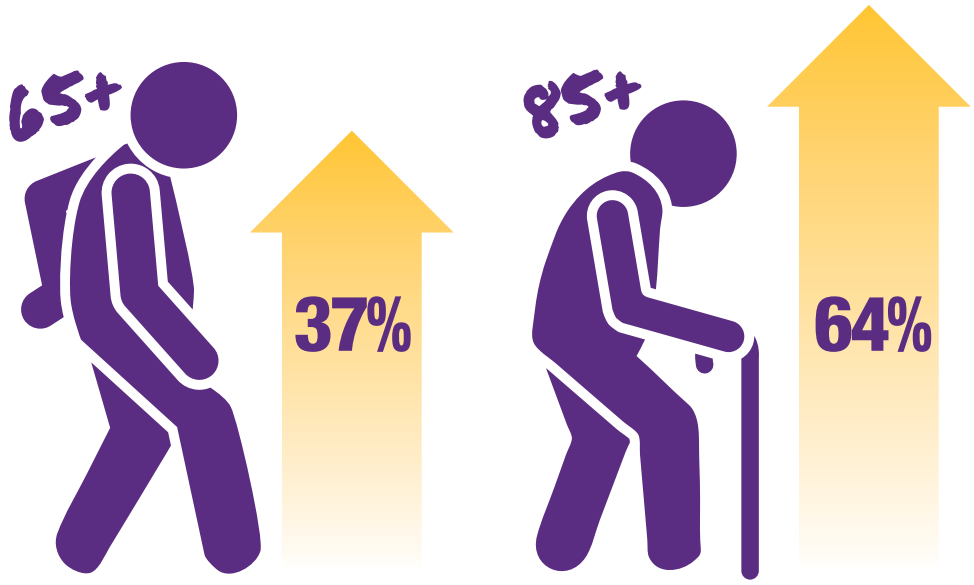
In 2017 the cost of stroke in the 32 European countries studied was €60 billion. In this chapter we predict the costs of stroke in 2030, 2035 and 2040. In order to do so, the first step was to estimate the future incidence and prevalence of stroke.

Although the incidence of strokes has been declining over the last two decades[203], after adjustments for age and gender related prevalence), recent data shows an increase in strokes in younger people[204]. This, together with increases in the numbers of people with conditions that increase the risk of stroke, such as diabetes and atrial fibrillation, make it difficult to assess future incidence[1 205]. So this study is based upon 2017 data (from the Global Burden of Disease study[1] with projections on future population numbers from Eurostat[3] and, for Israel, the OECD[206]).

And while there has been a welcome decrease in stroke related deaths[207], there is some evidence suggesting that the number of deaths within the first year after a stroke has not changed[203 208 209]. Nor is it not clear what impact this may have on the number of people living with the life changing, long-term impact of stroke. So, again, the study assumes the same stroke mortality rates for 2030, 2035 and 2040 as in 2017[1 3 146 146].

The research used the country, age and sex-specific stroke prevalence data from 2017 and mapped this against projections of the future age- and sex-specific populations of the 32 countries. With the projections showing more people living to a greater age, the number of people having a stroke and living with stroke is set to increase. Using 2017 prices this has implications for the future cost of stroke.

In 2030, for example, the total populations of the 32 countries is predicted to increase by 4%. However, the number of people aged 65 and over is set to rise by 37% and, even more dramatically, there will be an estimated 64% increase in the number of people aged 85 and over.



As age is the biggest, non-modifiable risk factor for stroke, we are set to see a dramatic rise in the number of new strokes and the number of people living with stroke, concentrated in these older age groups. The predicted increase in overall population compared to 2017 remains 4% for 2035 and 2040, but the increase in the number of older people means that stroke incidence is set to increase by 32% in 2035 and 41% in 2040, for example.

The following tables (Table 12 to 14) show changes from 2017, for the years 2030, 2035 and 2040 in terms of:

- the percentage overall population for the 32 countries, including changes in the number over 65 and over 80;
- the percentage change in the number of people living with stroke (prevalent stroke), again including the over 65 and over 80 age groups;
- the percentage change in the number of new strokes (incidence) including the same age groupings.

Table 12. Changes in population and stroke incidence/prevalence between 2017 and 2030

	POPULATION			PREVALENT STROKE CASES			INCIDENT STROKE CASES		
	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS
AUSTRIA	13%	49%	64%	37%	52%	64%	39%	53%	66%
BELGIUM	11%	39%	48%	30%	43%	49%	33%	45%	50%
BULGARIA	-13%	9%	68%	10%	19%	68%	15%	23%	69%
CROATIA	-6%	24%	59%	17%	30%	62%	22%	32%	64%
CYPRUS	10%	52%	141%	53%	72%	150%	66%	84%	158%
CZECH REPUBLIC	0%	25%	105%	33%	43%	105%	37%	47%	105%
DENMARK	12%	36%	116%	34%	47%	117%	43%	56%	116%
ESTONIA	-2%	22%	53%	20%	28%	50%	21%	29%	52%
FINLAND	4%	29%	90%	28%	43%	90%	36%	49%	90%
FRANCE	7%	38%	58%	31%	46%	57%	35%	48%	57%
GERMANY	2%	35%	55%	23%	36%	54%	25%	37%	57%
GREECE	-10%	25%	48%	17%	26%	45%	22%	29%	49%
HUNGARY	-2%	22%	68%	23%	33%	67%	26%	35%	68%
IRELAND	10%	64%	109%	52%	72%	110%	58%	77%	110%
ITALY	-1%	33%	52%	25%	34%	52%	30%	36%	54%
LATVIA	-15%	16%	44%	10%	20%	40%	12%	21%	43%
LITHUANIA	-21%	21%	35%	8%	22%	32%	9%	23%	34%
LUXEMBOURG	37%	86%	83%	69%	87%	84%	74%	87%	87%
MALTA	9%	42%	183%	44%	63%	188%	59%	77%	190%
NETHERLANDS	10%	48%	107%	39%	59%	108%	47%	66%	106%
POLAND	-4%	42%	71%	35%	56%	68%	41%	60%	69%
PORTUGAL	-6%	30%	62%	24%	35%	63%	31%	40%	67%
ROMANIA	-11%	22%	52%	17%	27%	51%	21%	29%	53%
SLOVAKIA	0%	49%	93%	41%	64%	91%	46%	67%	91%
SLOVENIA	0%	42%	66%	35%	52%	70%	39%	55%	73%
SPAIN	2%	48%	53%	34%	47%	52%	37%	49%	56%
SWEDEN	16%	29%	83%	31%	39%	85%	38%	45%	83%
TOTAL EU-27	**2%**	**36%**	**61%**	**27%**	**40%**	**61%**	**31%**	**42%**	**62%**
UK	12%	39%	76%	33%	45%	77%	39%	50%	76%
TOTAL EU-28	**3%**	**36%**	**62%**	**28%**	**41%**	**63%**	**32%**	**43%**	**64%**

	POPULATION			PREVALENT STROKE CASES			INCIDENT STROKE CASES		
	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS
ICELAND	17%	68%	73%	55%	76%	73%	60%	78%	74%
ISRAEL	30%	62%	116%	60%	76%	117%	66%	82%	117%
NORWAY	16%	49%	81%	44%	60%	81%	49%	63%	79%
SWITZERLAND	17%	58%	106%	48%	64%	105%	54%	69%	109%
TOTAL EUROPE	**4%**	**37%**	**64%**	**29%**	**42%**	**64%**	**32%**	**44%**	**65%**

Table 13. Changes in population and stroke incidence/prevalence between 2017 and 2035

	POPULATION			PREVALENT STROKE CASES			INCIDENT STROKE CASES		
	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS
AUSTRIA	13%	49%	64%	37%	52%	64%	39%	53%	66%
BELGIUM	11%	39%	48%	30%	43%	49%	33%	45%	50%
BULGARIA	-13%	9%	68%	10%	19%	68%	15%	23%	69%
CROATIA	-6%	24%	59%	17%	30%	62%	22%	32%	64%
CYPRUS	10%	52%	141%	53%	72%	150%	66%	84%	158%
CZECH REPUBLIC	0%	25%	105%	33%	43%	105%	37%	47%	105%
DENMARK	12%	36%	116%	34%	47%	117%	43%	56%	116%
ESTONIA	-2%	22%	53%	20%	28%	50%	21%	29%	52%
FINLAND	4%	29%	90%	28%	43%	90%	36%	49%	90%
FRANCE	7%	38%	58%	31%	46%	57%	35%	48%	57%
GERMANY	2%	35%	55%	23%	36%	54%	25%	37%	57%
GREECE	-10%	25%	48%	17%	26%	45%	22%	29%	49%
HUNGARY	-2%	22%	68%	23%	33%	67%	26%	35%	68%
IRELAND	10%	64%	109%	52%	72%	110%	58%	77%	110%
ITALY	-1%	33%	52%	25%	34%	52%	30%	36%	54%
LATVIA	-15%	16%	44%	10%	20%	40%	12%	21%	43%
LITHUANIA	-21%	21%	35%	8%	22%	32%	9%	23%	34%
LUXEMBOURG	37%	86%	83%	69%	87%	84%	74%	87%	87%
MALTA	9%	42%	183%	44%	63%	188%	59%	77%	190%
NETHERLANDS	10%	48%	107%	39%	59%	108%	47%	66%	106%
POLAND	-4%	42%	71%	35%	56%	68%	41%	60%	69%
PORTUGAL	-6%	30%	62%	24%	35%	63%	31%	40%	67%

	POPULATION			PREVALENT STROKE CASES			INCIDENT STROKE CASES		
	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS
ROMANIA	-11%	22%	52%	17%	27%	51%	21%	29%	53%
SLOVAKIA	0%	49%	93%	41%	64%	91%	46%	67%	91%
SLOVENIA	0%	42%	66%	35%	52%	70%	39%	55%	73%
SPAIN	2%	48%	53%	34%	47%	52%	37%	49%	56%
SWEDEN	16%	29%	83%	31%	39%	85%	38%	45%	83%
TOTAL EU-27	**2%**	**36%**	**61%**	**27%**	**40%**	**61%**	**31%**	**42%**	**62%**
UK	12%	39%	76%	33%	45%	77%	39%	50%	76%
TOTAL EU-28	**3%**	**36%**	**62%**	**28%**	**41%**	**63%**	**32%**	**43%**	**64%**
ICELAND	17%	68%	73%	55%	76%	73%	60%	78%	74%
ISRAEL	30%	62%	116%	60%	76%	117%	66%	82%	117%
NORWAY	16%	49%	81%	44%	60%	81%	49%	63%	79%
SWITZERLAND	17%	58%	106%	48%	64%	105%	54%	69%	109%
TOTAL EUROPE	**4%**	**37%**	**64%**	**29%**	**42%**	**64%**	**32%**	**44%**	**65%**

Table 14. Changes in population and stroke incidence/prevalence between 2017 and 2040

	POPULATION			PREVALENT STROKE CASES			INCIDENT STROKE CASES		
	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS
AUSTRIA	15%	58%	79%	47%	66%	79%	50%	68%	81%
BELGIUM	13%	46%	73%	39%	55%	75%	44%	59%	77%
BULGARIA	-16%	13%	92%	11%	22%	87%	17%	28%	91%
CROATIA	-8%	26%	97%	21%	36%	100%	26%	38%	103%
CYPRUS	12%	63%	189%	67%	90%	204%	85%	108%	218%
CZECH REPUBLIC	0%	35%	140%	38%	52%	141%	43%	57%	143%
DENMARK	14%	42%	133%	41%	56%	135%	51%	67%	138%
ESTONIA	-2%	28%	78%	24%	34%	74%	25%	36%	77%
FINLAND	4%	28%	117%	31%	45%	118%	42%	56%	122%
FRANCE	9%	45%	88%	39%	57%	90%	46%	63%	92%
GERMANY	2%	38%	77%	29%	45%	75%	33%	48%	76%
GREECE	-13%	33%	64%	22%	35%	62%	30%	40%	67%
HUNGARY	-3%	29%	111%	27%	40%	109%	31%	43%	110%
IRELAND	13%	85%	155%	67%	97%	158%	76%	105%	160%
ITALY	-1%	43%	65%	32%	47%	66%	39%	50%	69%

	POPULATION			PREVALENT STROKE CASES			INCIDENT STROKE CASES		
	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS	TOTAL	≥65 YEARS	≥85 YEARS
LATVIA	-18%	20%	60%	13%	25%	56%	15%	27%	59%
LITHUANIA	-25%	23%	51%	10%	28%	48%	11%	29%	51%
LUXEMBOURG	46%	112%	126%	94%	120%	128%	101%	122%	132%
MALTA	10%	46%	228%	51%	70%	241%	69%	88%	252%
NETHERLANDS	11%	54%	137%	46%	71%	139%	58%	81%	142%
POLAND	-6%	48%	133%	42%	66%	131%	50%	71%	133%
PORTUGAL	-7%	39%	85%	29%	46%	87%	40%	53%	92%
ROMANIA	-13%	30%	93%	21%	36%	93%	26%	38%	94%
SLOVAKIA	-1%	60%	162%	50%	78%	160%	56%	81%	160%
SLOVENIA	0%	49%	112%	43%	65%	117%	48%	68%	119%
SPAIN	4%	64%	73%	44%	65%	72%	49%	69%	78%
SWEDEN	20%	35%	94%	37%	46%	96%	46%	55%	99%
TOTAL EU-27	**2%**	**43%**	**86%**	**34%**	**51%**	**89%**	**39%**	**54%**	**90%**
UK	14%	46%	93%	41%	57%	95%	50%	64%	97%
TOTAL EU-28	**3%**	**44%**	**87%**	**34%**	**51%**	**90%**	**40%**	**55%**	**91%**
ICELAND	20%	83%	118%	70%	98%	118%	79%	103%	120%
ISRAEL	40%	85%	181%	78%	102%	182%	88%	111%	181%
NORWAY	19%	62%	109%	56%	75%	111%	62%	81%	111%
SWITZERLAND	19%	68%	134%	59%	80%	132%	68%	87%	140%
TOTAL EUROPE	**4%**	**45%**	**89%**	**35%**	**52%**	**91%**	**41%**	**56%**	**93%**

The projected number of people living with stroke is projected to rise from 9 million in 2017 to:

- 11 million in 2030, an increase of 21%;
- 11.5 million in 2035, an increase of 29%;
- 12 million in 2040, an increase of 35%.

The number of people suffering a stroke for the first time is predicted to increase from 1.5 million in 2017 to:

- 1.7 million in 2030, an increase of 23%;
- 1.9 million in 2035, an increase of 32%;
- 2 million in 2040, an increase of 41%.

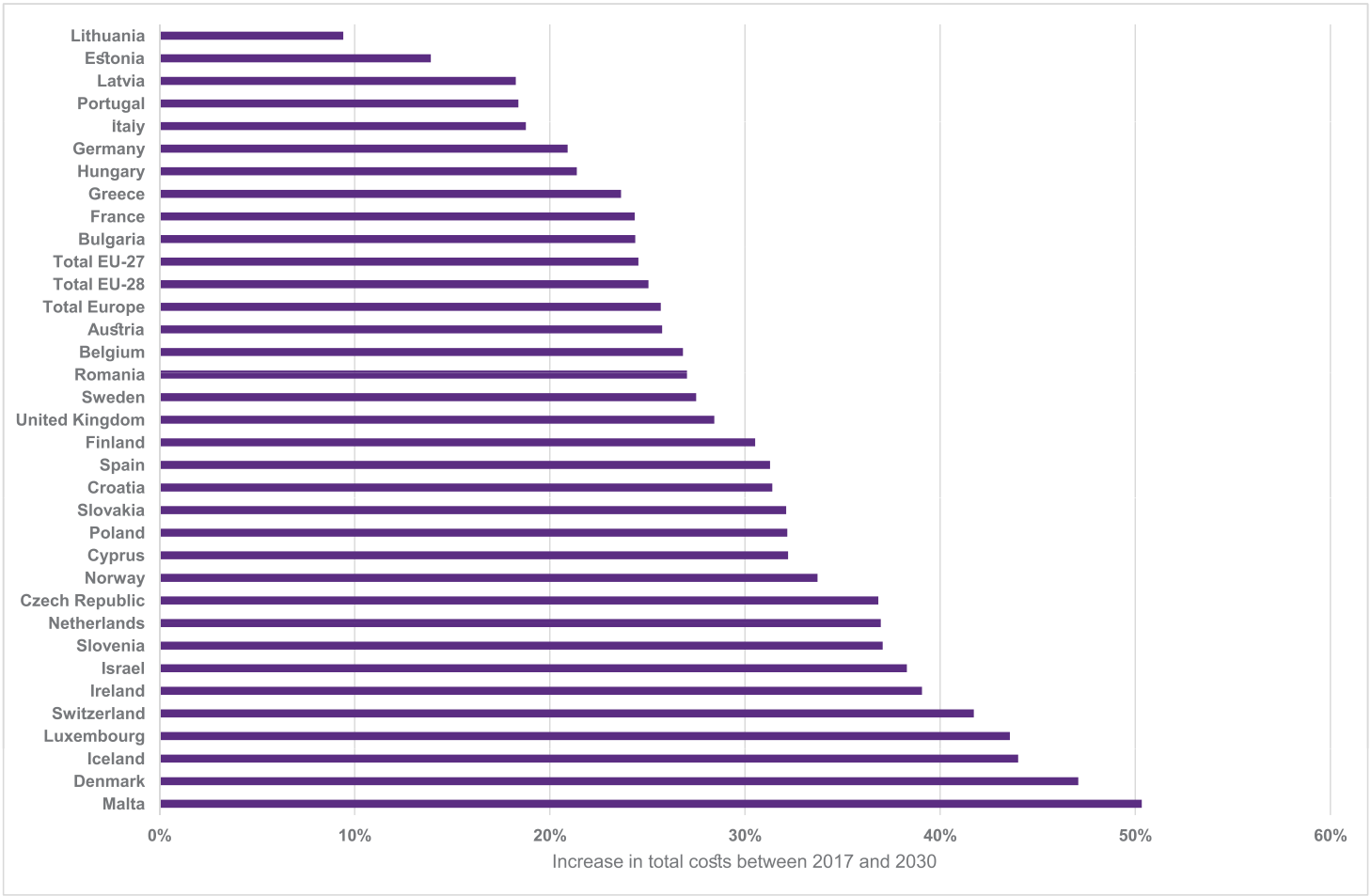
So, how will this rise in the number of people having a stroke and living with stroke in 2030, 2035 and 2040 impact on the cost of stroke?

Between 2017 and 2030 overall costs of stroke are projected to rise by €25 per citizen. This goes up by €33 per citizen from 2017 to 2035 and by €42 per citizen from 2017 to 2040. However, there was great variation between countries, with Finland experiencing the biggest increase in costs per citizen in all three years and Cyprus showing the lowest increase in 2035 and 2040.

COSTS OF STROKE IN 2030

Stroke is projected to cost the 32 European economies under study a total of €75 billion in 2030 with healthcare costs projected to be €33 billion in 2030, ranging from a lower value of €24 billion to a higher value of €45 billion. Figure 4 shows the increase in total stroke costs between 2017 and 2030.

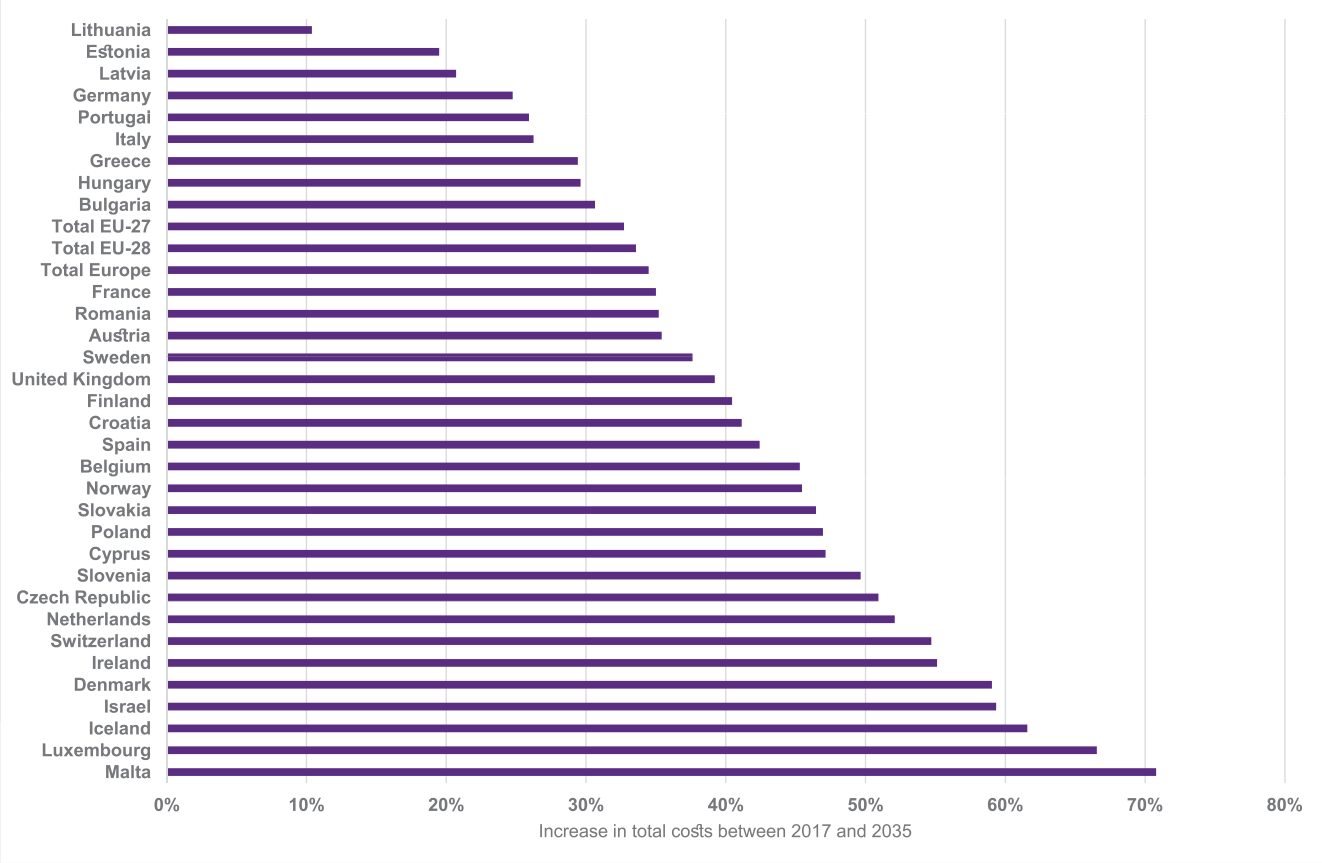
Figure 4. Increases in total stroke costs between 2017 and 2030



COSTS OF STROKE IN 2035

Stroke is projected to cost the 32 European economies under study a total of €80 billion in 2035 with healthcare costs projected to be €35 billion, ranging from a lower value of €26 billion to a higher value of €48 billion. This graph shows the increase in total stroke costs between 2017 and 2035.

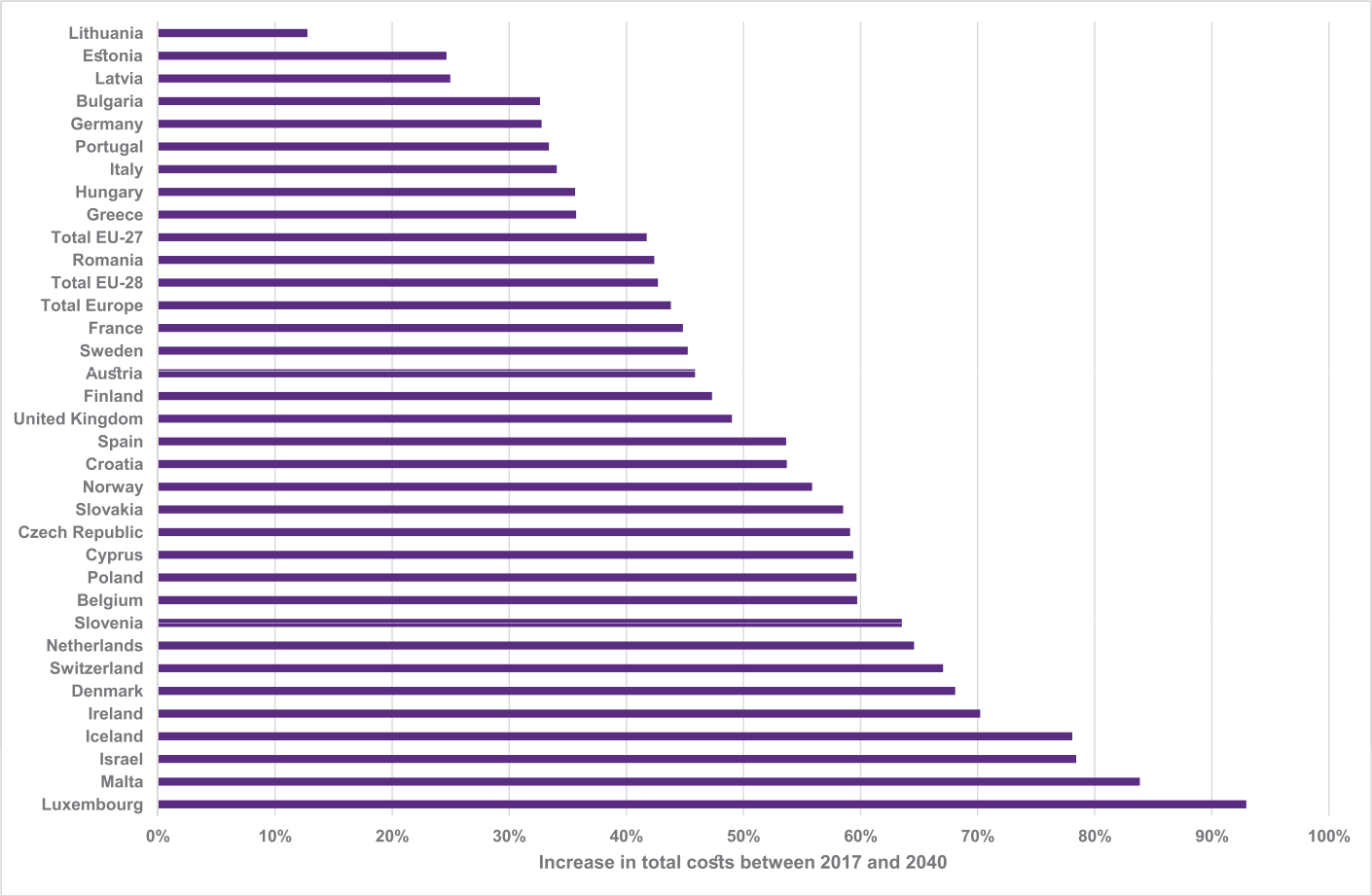
Figure 5. Increases in total stroke costs between 2017 and 2035



COSTS OF STROKE IN 2040

Stroke is projected to cost the 32 European economies under study a total of €86 billion in 2040 and healthcare systems costs are projected to be €37 billion in 2040, €27 billion to a higher value of €51 billion. Figure 6 shows the increase in total stroke costs between 2017 and 2040.

Figure 6. Increases in total stroke costs between 2017 and 2040



INVESTING IN STROKE CARE: ECONOMIC IMPACT

In this chapter we look at what impact three different interventions in stroke care and prevention would have on the economic burden of stroke. The numbers of people having a stroke, the severity of their stroke, and their recovery from stroke all influence the overall economic impact of stroke.

- The first intervention is tackling atrial fibrillation (uneven heartbeat) through the use of warfarin, or new oral anti-coagulation drugs instead of aspirin;
- The second is rolling out routine use of thrombectomy (the mechanical removal of blood clots in ischaemic stroke);
- The third is provision of rehabilitation services and support as outlined in stroke guidelines.

For each of these three interventions the study makes projections of costs over a five-year period, starting from the baseline of 2017. In order to do so, we have used the concept of QALYs to determine the cost effectiveness of the interventions in addition to comparing the number of cases, healthcare costs, informal care costs and productivity losses associated with implementing the intervention versus current practice / standard care.

QALYs have been used in the UK by the National Institute for Health and Care Excellence (NICE), which provides national guidance and advice to improve health and social care and makes decisions about what interventions are cost effective and should be routinely available. NICE defines QALYs as: "A measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality of life. One QALY is equal to one year of life in perfect health. QALYs are calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighting each year with a quality-of-life score (on a 0 to 1 scale). It is often measured in terms of the person's ability to carry out the activities of daily life, and freedom from pain and mental disturbance. NICE also determine a financial threshold of €22,727 per QALY gained (£20,000,[210] exchange rate: €1 = £0.88) above which an intervention is deemed to not be cost effective. The WHO also provides guidance on cost effectiveness.

The model we used to determine the costs of these three interventions simulated costs, survival and (quality adjusted) life expectancy following the onset of stroke. It is based on six levels of stroke -related disability at three months following the stroke using the modified Rankin Scale (mRS).

Following a stroke, patients might die or, at three months, have:

0	No symptoms
1	No significant disability (able to carry out all usual activities despite some symptoms)
2	Slight disability (able to look after own affairs without assistance, but unable to carry out all previous activities
3	Moderate disability (requires some help, but able to walk unassisted)
4	Moderate severe disability (unable to attend to own bodily needs without assistance and unable to walk unassisted)
5	Severe disability (requiring constant nursing care and attention, bedridden and incontinent)

Anticoagulant therapy was modelled via a potential reduction in the incidence of ischaemic stroke and a potential increase in major bleeding events in the atrial fibrillation population, compared to current practice. Both mechanical thrombectomy and community-based rehabilitation were modelled via a potential change in severity of stroke-induced disability and death at three months after stroke onset compared to standard care.

We used evidence from the Oxford Vascular Study (OXVASC),[211 212] to assess survival at three months and up to five years after stroke. Published Cox-regressions,[211 212] adjusted for by age, gender, and three month mRS score after stroke onset were used. We assumed that all cause-mortality after stroke given a particular mRS score would be the same across the 32 countries conditional on age and gender, but mortality differed across countries given each country's differing age and gender population.

Quality of life as measured using the Euroqol 5 Dimensions 3 Levels (EQ-5D-3L) (measuring mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) was obtained from OXVASC.[213] In OXVASC, EQ-5D responses were obtained from stroke patients at 1 to 3, 6, 12, 24 and 60 months, and converted into utility estimates using the UK tariff.[214] For this study, we used published regression analyses evaluating utility adjusting for mRS scores age and gender.[213] As with survival, we assumed that quality of life, given a particular mRS score, would not vary between countries. However, by including age and gender as part of the regression analysis, utility was allowed to differ between countries due to the differing age and gender population of each country cohort.

Healthcare resource use after stroke was derived from OXVASC.[211 212] As part of OXVASC, healthcare resource use was obtained from stroke onset until five years after stroke or death, whichever occurred first. Resource use collected included: inpatient and day case stays in hospital; outpatient visits; and A&E visits. Mean resource use by mRS score in OXVASC is reported in Table 15.

Table 15. Mean resource (S.D.) use by 3-month mRS in OXVASC

	MRS 0	MRS 1	MRS 2	MRS 3	MRS 4	MRS 5
			LENGTH OF STAY, DAYS			
STROKE ONSET TO 90 DAYS	1.30 (3.04)	2.68 (6.63)	6.37 (10.8)	21.3 (27.3)	53.4 (33.6)	69.6 (27.7)
90 DAYS TO 1 YEAR	0.91 (3.71)	1.51 (6.69)	3.94 (15.4)	13.2 (32.6)	32.1 (47.0)	48.7 (58.2)
1 YEAR TO 2 YEARS	2.44 (14.3)	2.74 (12.7)	4.46 (19.0)	8.91 (27.0)	5.78 (14.8)	4.92 (15.2)
2 YEARS TO 3 YEARS	2.27 (10.2)	2.67 (16.5)	5.12 (19.8)	12.2 (29.6)	7.31 (25.7)	3.78 (11.5)
3 YEARS TO 4 YEARS	1.09 (4.64)	2.41 (9.74)	5.62 (18.8)	9.88 (23.7)	6.4 (18.4)	1.69 (4.71)
4 YEARS TO 5 YEARS	2.03 (9.51)	3.57 (14.7)	4.13 (17.6)	10.3 (26.5)	6.30 (18.5)	1.25 (4.84)
			OUTPATIENT VISITS			
STROKE ONSET TO 90 DAYS	3.35 (2.12)	3.06 (2.15)	2.96 (0.26)	2.48 (2.12)	1.39 (1.68)	1.35 (2.10)
90 DAYS TO 1 YEAR	2.02 (2.24)	2.60 (3.59)	3.18 (4.57)	2.60 (3.22)	3.57 (7.17)	1.67 (4.31)
1 YEAR TO 2 YEARS	2.17 (2.88)	2.87 (4.56)	3.12 (5.40)	2.47 (3.03)	2.88 (4.55)	1.85 (3.19)
2 YEARS TO 3 YEARS	1.52 (2.16)	2.28 (3.94)	2.56 (5.13)	2.22 (2.86)	2.10 (3.64)	1.78 (3.86)
3 YEARS TO 4 YEARS	1.96 (3.59)	2.10 (4.39)	2.43 (5.04)	2.31 (3.33)	1.78 (3.33)	1.19 (2.95)
4 YEARS TO 5 YEARS	1.90 (2.98)	2.53 (6.23)	2.54 (5.42)	2.83 (6.11)	1.68 (3.42)	0.96 (1.50)
			A&E VISITS			
STROKE ONSET TO 90 DAYS	0.36 (0.52)	0.37 (0.57)	0.48 (0.62)	0.57 (0.66)	0.80 (0.71)	0.74 (0.59)

	MRS 0	MRS 1	MRS 2	MRS 3	MRS 4	MRS 5
	LENGTH OF STAY, DAYS					
90 DAYS TO 1 YEAR	0.18 (0.47)	0.18 (0.52)	0.26 (0.68)	0.44 (0.89)	0.34 (0.70)	0.32 (0.76)
1 YEAR TO 2 YEARS	0.20 (0.57)	0.19 (0.57)	0.27 (0.63)	0.39 (0.76)	0.35 (0.64)	0.30 (0.61)
2 YEARS TO 3 YEARS	0.17 (0.62)	0.15 (0.47)	0.34 (0.84)	0.55 (1.03)	0.44 (0.87)	0.30 (0.74)
3 YEARS TO 4 YEARS	0.24 (0.84)	0.21 (0.62)	0.32 (0.71)	0.65 (1.46)	0.29 (0.67)	0.31 (0.56)
4 YEARS TO 5 YEARS	0.22 (0.90)	0.22 (0.83)	0.25 (0.57)	0.49 (0.91)	0.30 (0.66)	0.21 (0.63)

For each type of resource use, we used regression analysis (a statistical method that allows examination of the relationship between two or more variables) evaluating resource use adjusted for by three-month mRS score, age and gender. In addition to resource use varying by the age and gender structure of the stroke population in each country, we also adjusted resource estimates from OXVASC using country-specific resource use. So, for example, with length of stay for stroke in the UK being 18 days and that in Austria being 19,[3] for the Austrian version of the model we adjusted the number of days in hospital derived from OXVASC by a factor of 1.08 reflecting longer lengths of stay in Austria. For outpatient and A&E visits, we adjusted OXVASC estimates using the division of per capita visits due to stroke in the UK over per capita stroke-related visits in the country under study. Table 16 reports the weights used to adjust resource use for each country in the first three months following stroke.

Table 16. Country-specific resource use weights for resource use within three months from stroke onset. UK = 1

	DAYS IN HOSPITAL	OUTPATIENT VISITS	A&E VISITS	DAYS IN NURSING HOME
AUSTRIA	1.078	3.107	1.651	0.911
BELGIUM	0.803	0.884	0.529	4.070
BULGARIA	0.293	0.618	0.363	0.570
CROATIA	0.661	1.097	0.412	0.209
CYPRUS	0.511	4.927	4.849	0.451
CZECH REPUBLIC	1.244	4.725	0.234	0.911
DENMARK	0.314	0.636	0.639	1.199
ESTONIA	0.835	2.320	1.807	0.552

	DAYS IN HOSPITAL	OUTPATIENT VISITS	A&E VISITS	DAYS IN NURSING HOME
FINLAND	1.154	0.840	0.701	0.868
FRANCE	0.557	0.767	1.382	1.405
GERMANY	0.922	2.712	0.204	0.675
GREECE	0.524	0.280	1.546	0.530
HUNGARY	0.787	5.972	0.281	0.534
ICELAND	0.890	2.889	1.197	1.322
IRELAND	0.934	0.876	2.018	0.407
ISRAEL	0.620	2.312	3.015	0.453
ITALY	0.814	1.600	1.397	0.606
LATVIA	0.568	0.795	0.540	0.516
LITHUANIA	0.637	1.663	0.694	1.155
LUXEMBOURG	0.886	2.252	0.924	2.083
MALTA	1.270	0.666	0.992	0.364
NETHERLANDS	0.494	1.680	0.402	0.758
NORWAY	0.630	0.960	0.841	1.062
POLAND	0.596	1.824	0.705	0.246
PORTUGAL	0.694	1.229	3.267	0.444
ROMANIA	0.482	2.363	0.140	0.857
SLOVAKIA	0.585	5.990	1.119	0.662
SLOVENIA	0.846	1.353	0.712	0.622
SPAIN	0.523	1.232	2.373	0.461
SWEDEN	0.551	1.066	1.142	1.117
SWITZERLAND	0.880	0.507	0.552	1.738

Risk of institutionalisation in a nursing or residential care was derived from OXVASC.[211 212] We used a published Cox-regression analysis to identify the risk of institutionalisation over a five-year period controlling for age, gender and three month mRS score,[211 212] and converted these into days in a nursing/residential home. As with healthcare resource use, we adjusted OXVASC long-term institutionalisation days using country-specific resource use. For this we divided the per capita rate of institutionalisation in those aged 65 years or over in the UK by the same per capita rate in each of the 32 countries (Table 16).

In Chapter 2, we evaluated the annual hours of care received by those stroke survivors who survived and were severely hampered in their daily activities. As a result, in the model, for those stroke survivors who at three

months after stroke onset had an mRS score of 4 or 5, and for half of those with a mRS score of 3, we applied the country-, age- and gender- specific annual hours of care calculated.

As the stroke extrapolation model predicted death over a maximum period of five years after stroke onset, we estimated for those under 65 years of age the productivity losses accrued due to early death. Mortality losses were valued using the country- and gender-specific average annual earnings[3 148], taking into account country-, age- and gender-specific employment rates as estimated in Chapter 2.[3 147]

We also included morbidity losses (i.e. costs due to temporary or permanent absence from work) in the model. We assumed that for patients surviving stroke and who remained non-disabled (i.e. mRS≤2), their absence from work would be temporary. Hence, we used the country-specific average days off work due to stroke as estimated in Chapter 2. For those patients disabled after stroke (i.e. mRS>2), we assumed that their absence from work would be permanent. The product of working days lost and mean daily earnings provided the morbidity losses.[3] We used the "friction period" approach, as absent workers are likely to be replaced, whereby only the first 90 days of work absence were counted.[201]

We used the results from our research outlined in Chapter 2 to account for variations between the 32 countries. This was accounted for by using country-specific: age/gender distributions, atrial fibrillation prevalence and stroke incidence rates, unit costs, health and social care resource use, probability of receiving as well as amount of informal care, employment rates and productivity losses. This allowed the models to generate results for each of the 32 countries under analysis.

INTERVENTIONS TACKLING ATRIAL FIBRILLATION

Atrial fibrillation is a major risk factor for stroke. Treatment with anticoagulant drugs reduces the risk of blood clots forming. These blood clots can travel through the vascular system to the brain, causing a blockage - an ischaemic stroke. There is evidence that a large proportion of people with atrial fibrillation who have an ischaemic stroke are not being treated with anticoagulant drugs.

A range of anticoagulants are currently licensed and used throughout Europe. These include warfarin and new oral anticoagulants (NOACs: apixaban, dabigatran, edoxaban and rivaroxaban). In this study, we evaluated the impact of routine use of anticoagulants in atrial fibrillation patients.

- Warfarin has been available since the 1950s[215] and its costs are low, therefore potentially decreasing the barriers to rapid uptake across Europe. 28 tablets of warfarin 1 mg cost €0.48.[216]

- NOACs, on the other hand, are more costly,[216] but have broadly shown to be more effective at reducing the risk of ischaemic stroke, major bleeding events and all-cause mortality, than warfarin.[217]

Anticoagulants are not suitable for all people with atrial fibrillation because the risk of bleeding, compared to just giving aspirin, can be higher. A scoring system to assess the risk of major bleeding for people using anticoagulants has been developed, called HAS-BLED.

In this study, we assumed that patients with a HAS-BLED score larger than 2 would not be eligible to receive any anticoagulant, and thus would continue to be treated with aspirin.[218]

Based on population-based evidence, we assumed this to be 15% of the atrial fibrillation population, irrespective of age.[205] Due to very low prevalence of atrial fibrillation in the under 30s,[1] we restricted our target population to those with atrial fibrillation aged ≥ 30 years. So routine use of warfarin would cover 85% of people with atrial fibrillation.

We defined "current practice" assuming that an average 25% of the eligible atrial fibrillation-population would be already on warfarin (this proportion varied with age),[205] and that the rest would be on daily antiplatelet therapy with aspirin 150mg.[205] We then compared routine use of warfarin and NOACs to current practice (Figures 7 and 8).

For NOACs, we assumed that 15% of the population would remain on antiplatelet therapy (aspirin) due to high HAS-BLED scores, 25% would still be taking warfarin because they are perceived to be at risk of missing dosages of the medication. If a dose of warfarin is missed, re-starting treatment with warfarin would still be effective. In contrast, NOACs are shorter-acting than warfarin, so if a dose of NOAC is missed, patients can quickly lose the anticoagulation effect and increase their risk of a blood clot.[219] The remaining 60% of patients would receive a NOAC. Given that there are currently four classes of NOACs, we modelled that of the 60% of patients receiving a NOAC, 25% of them would receive apixaban (5mg twice daily), 25% dibagatran (150mg twice daily), 25% edoxaban (60mg once daily), and the remaining 25% would receive rivaroxaban (20mg once daily). We also modelled the use of each individual NOAC to current practice. For results of these individual analyses please visit www.safestroke.eu/economic-impact-of-stroke/

The dose of warfarin will vary between individuals depending on how long it takes blood to form a blood clot (known as the international normalised ratio or INR). We followed general guidance and assumed that patients would be on a daily dosage of 10mg during the first day of treatment, and 2mg thereafter.[216] For NOACs, we assumed that patients would receive dosages as recommended in the British National Formulary.[216]

Figure 7. Comparison of routine use of warfarin with current practice

Figure 8. Comparison of routine use of NOACs with current practice

The table below (Table 17) shows that there are almost seven million people with atrial fibrillation in the 32 countries under study, with almost six million of them having the potential to benefit from anticoagulation therapy. Country, age, and gender-specific numbers of cases with atrial fibrillation were derived from the Global Burden of Disease study.[1]

Table 17. Number of people with atrial fibrillation

	AF PATIENTS	AF PATIENTS ELIGIBLE FOR ANTICOAGULANT THERAPY
AUSTRIA	142,603	121,212
BELGIUM	137,448	116,831
BULGARIA	88,079	74,867
CROATIA	43,670	37,119
CYPRUS	10,161	8,636
CZECH REPUBLIC	135,868	115,488
DENMARK	74,597	63,408
ESTONIA	16,619	14,126
FINLAND	87,422	74,309
FRANCE	820,312	697,265
GERMANY	1,201,402	1,021,191
GREECE	139,047	118,190
HUNGARY	125,060	106,301
IRELAND	42,228	35,893
ITALY	847,845	720,668
LATVIA	26,232	22,297
LITHUANIA	36,884	31,351
LUXEMBOURG	7,582	6,445
MALTA	5,583	4,745
NETHERLANDS	197,572	167,936
POLAND	495,314	421,017
PORTUGAL	102,488	87,115
ROMANIA	196,967	167,422
SLOVAKIA	61,154	51,981
SLOVENIA	31,271	26,580
SPAIN	588,301	500,056
SWEDEN	174,243	148,107
TOTAL EU-27	**5,835,950**	**4,960,557**
UK	934,851	794,623

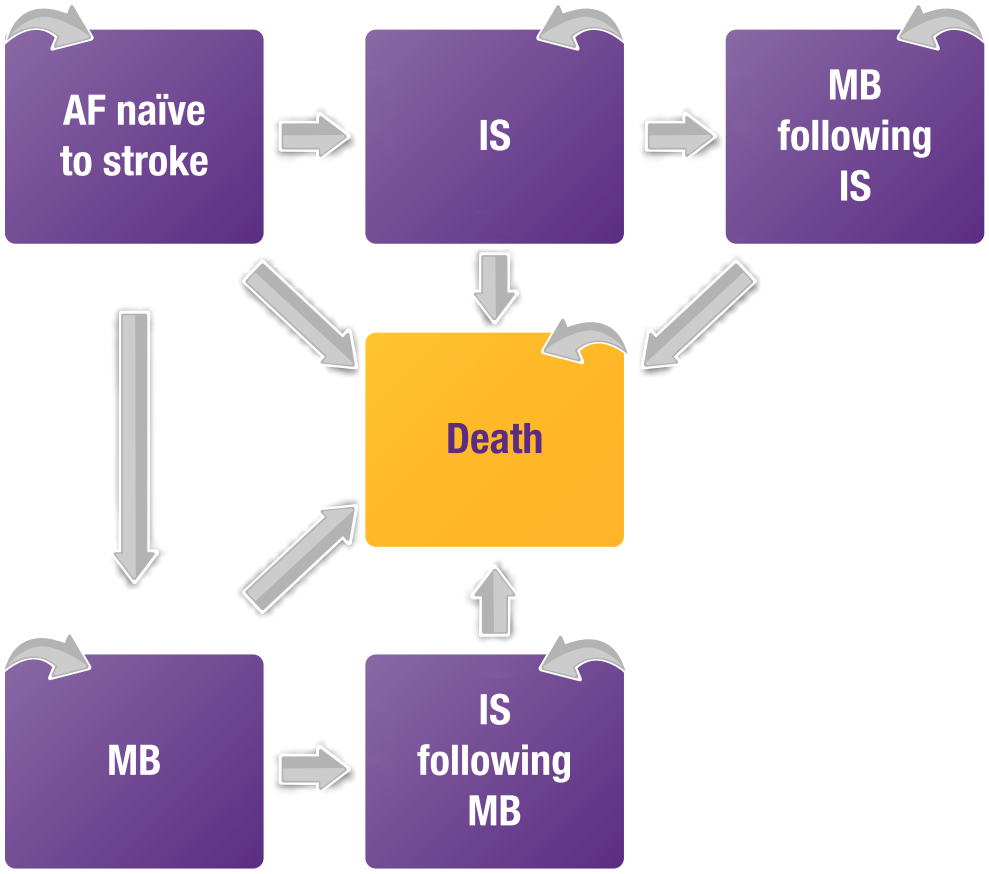
	AF PATIENTS	AF PATIENTS ELIGIBLE FOR ANTICOAGULANT THERAPY
TOTAL EU-28	**6,770,801**	**5,755,181**
ICELAND	3,399	2,889
ISRAEL	61,750	52,488
NORWAY	69,017	58,665
SWITZERLAND	80,875	68,743
TOTAL 32 COUNTRIES	**6,985,842**	**5,937,966**

To generate a picture of the economic costs of treating or not treating atrial fibrillation with either warfarin or a NOAC, we used the following model following a one-year cycle:

- someone with atrial fibrillation (who has not already had a stroke) could have an ischaemic stroke;
- they could have a major bleed requiring hospital treatment;
- they could die as a result of both.

The modelling approach is summarised in Figure 9 below.

Figure 9. Anticoagulant therapy model structure



For people who have an ischaemic stroke, their condition was further divided in to six levels, depending on the severity of the long-term impact of the stroke (measured at three months using the mRS which assesses the level of disability that someone is left with after stroke). During the one-year cycle, there may be no change; or they could have a major bleed; or they could die.

For those who were already taking warfarin at the time of their ischaemic stroke, we assumed they would continue to take it unless or until they then had a major bleeding event.

People with non-fatal major bleeds may either recover completely or be disabled. They could also have an ischaemic stroke and they could die. We assumed that those on warfarin would stop taking it following a major bleed and be given aspirin instead.

We based our assessment of the risk of ischaemic stroke in the atrial fibrillation population by using the Birmingham Atrial Fibrillation Treatment of the Aged Study (BAFTA) trial[220] with further analysis from the OXVASC,[205] providing probabilities of different outcomes flowing ischaemic stroke. The risks of ischaemic stroke for people on warfarin/ NOACs were obtained by multiplying the absolute risk of ischaemic stroke under aspirin[220] by the relative effectiveness of warfarin / NOACs obtained from a meta-analysis.[217]

Stroke survivors were still at risk of major bleeding and death due to bleeding. We assumed that these warfarin-related bleeding risks would be the same as those estimated for the atrial fibrillation population naïve to stroke. Age-dependent risk of major bleeding, including disabling, non-disabling and fatal, in patients on antiplatelet therapy was obtained from the literature.[221] The risk of bleeding on warfarin / NOACs were obtained by multiplying the absolute risk of major bleeding whilst on aspirin by the relative bleeding hazard rate on warfarin / NOACs.[217]

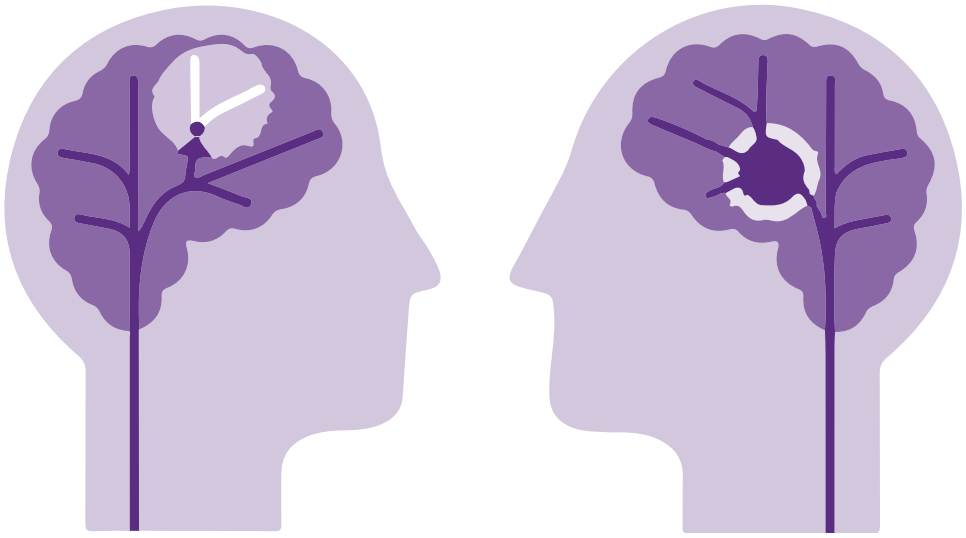
The risk of death due to major bleeding was obtained from OXVASC.[221] We assumed that the risk of mortality following a major non-disabling bleed would correspond to that of a stroke survivor with a mRS of 1. We further assumed that the risk of mortality following a major disabling bleeding event would correspond to that of a stroke survivor with a mRS of 4. Risk of all cause-death for atrial fibrillation patients naïve to stroke, under current practice, was obtained from country-specific life tables,[222] taking into account the additional risk of being in an atrial fibrillation state[223] and removing the risk of stroke from all cause-mortality.[3] The risks of all cause-death for atrial fibrillation patients naïve to stroke on warfarin / NOACs were obtained by multiplying the absolute risk under aspirin by the relative effectiveness of warfarin / NOACs obtained from a meta-analysis.[217]

We assumed that the only costs patients incurred were those covering the medications. Using the daily costs of aspirin, warfarin and NOAC from the

British National Formulary, our analysis is based upon the following:

- aspirin (1250mg) costs €0.07 per day. A packet of 75mg tablets cost €0.794, therefore daily cost was €0.94 / 28 x 2 = €0.07;
- warfarin costs €0.04 per day. A packet of 28 tablets with 1mg cost €0.62, therefore daily cost was €0.62 / 28 x 2 = €0.04 (plus an initial cost for the higher first does on day on of €0.05);
- apixaban (5 mg twice daily) costs €2.16 per day: a packet of 56 tablets with 5mg costs €60.45 therefore, €60.45 / 56 x 2 = €2.16;
- dabigatran (150 mg twice daily) costs €1.93 per day: a packet of 60 tablets with 150mg costs €57.95 therefore, €57.95 / 60 x 2 = €1.93;
- edoxaban (60 mg once daily) costs €1.99 per day: a packet of 28 tablets with 60mg costs €55.68 therefore, €55.68/ 28 = €1.99;
- rivaroxaban (20 mg once daily) costs €2.04 per day: a packet of 28 tablets with 20mg costs €57.27 therefore, €57.27 / 28 = €2.04.

Resource use after major bleeding was obtained from OXVASC in a study assessing the bleeding risks, outcome and costs after bleeding and major bleeding.[221] With resource use to varying across countries, we applied country-specific weights separately for the first three months from onset and from three months to five years.



In terms of productivity losses, we included the costs of:

- foregone earnings due to early mortality due to stroke or major bleeding;
- early death from all causes for people with atrial fibrillation who had not had a stroke;
- temporary or permanent absence from work. We assumed that for patients surviving an ischaemic stroke or major bleed and who remained non-disabled (i.e. mRS<2), the absence from work would be temporary. For those patients disabled after stroke or major bleeding (i.e. mRS>2), we assumed that their absence from work would be permanent.

We assessed the difference in costs and QALYs for each intervention compared to aspirin. Where the intervention was more costly but also more effective, or was less costly but less effective, we evaluated the "incremental cost-effectiveness ratio" (ICER), estimated by dividing the difference in costs by the difference in QALYs.

We used two thresholds in order to judge the cost-effectiveness of the interventions being evaluated:

- The cost-effectiveness threshold decided by NICE of €22,727 per QALY gained (£20,000,[210] exchange rate: €1 = £0.88);
- Using the country's per capita GDP for 2017, as recommended by the WHO.[3 34]

RESULTS FOR WARFARIN

When warfarin is routinely used, the average QALYs over five years were 2.21 per patient treated compared with 2.19 QALYs under current practice. That is a QALY gain of 0.019 per atrial fibrillation patient. As a result, at the population level, the total QALYs across the 32 European countries were 15.4 million with routine use of warfarin and 15.3 million with current practice, an increase of 0.14 million QALYs (Table 18). For all countries, routine use of warfarin generated additional QALYs, relative to current practice.

Table 18. QALYs gained at the population level

	ROUTINE USE OF WARFARIN	CURRENT PRACTICE	DIFFERENCE
AUSTRIA	322,456	317,547	4,909
BELGIUM	304,240	299,159	5,081
BULGARIA	198,584	195,557	3,027
CROATIA	99,731	98,250	1,481
CYPRUS	23,060	22,726	334
CZECH REPUBLIC	315,577	311,210	4,367
DENMARK	168,952	166,375	2,577
ESTONIA	37,327	36,733	593
FINLAND	197,732	194,715	3,017
FRANCE	1,817,891	1,787,222	30,668
GERMANY	2,635,795	2,591,201	44,594
GREECE	301,481	296,145	5,335
HUNGARY	279,399	274,937	4,462
IRELAND	97,478	96,106	1,371
ITALY	1,855,553	1,823,832	31,721
LATVIA	59,263	58,335	929
LITHUANIA	82,094	80,761	1,333
LUXEMBOURG	17,136	16,867	269
MALTA	12,640	12,453	187
NETHERLANDS	448,841	442,127	6,714
POLAND	1,136,397	1,119,657	16,740
PORTUGAL	225,284	221,484	3,800
ROMANIA	439,295	432,131	7,163
SLOVAKIA	143,097	141,157	1,940

	ROUTINE USE OF WARFARIN	CURRENT PRACTICE	DIFFERENCE
SLOVENIA	72,262	71,241	1,021
SPAIN	1,294,199	1,271,932	22,267
SWEDEN	393,035	387,020	6,015
TOTAL EU-27	**12,888,172**	**12,762,893**	**125,279**
UK	2,106,291	2,073,206	33,085
TOTAL EU-28	**14,977,827**	**14,835,975**	**141,852**
ICELAND	7,809	7,698	112
ISRAEL	140,909	138,784	2,125
NORWAY	151,415	148,869	2,547
SWITZERLAND	182,653	179,852	2,800
TOTAL 32 COUNTRIES	**15,447,133**	**15,311,120**	**136,014**

On average, across the 32 countries under study, the average cost of therapy was:

- €51.4 for those treated with routine use of warfarin;
- €64.9 for patients receiving current therapy (aspirin only).

At the population level, this translated to costs of €359 million as opposed to €453 million with current practice (Table 19). Subsequent health and social care costs were also lower for routine use of warfarin than the comparator (€8.7 billion vs. €14.8 billion, respectively), even though costs associated with treatment of major bleeding were higher in the routine warfarin scenario.

Table 19. Population-level health and social care costs for patients routinely receiving warfarin and current practice, € thousands

	ROUTINE USE OF WARFARIN							CURRENT PRACTICE						
			SUBSEQUENT COSTS							SUBSEQUENT COSTS				
	THERAPY	BLEEDING	INPATIENT	OUTPATIENT	A&E	SOCIAL CARE	TOTAL COSTS	THERAPY	BLEEDING	INPATIENT	OUTPATIENT	A&E	SOCIAL CARE	TOTAL COSTS
AUSTRIA	7,546	11,345	141,113	2,302	877	743	163,926	9,424	9,396	247,703	4,025	1,539	1,306	273,394
BELGIUM	7,075	12,922	167,921	1,017	216	54,800	243,951	8,839	10,650	295,782	1,791	382	97,780	415,224
BULGARIA	4,554	271	8,265	164	26	689	13,968	5,670	225	14,484	286	46	1,220	21,930
CROATIA	2,283	378	5,578	96	139	933	9,406	2,841	314	9,775	169	243	1,653	14,995
CYPRUS	526	91	855	139	57	1,026	2,695	656	76	1,498	244	101	1,820	4,393
CZECH REPUBLIC	7,219	4,639	56,095	1,063	61	4,068	73,145	8,984	3,866	97,984	1,851	107	7,183	119,975
DENMARK	3,923	4,426	76,502	495	188	39,175	124,709	4,902	3,663	134,174	866	330	69,486	213,422
ESTONIA	861	432	5,160	199	41	1,291	7,985	1,072	359	9,050	348	72	2,293	13,193
FINLAND	4,606	9,185	113,264	3,529	718	47,182	178,483	5,762	7,592	198,864	6,185	1,261	83,861	303,525
FRANCE	42,902	40,978	610,905	12,551	2,857	182,559	892,753	53,766	33,674	1,077,758	22,128	5,038	326,167	1,518,530
GERMANY	61,413	120,734	2,210,692	35,246	767	424,889	2,853,740	76,800	99,565	3,889,376	61,962	1,350	756,746	4,885,798
GREECE	7,069	4,452	92,438	303	483	10,089	114,833	8,857	3,657	163,073	534	851	18,012	194,984
HUNGARY	6,373	1,787	29,091	371	95	10,095	47,812	7,924	1,484	50,895	645	166	17,865	78,980
IRELAND	2,236	3,041	30,128	552	521	10,561	47,039	2,789	2,525	52,841	966	914	18,758	78,793
ITALY	43,786	58,409	712,295	12,662	8,412	180,946	1,016,511	54,902	48,036	1,253,872	22,268	14,819	322,726	1,716,623
LATVIA	1,368	171	2,532	101	15	568	4,754	1,700	142	4,436	176	26	1,006	7,487
LITHUANIA	1,890	327	6,011	172	15	2,072	10,487	2,348	272	10,553	301	26	3,681	17,181
LUXEMBOURG	399	949	12,146	160	15	4,863	18,533	499	784	21,375	282	26	8,664	31,629
MALTA	294	332	3,704	25	14	996	5,365	368	275	6,499	43	25	1,769	8,979
NETHERLANDS	10,373	16,558	199,656	5,569	358	96,996	329,511	12,958	13,711	350,443	9,758	629	172,369	559,869
POLAND	25,984	6,285	88,471	4,722	193	34,621	160,275	32,322	5,224	155,180	8,257	338	61,460	262,780
PORTUGAL	5,277	2,814	31,395	997	908	2,757	44,149	6,607	2,316	55,285	1,756	1,599	4,920	72,484
ROMANIA	10,106	1,158	21,896	681	51	8,345	42,236	12,587	959	38,419	1,192	89	14,814	68,060
SLOVAKIA	3,256	751	11,342	896	54	3,651	19,950	4,041	628	19,835	1,560	95	6,453	32,611
SLOVENIA	1,676	1,010	12,611	169	54	4,886	20,406	2,092	838	22,126	296	95	8,674	34,122
SPAIN	30,474	27,982	376,264	11,936	7,858	74,833	529,346	38,155	22,992	663,896	21,058	13,871	133,787	893,759
SWEDEN	9,173	10,808	142,805	7,982	2,039	99,212	272,019	11,487	8,932	250,613	13,967	3,577	176,202	464,778
TOTAL EU-27	**299,832**	**336,407**	**4,904,754**	**130,431**	**24,825**	**1,414,448**	**7,110,697**	**378,195**	**279,120**	**8,671,383**	**230,051**	**43,890**	**2,528,095**	**12,130,736**
UK	48,916	74,051	795,540	14,459	5,010	273,290	1,211,265	61,111	61,184	1,397,868	25,373	8,819	486,455	2,040,810
TOTAL EU-28	**348,237**	**395,388**	**5,691,995**	**156,145**	**29,749**	**1,692,353**	**8,313,866**	**439,302**	**328,168**	**10,063,412**	**275,392**	**52,600**	**3,024,743**	**14,183,617**
ICELAND	180	457	4,642	122	28	1,995	7,424	225	378	8,160	214	49	3,553	12,579
ISRAEL	3,254	2,277	17,135	374	690	5,380	29,109	4,062	1,884	30,098	652	1,209	9,581	47,486
NORWAY	3,555	7,631	119,839	1,033	269	73,933	206,259	4,458	6,278	210,836	1,812	473	131,701	355,558
SWITZERLAND	4,254	10,498	153,237	314	206	67,104	235,613	5,322	8,672	269,598	553	363	119,509	404,017
TOTAL 32 COUNTRIES	**359,064**	**417,167**	**5,877,734**	**152,326**	**30,981**	**1,831,770**	**8,669,042**	**453,367**	**346,438**	**10,396,422**	**268,728**	**54,796**	**3,274,972**	**14,794,723**

Therefore, routinely treating eligible atrial fibrillation-patients with warfarin would generate cost-savings to the health and social care budget across Europe of €6.1 billion.

Routine use of warfarin generated cost savings in all of the 32 countries under study, relative to current practice. The countries where the biggest savings, in terms of health and social care costs if warfarin were to be routinely administered, were Germany, with five-year savings of €2 billion, followed by the UK (savings of €842 million), followed by Italy (savings of €710 million).

When we include the overall societal costs, savings of around €7 billion could be made over five years in the 32 countries under study (Table 20).

Table 20. Societal costs under routine use of warfarin vs current practice, € thousands

	ROUTINE USE OF WARFARIN				CURRENT PRACTICE			
	HEALTH & SOCIAL CARE	INFORMAL CARE	PRODUCTIVITY LOSSES	TOTAL COSTS	HEALTH & SOCIAL CARE	INFORMAL CARE	PRODUCTIVITY LOSSES	TOTAL COSTS
AUSTRIA	163,926	11,264	41,554	216,744	273,394	19,898	55,442	348,734
BELGIUM	243,951	8,330	41,958	294,239	415,224	14,779	57,222	487,225
BULGARIA	13,968	1,099	7,532	22,599	21,930	1,935	8,996	32,861
CROATIA	9,406	1,199	5,331	15,936	14,995	2,113	6,830	23,939
CYPRUS	2,695	445	1,830	4,970	4,393	784	2,386	7,564
CZECH REPUBLIC	73,145	4,817	20,504	98,466	119,975	8,461	25,118	153,554
DENMARK	124,709	6,445	35,313	166,467	213,422	11,368	45,163	269,953
ESTONIA	7,985	434	3,296	11,715	13,193	766	3,997	17,955
FINLAND	178,483	2,313	27,116	207,912	303,525	4,084	35,672	343,282
FRANCE	892,753	43,972	182,691	1,119,416	1,518,530	78,111	250,350	1,846,992
GERMANY	2,853,740	90,455	477,925	3,422,121	4,885,798	160,187	620,448	5,666,433
GREECE	114,833	6,940	16,048	137,821	194,984	12,325	22,151	229,461
HUNGARY	47,812	2,143	19,619	69,574	78,980	3,770	23,268	106,019
IRELAND	47,039	3,454	15,020	65,513	78,793	6,099	19,793	104,685
ITALY	1,016,511	61,466	136,098	1,214,075	1,716,623	109,013	188,753	2,014,390
LATVIA	4,754	575	4,530	9,859	7,487	1,013	5,378	13,879
LITHUANIA	10,487	720	5,930	17,137	17,181	1,272	7,040	25,493
LUXEMBOURG	18,533	548	2,334	21,414	31,629	970	3,297	35,896
MALTA	5,365	242	706	6,314	8,979	428	957	10,364
NETHERLANDS	329,511	7,062	71,445	408,018	559,869	12,477	92,360	664,706
POLAND	160,275	7,203	76,657	244,135	262,780	12,708	93,061	368,550
PORTUGAL	44,149	3,182	12,358	59,689	72,484	5,648	16,326	94,458
ROMANIA	42,236	3,753	19,155	65,145	68,060	6,624	23,292	97,976
SLOVAKIA	19,950	1,230	9,626	30,806	32,611	2,162	11,764	46,537
SLOVENIA	20,406	1,166	5,058	26,630	34,122	2,059	6,723	42,904
SPAIN	529,346	46,463	96,195	672,004	893,759	82,596	132,832	1,109,188
SWEDEN	272,019	5,357	49,276	326,652	464,778	9,459	65,177	539,414
TOTAL EU-27	**7,110,697**	**312,549**	**1,551,979**	**8,975,225**	**12,130,736**	**555,769**	**1,964,786**	**14,651,292**
UK	1,211,265	49,214	278,819	1,539,297	2,040,810	87,105	362,068	2,489,983
TOTAL EU-28	**8,313,866**	**361,504**	**1,847,857**	**10,523,227**	**14,183,617**	**642,818**	**2,336,102**	**17,162,537**
ICELAND	7,424	114	1,321	8,859	12,579	202	1,740	14,521
ISRAEL	29,109	4,254	14,253	47,616	47,486	7,533	18,555	73,574
NORWAY	206,259	3,053	22,442	231,754	355,558	5,405	30,829	391,792
SWITZERLAND	235,613	7,070	38,543	281,226	404,017	12,519	51,103	467,639
TOTAL 32 COUNTRIES	**8,669,042**	**375,824**	**1,937,811**	**10,982,677**	**14,794,723**	**668,535**	**2,445,367**	**17,908,625**

The countries with the largest cost-savings were Germany (€2.2 billion), followed by the UK (€950 million) and Italy (€800 million). As with the health and social care perspective, routine use of warfarin generated overall societal cost-savings, when compared to current practice, in all of the 32 countries under study. The countries with the highest savings, per patient with atrial fibrillation, were Norway (€2,782), followed by Switzerland (€2,710) and Luxembourg (€2,246) compared to an average €1,166 for Europe.

Routinely treating every eligibly atrial fibrillation patient with warfarin would save almost €7 billion and add just over 136,000 QALYs over five years.

RESULTS FOR NOACs

When NOACs are routinely used, the average QALYs over five years were 2.24 per patient treated compared with 2.19 QALYs under current practice. That is a QALY gain of 0.044 per atrial fibrillation patient. As a result, at the population level, the total QALYs across the 32 European countries were 15.6 million with routine use of NOACs and 15.3 million with current practice, an increase of 0.31 million QALYs (Table 21). For all countries, routine use of NOACs generated additional QALYs, relative to current practice.

Table 21. QALYs gained at the population level

	ROUTINE USE OF NOACS	CURRENT PRACTICE	DIFFERENCE
AUSTRIA	325,152	317,547	7,605
BELGIUM	307,220	299,159	8,061
BULGARIA	200,359	195,557	4,802
CROATIA	100,588	98,250	2,338
CYPRUS	23,275	22,726	549
CZECH REPUBLIC	318,024	311,210	6,814
DENMARK	170,405	166,375	4,030
ESTONIA	37,661	36,733	928
FINLAND	199,432	194,715	4,717
FRANCE	1,834,590	1,787,222	47,368
GERMANY	2,662,251	2,591,201	71,050
GREECE	304,653	296,145	8,508
HUNGARY	282,044	274,937	7,107
IRELAND	98,292	96,106	2,186
ITALY	1,873,705	1,823,832	49,873

	ROUTINE USE OF NOACS	CURRENT PRACTICE	DIFFERENCE
LATVIA	59,769	58,335	1,434
LITHUANIA	82,868	80,761	2,107
LUXEMBOURG	17,285	16,867	418
MALTA	12,750	12,453	297
NETHERLANDS	452,767	442,127	10,640
POLAND	1,145,905	1,119,657	26,248
PORTUGAL	227,512	221,484	6,028
ROMANIA	443,409	432,131	11,278
SLOVAKIA	144,183	141,157	3,026
SLOVENIA	72,816	71,241	1,575
SPAIN	1,306,745	1,271,932	34,813
SWEDEN	396,452	387,020	9,432
TOTAL EU-27	**13,031,458**	**12,762,893**	**268,565**
UK	2,125,182	2,073,206	51,976
TOTAL EU-28	**15,144,126**	**14,835,975**	**308,151**
ICELAND	7,876	7,698	178
ISRAEL	142,130	138,784	3,346
NORWAY	152,907	148,869	4,038
SWITZERLAND	184,264	179,852	4,412
TOTAL 32 COUNTRIES	**15,621,079**	**15,311,120**	**309,959**

On average, across the 32 countries under study, the average cost of therapy was:

- €1,344 for those treated with routine use of NOACs;
- €65 for patients receiving current therapy.

At the population level, this translated to costs of €9,385 million as opposed to €453 million with current practice (Table 22). Subsequent health and social care costs were lower for routine use of NOACs than the comparator (€7.5 billion vs. €14.0 billion, respectively), even though costs associated with treatment of major bleeding were marginally higher in the routine NOAC scenario.

Table 22. Population-level health and social care costs for patients routinely receiving NOACs and current practice, € thousands

	ROUTINE USE OF NOACS							CURRENT PRACTICE						
			SUBSEQUENT COSTS							SUBSEQUENT COSTS				
	THERAPY	BLEEDING	INPATIENT	OUTPATIENT	A&E	SOCIAL CARE	TOTAL COSTS	THERAPY	BLEEDING	INPATIENT	OUTPATIENT	A&E	SOCIAL CARE	TOTAL COSTS
AUSTRIA	194,014	10,442	134,794	2,200	838	710	342,998	9,424	9,396	247,703	4,025	1,539	1,306	273,394
BELGIUM	184,731	11,889	160,459	972	207	52,219	410,476	8,839	10,650	295,782	1,791	382	97,780	415,224
BULGARIA	115,525	250	7,899	157	25	657	124,512	5,670	225	14,484	286	46	1,220	21,930
CROATIA	57,608	348	5,330	92	133	889	64,400	2,841	314	9,775	169	243	1,653	14,995
CYPRUS	13,355	84	818	133	55	979	15,423	656	76	1,498	244	101	1,820	4,393
CZECH REPUBLIC	180,594	4,278	53,603	1,016	59	3,879	243,428	8,984	3,866	97,984	1,851	107	7,183	119,975
DENMARK	101,233	4,073	73,093	473	180	37,342	216,394	4,902	3,663	134,174	866	330	69,486	213,422
ESTONIA	21,845	399	4,932	190	39	1,231	28,635	1,072	359	9,050	348	72	2,293	13,193
FINLAND	119,495	8,449	108,205	3,372	686	44,961	285,167	5,762	7,592	198,864	6,185	1,261	83,861	303,525
FRANCE	1,136,300	37,633	583,357	11,982	2,728	173,875	1,945,875	53,766	33,674	1,077,758	22,128	5,038	326,167	1,518,530
GERMANY	1,613,995	111,119	2,113,051	33,678	733	405,018	4,277,593	76,800	99,565	3,889,376	61,962	1,350	756,746	4,885,798
GREECE	188,554	4,093	88,341	290	461	9,616	291,354	8,857	3,657	163,073	534	851	18,012	194,984
HUNGARY	161,395	1,649	27,819	354	91	9,629	200,937	7,924	1,484	50,895	645	166	17,865	78,980
IRELAND	56,787	2,801	28,784	527	498	10,065	99,462	2,789	2,525	52,841	966	914	18,758	78,793
ITALY	1,165,593	53,680	680,715	12,099	8,037	172,429	2,092,553	54,902	48,036	1,253,872	22,268	14,819	322,726	1,716,623
LATVIA	34,427	158	2,419	97	14	541	37,655	1,700	142	4,436	176	26	1,006	7,487
LITHUANIA	47,847	302	5,745	165	14	1,976	56,048	2,348	272	10,553	301	26	3,681	17,181
LUXEMBOURG	10,315	873	11,600	153	14	4,632	27,588	499	784	21,375	282	26	8,664	31,629
MALTA	7,627	306	3,539	24	14	950	12,458	368	275	6,499	43	25	1,769	8,979
NETHERLANDS	267,012	15,243	190,767	5,321	342	92,440	571,126	12,958	13,711	350,443	9,758	629	172,369	559,869
POLAND	653,078	5,795	84,515	4,511	184	32,992	781,075	32,322	5,224	155,180	8,257	338	61,460	262,780
PORTUGAL	139,331	2,588	30,004	953	867	2,627	176,370	6,607	2,316	55,285	1,756	1,599	4,920	72,484
ROMANIA	258,803	1,067	20,927	651	49	7,956	289,452	12,587	959	38,419	1,192	89	14,814	68,060
SLOVAKIA	80,158	694	10,835	857	52	3,480	96,075	4,041	628	19,835	1,560	95	6,453	32,611
SLOVENIA	42,619	930	12,041	162	52	4,655	60,459	2,092	838	22,126	296	95	8,674	34,122
SPAIN	806,228	25,711	359,421	11,397	7,504	71,282	1,281,542	38,155	22,992	663,896	21,058	13,871	133,787	893,759
SWEDEN	239,276	9,941	136,445	7,629	1,948	94,559	489,797	11,487	8,932	250,613	13,967	3,577	176,202	464,778
TOTAL EU-27	**7,843,382**	**309,928**	**4,692,071**	**124,734**	**23,745**	**1,348,986**	**14,342,845**	**378,195**	**279,120**	**8,671,383**	**230,051**	**43,890**	**2,528,095**	**12,130,736**
UK	1,266,770	68,133	760,085	13,813	4,784	260,408	2,373,992	61,111	61,184	1,397,868	25,373	8,819	486,455	2,040,810
TOTAL EU-28	**9,100,349**	**364,285**	**5,445,240**	**149,327**	**28,455**	**1,614,045**	**16,701,699**	**439,302**	**328,168**	**10,063,412**	**275,392**	**52,600**	**3,024,743**	**14,183,617**
ICELAND	4,601	420	4,434	117	27	1,900	11,499	225	378	8,160	214	49	3,553	12,579
ISRAEL	83,579	2,096	16,370	358	659	5,125	108,186	4,062	1,884	30,098	652	1,209	9,581	47,486
NORWAY	94,488	7,015	114,538	987	257	70,469	287,754	4,458	6,278	210,836	1,812	473	131,701	355,558
SWITZERLAND	110,609	9,655	146,368	300	197	63,935	331,064	5,322	8,672	269,598	553	363	119,509	404,017
TOTAL EUROPE	**9,385,518**	**384,400**	**5,623,638**	**145,695**	**29,638**	**1,747,147**	**17,316,036**	**453,367**	**346,438**	**10,396,422**	**268,728**	**54,796**	**3,274,972**	**14,794,723**

Therefore, routinely treating eligible atrial fibrillation-patients with NOACs would generate additional costs to the health and social care budget across Europe of €2.5 billion.

Routine use of NOACs generated care cost savings in seven countries (Belgium, Finland, Germany, Iceland, Luxembourg, Norway and Switzerland), relative to current practice. The countries where the biggest savings, in terms of health and social care costs if NOACs were to be routinely administered, were Germany, with five year savings of €608 million, followed by Switzerland (savings of €73 million), followed by Norway (savings of €68 million).

When we include the overall societal costs, the additional costs of routine NOAC use were €1.5 billion over five years (Table 23).

Table 23. Societal costs under routine use of warfarin vs current practice, € thousands

	ROUTINE USE OF NOACS				CURRENT PRACTICE			
	HEALTH & SOCIAL CARE	INFORMAL CARE	PRODUCTIVITY LOSSES	TOTAL COSTS	HEALTH & SOCIAL CARE	INFORMAL CARE	PRODUCTIVITY LOSSES	TOTAL COSTS
AUSTRIA	342,998	10,746	39,402	393,145	273,394	19,898	55,442	348,734
BELGIUM	410,476	7,948	39,793	458,217	415,224	14,779	57,222	487,225
BULGARIA	124,512	1,049	7,170	132,731	21,930	1,935	8,996	32,861
CROATIA	64,400	1,144	5,067	70,611	14,995	2,113	6,830	23,939
CYPRUS	15,423	424.5	1,734	17,582	4,393	784	2,386	7,564
CZECH REPUBLIC	243,428	4,598	19,482	267,508	119,975	8,461	25,118	153,554
DENMARK	216,394	6,151	33,483	256,027	213,422	11,368	45,163	269,953
ESTONIA	28,635	414.25	3,135	32,184	13,193	766	3,997	17,955
FINLAND	285,167	2,207	25,712	313,085	303,525	4,084	35,672	343,282
FRANCE	1,945,875	41,930	173,196	2,161,001	1,518,530	78,111	250,350	1,846,992
GERMANY	4,277,593	86,335	453,418	4,817,345	4,885,798	160,187	620,448	5,666,433
GREECE	291,354	6,622	15,213	313,189	194,984	12,325	22,151	229,461
HUNGARY	200,937	2,047	18,691	221,675	78,980	3,770	23,268	106,019
IRELAND	99,462	3,295	14,221	116,978	78,793	6,099	19,793	104,685
ITALY	2,092,553	58,644	128,829	2,280,026	1,716,623	109,013	188,753	2,014,390
LATVIA	37,655	549	4,314	42,517	7,487	1,013	5,378	13,879
LITHUANIA	56,048	688	5,647	62,382	17,181	1,272	7,040	25,493
LUXEMBOURG	27,588	522.5	2,212	30,322	31,629	970	3,297	35,896
MALTA	12,458	231.25	669	13,358	8,979	428	957	10,364
NETHERLANDS	571,126	6,739	67,679	645,543	559,869	12,477	92,360	664,706
POLAND	781,075	6,872	72,902	860,850	262,780	12,708	93,061	368,550
PORTUGAL	176,370	3,036	11,711	191,118	72,484	5,648	16,326	94,458
ROMANIA	289,452	3,582	18,228	311,262	68,060	6,624	23,292	97,976
SLOVAKIA	96,075	1,174	9,156	106,405	32,611	2,162	11,764	46,537
SLOVENIA	60,459	1,112	4,800	66,371	34,122	2,059	6,723	42,904
SPAIN	1,281,542	44,312	91,092	1,416,946	893,759	82,596	132,832	1,109,188
SWEDEN	489,797	5,112	46,632	541,541	464,778	9,459	65,177	539,414
TOTAL EU-27	**14,342,845**	**298,493**	**1,464,751**	**16,106,088**	**12,130,736**	**555,769**	**1,964,786**	**14,651,292**
UK	2,373,992	46,949	264,151	2,685,093	2,040,810	87,105	362,068	2,489,983
TOTAL EU-28	**16,701,699**	**345,249**	**1,743,432**	**18,790,380**	**14,183,617**	**642,818**	**2,336,102**	**17,162,537**
ICELAND	11,499	109	1,248	12,856	12,579	202	1,740	14,521
ISRAEL	108,186	4,057	13,488	125,731	47,486	7,533	18,555	73,574
NORWAY	287,754	2,914	21,258	311,925	355,558	5,405	30,829	391,792
SWITZERLAND	331,064	6,744	36,476	374,283	404,017	12,519	51,103	467,639
TOTAL 32 COUNTRIES	**17,316,036**	**358,958**	**1,827,355**	**19,502,349**	**14,794,723**	**668,535**	**2,445,367**	**17,908,625**

Using a societal perspective, routine NOAC use generated cost savings in nine European countries: Belgium, Denmark, Finland, Germany, Iceland, Luxembourg, the Netherlands, Norway and Switzerland. The countries with the largest cost-savings were Germany (€850 million), followed by Switzerland (€93 million) and Norway (€80 million).

Using a cost per QALY threshold of €22,727, both from a health and social care, and a societal perspective, routine use of NOACs was cost-effective in all 32 countries. If using a country's per capita GDP as a threshold, routine use of NOACs was not cost-effective in eight Eastern European countries: Bulgaria, Croatia, Hungary, Romania, Latvia, Lithuania, Poland and Slovakia (Table 24).

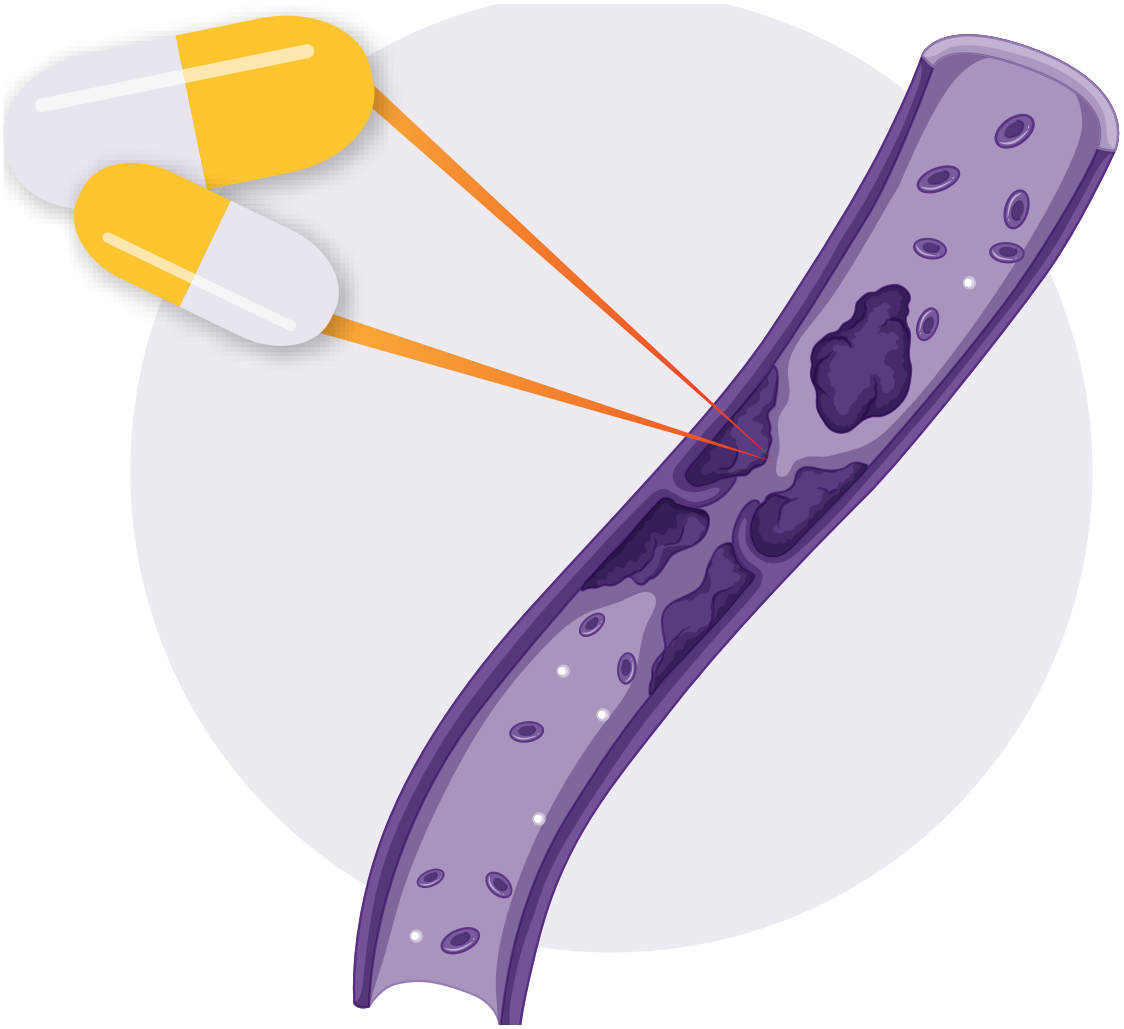


Table 24. Incremental cost (€) per QALY gained from a health and social care, and societal perspectives

COUNTRY	HEALTH AND SOCIAL CARE	COST-EFFECTIVE AT € €22,727 PER ADDITIONAL QALY?	SOCIETY	COST-EFFECTIVE AT € €22,727 PER ADDITIONAL QALY?	COST-EFFECTIVE COMPARED TO GDP PER CAPITA?
AUSTRIA	9,152	yes	5,840	yes	yes
BELGIUM	NOACs dominate	yes	NOACs dominate	yes	yes
BULGARIA	21,363	yes	20,799	yes	no
CROATIA	21,129	yes	19,960	yes	no
CYPRUS	20,110	yes	18,264	yes	yes
CZECH REPUBLIC	18,118	yes	16,723	yes	yes
DENMARK	737	yes	NOACs dominate	yes	yes
ESTONIA	16,645	yes	15,337	yes	yes
FINLAND	NOACs dominate	yes	NOACs dominate	yes	yes
FRANCE	9,022	yes	6,629	yes	yes
GERMANY	NOACs dominate	yes	NOACs dominate	yes	yes
GREECE	11,327	yes	9,841	yes	yes
HUNGARY	17,161	yes	16,274	yes	no
IRELAND	9,456	yes	5,624	yes	yes
ITALY	7,538	yes	5,326	yes	yes
LATVIA	21,038	yes	19,971	yes	no
LITHUANIA	18,451	yes	17,512	yes	no
LUXEMBOURG	NOACs dominate	yes	NOACs dominate	yes	yes
MALTA	11,724	yes	10,088	yes	yes
THE NETHERLANDS	1,058	yes	NOACs dominate	yes	yes
POLAND	19,746	yes	18,756	yes	no
PORTUGAL	17,233	yes	16,034	yes	yes
ROMANIA	19,631	yes	18,912	yes	no
SLOVAKIA	20,973	yes	19,784	yes	no
SLOVENIA	16,722	yes	14,899	yes	yes
SPAIN	11,139	yes	8,840	yes	yes
SWEDEN	2,653	yes	225	yes	yes
TOTAL EU-27	**8,237**	**yes**	**5,417**	**yes**	**yes**
UK	6,410	yes	3,754	yes	yes
TOTAL EU-28	**8,172**	**yes**	**5,283**	**yes**	**yes**
ICELAND	NOACs dominate	yes	NOACs dominate	yes	yes
ISRAEL	18,141	yes	15,588	yes	yes
NORWAY	NOACs dominate	yes	NOACs dominate	yes	yes
SWITZERLAND	NOACs dominate	yes	NOACs dominate	yes	yes
TOTAL 32 COUNTRIES	**8,134**	**yes**	**5,142**	**yes**	**yes**

MECHANICAL THROMBECTOMY

One of the most recent developments in the treatment of acute stroke has been the development of mechanical thrombectomy (MT). MT is a treatment that removes blood clots blocking large blood vessels in the brain with a procedure using an angiogram or a catheterisation and a device that grabs the clot, removes it, and then re-establishes blood flow to the brain. It is most often performed after intravenous thrombolysis (IVT) with alteplase, and performed within six hours from symptoms onset[224].

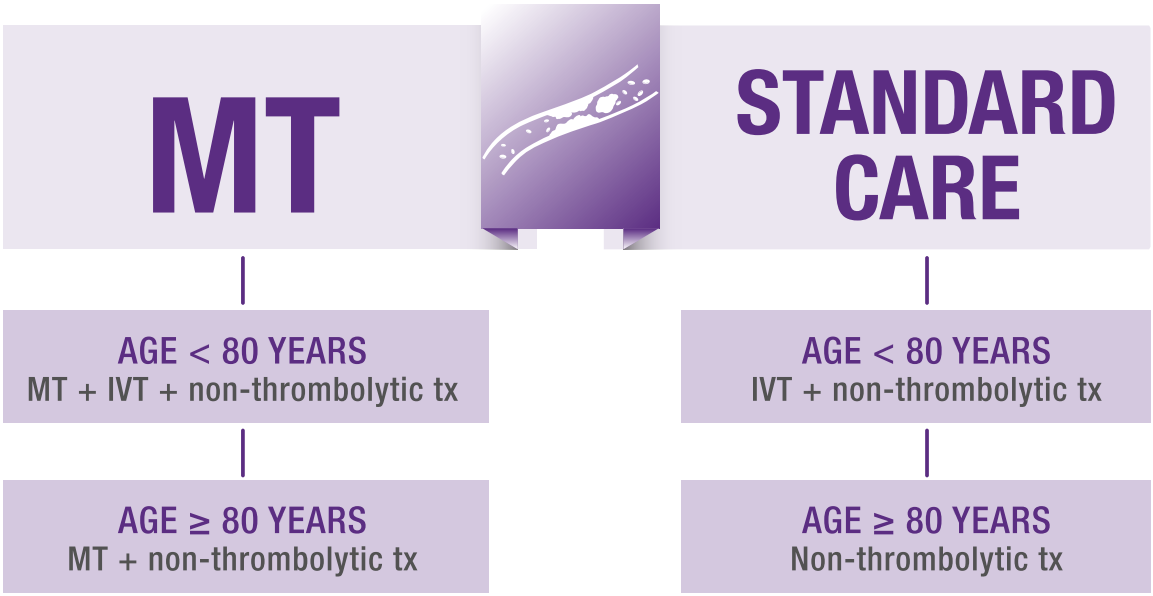
We compared MT with the use of IVT by itself, except for patients over the age of 80, where IVT is typically not administered, where we compared MT on its own with non-thrombolytic treatment.

The target population of MT treatment was defined as:

- Had a confirmed ischaemic stroke;
- Were admitted to hospital within 6 hours from symptoms onset;
- Were not disabled before the stroke (i.e. mRS < 3);
- Had a non-minor stroke as defined using a National Institutes of Health Stroke Scale (NIHSS) score ≥ 5; and
- ≥ 20 years old.

We compared MT treatment with standard care (Figure 11).

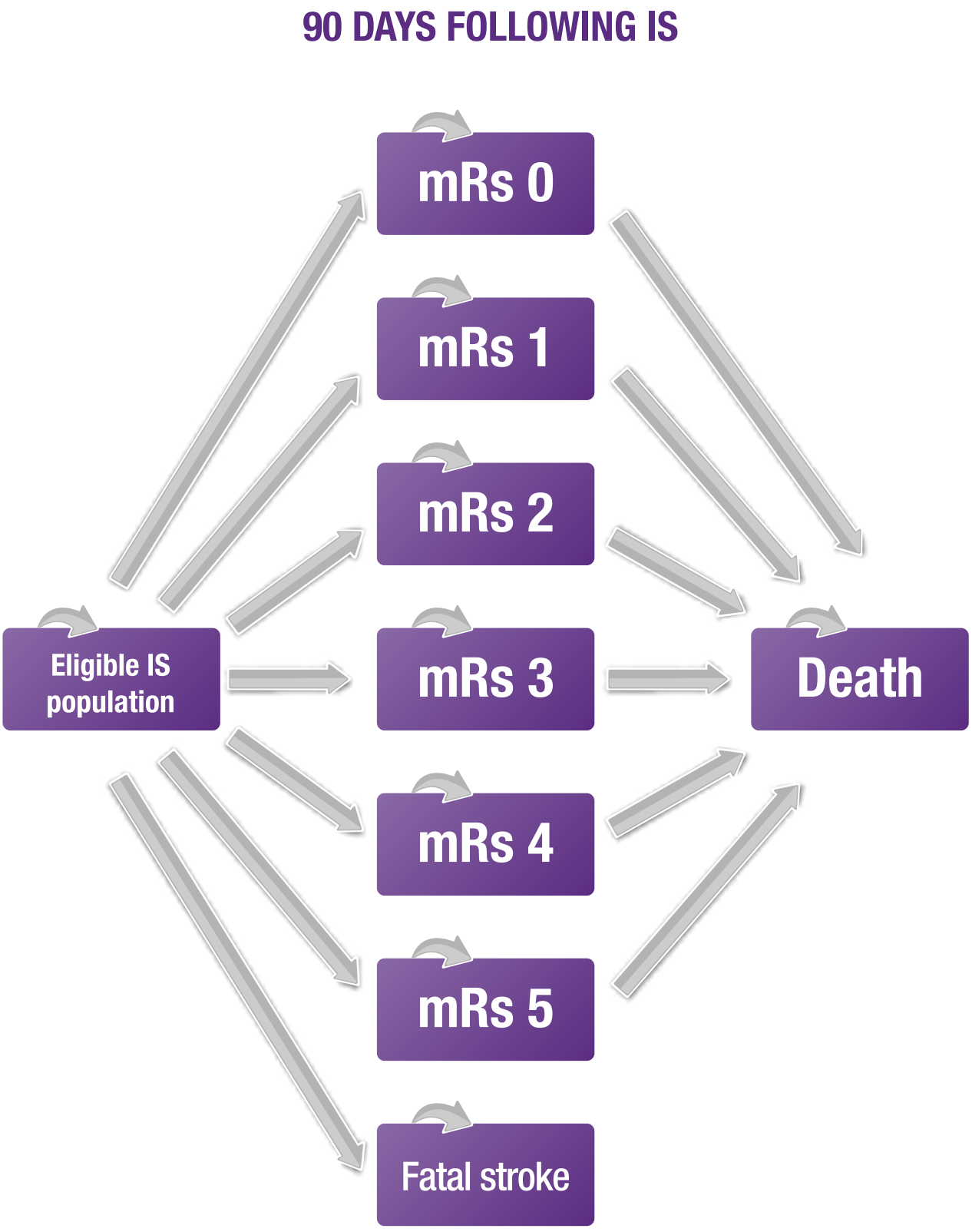
Figure 11. Comparison of MT with standard care



For all eligible patients under the age of 80, we assumed standard care across the 32 countries under study to be IVT alone. For patients over the age of 80, where IVT is typically not administered,[225] we compared MT on its own with non-thrombolytic treatment.

Over the course of the first year after having an ischaemic stroke, people could die from stroke or be assessed at three months for the level of disability the stroke had caused - levels 0 to 5 on the mRS (Figure 12). The survival, utilities and costs over the five-year time horizon were conditional on mRS state at three months. The simulation was run for 28 age group / gender combinations (two gender and 14 age 5-year groups). Results were combined based on group proportions for the defined country or group of countries. Country, age, and gender-specific numbers of new ischaemic strokes were derived from the Global Burden of Disease.[1]

Figure 12. Mechanical thrombectomy model structure



EFFECTIVENESS OF MT ON MRS SCORE AT 3 MONTHS

The effectiveness of MT + IVT over IVT alone in those younger than 80 years of age, and that of MT over standard care with no IVT, was derived from a meta-analysis of five randomised controlled trials.[225] The primary outcome of this study was 90-day mRS score and death, results of which are summarised in Table 25. The costs and (quality-adjusted) life expectancy over a five-year time horizon conditional on mRS at three months were then simulated to determine the differences between MT intervention and standard care.

Table 25. 90-day mRS scores according to treatment received225

	AGE < 80 YEARS		AGE ≥ 80 YEARS	
MRS SCORE	MT + IVT	IVT	MT	NO IVT
0	10.0%	5.0%	10.2%	3.6%
1	16.9%	7.9%	15.7%	6.2%
2	19.1%	13.6%	17.6%	12.5%
3	16.9%	16.4%	18.5%	8.7%
4	15.6%	24.7%	7.4%	31.2%
5	6.2%	13.5%	7.4%	15.0%
DEATH	15.3%	18.9%	23.1%	22.5%

INTERVENTION COSTS

Costs of MT and IVT were derived from a study undertaken in Italy [226]. For this study, we assumed that the costs of the MT device, alteplase to deliver IVT, and any other consumables and tests would be the same across countries. These costs were €4,409 for MT, €606 for IVT, and €123 for those receiving no IVT.

Healthcare staff needed to deliver the intervention included nurses, anaesthesiologists, assistants, neuro-radiologists and registrars. We assumed that all countries would require the same staff categories and hours to provide all ischaemic stroke treatments (MT, IVT, and non-thrombolysis) as that reported in two previous studies in Italy and the UK [226 227] (Table 26). Staff time was valued using country-specific unit costs.

Table 26. Ischaemic stroke resource use by treatment procedure

	ITEM	RESOURCE USE
MT PROCEDURE	Device	1.2
	Consumables	1
	Anaesthetist	4
	Anaesthetist assistant	4
	Radiographer	3
	Neuroradiologist	3
	Registrar	3
	Nurse	3
	Scrub Nurse	3
IVT PROCEDURE	Drug	1
	Blood test	1
	Nurse activate stroke team	0.08
	Stroke team assessment	0.5
	Registrar accompanies patient to CT scan	1
	Consultant reviews CT results and discusses with relatives	0.5
	Nurse assessment	0.08
	Registrar time for IV-tPA infusion	1.25
	Additional 12 routine observations	1
	1:1 care for 5 hours with senior nurse	5
	Junior staff review	0.42
	Overnight junior staff review	0.17
	Consultant review after infusion	0.33
NON-THROMBOLYSIS PROCEDURE	Blood test	1
	CT scan	1
	ER Doctor assessment	0.25
	Nurse to accompany to CT scan	1
	Nurse assessment	0.08
	Routine nurse observation 4 in 24 hours	0.33
	Junior staff review	0.21
	Consultant review at 24 hours	0.25

In 2017, just over one million people aged 20 years and over suffered an ischaemic stroke across Europe, with Germany, Italy and Poland having the highest incidence (Table 27). Of these, 27% (267,514) were eligible for mechanical thrombectomy.

Table 27. Number of ischaemic stroke cases in individuals aged 20 years and over in 2017

	INCIDENT ISCHAEMIC STROKE CASES	MT-ELIGIBLE INCIDENT ISCHAEMIC STROKE CASES
AUSTRIA	16,498	4,191
BELGIUM	19,559	4,846
BULGARIA	29,054	7,279
CROATIA	16,601	4,170
CYPRUS	930	238
CZECH REPUBLIC	31,001	7,783
DENMARK	8,340	2,125
ESTONIA	3,735	932
FINLAND	12,663	3,293
FRANCE	88,468	23,286
GERMANY	175,081	44,624
GREECE	22,101	5,855
HUNGARY	32,567	8,146
IRELAND	4,877	1,226
ITALY	110,530	29,504
LATVIA	10,088	2,533
LITHUANIA	12,507	3,126
LUXEMBOURG	719	185
MALTA	547	136
NETHERLANDS	23,738	6,059
POLAND	101,706	25,612
PORTUGAL	18,031	4,751
ROMANIA	79,443	19,822
SLOVAKIA	16,429	4,033
SLOVENIA	4,690	1,196
SPAIN	67,358	17,632
SWEDEN	17,262	4,480
TOTAL EU-27	**924,520**	**237,065**

	INCIDENT ISCHAEMIC STROKE CASES	MT-ELIGIBLE INCIDENT ISCHAEMIC STROKE CASES
UK	87,921	22,908
TOTAL EU-28	**1,012,441**	**259,974**
ICELAND	428	109
ISRAEL	7,531	1,912
NORWAY	8,324	2,132
SWITZERLAND	13,179	3,388
TOTAL 32 COUNTRIES	**1,041,903**	**267,514**

In our model, the cohort consisted of 267,514 patients undergoing either MT or standard care. For those undergoing MT, the average QALY gain over five years was 2.00, compared with 1.62 for those undergoing standard care. As a result, at the population level, the total QALYs gained across the 32 European countries was 534,430 with MT and 433,103 with standard care, with MT generating an additional 101,327 QALYs (Table 28). MT generated additional QALYs over standard care in all countries.

Table 28. QALYs gained at the population level

	MT	STANDARD CARE	DIFFERENCE
AUSTRIA	8,494	6,898	1,596
BELGIUM	9,711	7,873	1,838
BULGARIA	14,656	11,887	2,769
CROATIA	8,359	6,775	1,584
CYPRUS	481	390	91
CZECH REPUBLIC	15,791	12,823	2,968
DENMARK	4,283	3,475	808
ESTONIA	1,888	1,533	355
FINLAND	6,529	5,286	1,243
FRANCE	46,082	37,308	8,774
GERMANY	89,357	72,430	16,928
GREECE	11,453	9,255	2,198
HUNGARY	16,490	13,385	3,105
IRELAND	2,515	2,045	469
ITALY	57,336	46,291	11,045
LATVIA	5,076	4,114	962
LITHUANIA	6,323	5,132	1,191

	MT	STANDARD CARE	DIFFERENCE
LUXEMBOURG	372	302	70
MALTA	277	225	52
NETHERLANDS	12,223	9,919	2,303
POLAND	51,727	41,979	9,748
PORTUGAL	9,311	7,526	1,785
ROMANIA	40,092	32,536	7,556
SLOVAKIA	8,301	6,753	1,548
SLOVENIA	2,392	1,938	453
SPAIN	35,128	28,466	6,663
SWEDEN	8,934	7,239	1,695
TOTAL EU-27	**473,577**	**383,777**	**89,800**
UK	45,621	36,962	8,659
TOTAL EU-28	**519,197**	**420,738**	**98,459**
ICELAND	221	180	42
ISRAEL	3,906	3,176	730
NORWAY	4,306	3,495	811
SWITZERLAND	6,801	5,515	1,286
TOTAL 32 COUNTRIES	**534,430**	**433,103**	**101,327**

On average across Europe, the average intervention cost with MT was €6,333 per patient treated, compared with €611 for standard care. At the population level, this translated into costs of €1.7 billion as opposed to €163 million. However, inpatient costs following the intervention were lower for MT than for standard care (€5.8 billion vs. €7.2 billion, respectively). Over the five years, treating all eligible patients with MT generated health and social care costs of €11 billion compared with €12 billion for standard care (Table 29), generating cost savings to the health and social care services across the 32 countries of €868 million. The countries with the biggest savings were Germany, with five-year savings of €435 million, followed by the UK (savings of €80 million), Switzerland (savings of €61 million) and Italy (savings of €59 million). However, MT did not generate cost savings when compared to standard care for all countries, including Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Greece, Hungary, Israel, Latvia, Lithuania, Poland, Portugal, Romania, Slovakia and Spain.

Table 29. Population-based health and social care costs for patients undergoing mechanical thrombectomy vs standard care, € thousands

	MECHANICAL THROMBECTOMY						STANDARD CARE					
		SUBSEQUENT COSTS						SUBSEQUENT COSTS				
	INTERVENTION	INPATIENT	OUTPATIENT	A&E	SOCIAL CARE	TOTAL COSTS	INTERVENTION	INPATIENT	OUTPATIENT	A&E	SOCIAL CARE	TOTAL COSTS
AUSTRIA	25,874	137,650	4,481	667	81,922	250,593	2,520	167,626	4,096	665	109,284	284,191
BELGIUM	29,284	141,254	1,977	212	84,076	256,804	2,677	175,177	1,825	209	112,419	292,308
BULGARIA	42,189	27,185	862	73	3,046	73,356	4,003	31,869	791	72	4,051	40,785
CROATIA	23,772	17,904	603	482	4,970	47,730	2,189	21,514	559	470	6,614	31,347
CYPRUS	1,381	515	193	36	1,241	3,366	123	653	177	36	1,661	2,650
CZECH REPUBLIC	44,522	105,308	3,993	125	13,516	167,463	4,139	129,428	3,658	124	18,047	155,395
DENMARK	13,461	66,789	791	152	53,799	134,992	1,341	80,326	727	150	71,734	154,279
ESTONIA	5,653	8,539	727	66	3,766	18,751	569	10,474	666	65	5,010	16,785
FINLAND	29,144	108,485	7,320	725	88,336	234,010	3,441	135,065	6,744	716	117,946	263,912
FRANCE	157,681	413,098	18,191	1,567	219,951	810,489	14,978	507,825	16,817	1,569	294,495	835,684
GERMANY	278,985	2,279,163	67,199	867	689,533	3,315,746	27,467	2,745,787	61,596	868	915,235	3,750,953
GREECE	34,648	103,821	643	443	17,833	157,388	2,840	125,277	601	437	23,839	152,994
HUNGARY	45,951	68,831	1,525	194	37,068	153,569	4,252	82,702	1,387	193	49,382	137,915
IRELAND	8,335	20,965	962	347	14,545	45,153	901	26,513	890	347	19,464	48,115
ITALY	184,095	525,373	20,119	6,272	280,277	1,016,137	15,624	661,168	18,477	6,203	374,058	1,075,530
LATVIA	15,060	8,331	651	50	3,026	27,119	1,477	9,987	599	49	4,014	16,127
LITHUANIA	18,201	17,510	940	39	9,009	45,699	1,742	20,962	862	39	11,993	35,599
LUXEMBOURG	1,129	7,317	224	8	5,349	14,028	103	9,094	207	8	7,156	16,569
MALTA	835	2,159	35	9	1,162	4,200	86	2,700	32	9	1,543	4,370
NETHERLANDS	40,804	158,045	9,557	309	142,734	351,449	4,206	195,799	8,783	308	190,949	400,044
POLAND	154,946	154,949	16,025	332	99,608	425,859	14,976	188,406	14,676	333	133,036	351,427
PORTUGAL	28,885	29,989	2,310	870	5,688	67,742	2,472	38,035	2,135	864	7,602	51,108
ROMANIA	113,106	75,916	4,154	159	42,882	236,217	10,631	90,107	3,795	158	57,124	161,816
SLOVAKIA	23,835	29,399	4,170	121	14,163	71,688	2,423	35,201	3,795	122	18,888	60,428
SLOVENIA	7,030	13,894	387	58	9,871	31,241	641	17,121	355	57	13,154	31,328
SPAIN	117,065	251,107	18,563	5,107	92,757	484,599	11,016	312,811	17,184	5,064	124,444	470,519
SWEDEN	41,749	93,162	10,174	1,181	118,987	265,252	5,100	115,225	9,298	1,177	158,872	289,671
TOTAL EU-27	**1,493,942**	**5,222,973**	**273,379**	**23,745**	**2,685,551**	**9,699,590**	**143,934**	**6,387,360**	**250,690**	**23,595**	**3,582,477**	**10,388,056**
UK	153,864	429,991	18,606	3,539	312,140	918,139	14,991	545,597	17,110	3,475	417,612	998,785
TOTAL EU-28	**1,641,753**	**5,719,149**	**309,689**	**27,187**	**3,048,405**	**10,746,184**	**157,878**	**7,003,485**	**284,036**	**27,003**	**4,067,597**	**11,540,000**
ICELAND	740	3,380	212	20	2,957	7,308	77	4,300	194	20	3,969	8,558
ISRAEL	11,789	8,595	489	237	7,449	28,560	1,144	11,659	435	253	9,983	23,473
NORWAY	14,771	93,728	1,552	198	95,000	205,250	1,554	114,284	1,417	196	126,983	244,434
SWITZERLAND	20,223	165,034	718	240	125,402	311,617	1,829	202,441	665	235	167,639	372,809
TOTAL 32 COUNTRIES	**1,694,124**	**5,842,753**	**298,649**	**27,385**	**3,286,365**	**11,149,276**	**163,374**	**7,167,625**	**273,708**	**27,254**	**4,385,384**	**12,017,345**

When productivity losses were included, overall societal costs were €12.2 billion with routine use of MT compared with €13.7 billion for standard care (Table 30), generating savings of €1.5 billion over a five-year period. As with the health and social care perspective, MT did not generate cost savings when compared to standard care for all countries. For Bulgaria, Croatia, Cyprus, Estonia, Hungary, Latvia, Lithuania, Poland, Portugal, Romania and Slovakia, the additional costs of providing MT were not offset by subsequent savings.

Table 30. Societal costs for patients undergoing MT vs standard care, € thousands

	MECHANICAL THROMBECTOMY				STANDARD CARE			
	HEALTH & SOCIAL CARE	INFORMAL CARE	PRODUCTIVITY LOSSES	TOTAL COSTS	HEALTH & SOCIAL CARE	INFORMAL CARE	PRODUCTIVITY LOSSES	TOTAL COSTS
AUSTRIA	250,593	14,149	12,444	277,186	284,191	25,344	16,225	325,760
BELGIUM	256,804	11,326	11,676	279,805	292,308	20,901	15,280	328,489
BULGARIA	73,356	4,328	2,631	80,315	40,785	7,591	3,529	51,906
CROATIA	47,730	5,394	1,998	55,122	31,347	9,576	2,615	43,539
CYPRUS	3,366	479	365	4,210	2,650	872	491	4,012
CZECH REPUBLIC	167,463	14,492	7,365	189,320	155,395	25,480	9,739	190,614
DENMARK	134,992	7,777	8,916	151,685	154,279	13,901	11,808	179,989
ESTONIA	18,751	1,179	1,103	21,033	16,785	2,050	1,433	20,269
FINLAND	234,010	3,431	7,506	244,947	263,912	6,344	9,756	280,012
FRANCE	810,489	44,147	42,408	897,044	835,684	84,296	55,029	975,009
GERMANY	3,315,746	128,200	160,960	3,604,907	3,750,953	231,433	211,390	4,193,777
GREECE	157,388	9,634	3,723	170,745	152,994	18,773	5,019	176,787
HUNGARY	153,569	7,103	5,166	165,838	137,915	12,425	6,929	157,269
IRELAND	45,153	4,621	4,497	54,271	48,115	8,164	6,015	62,294
ITALY	1,016,137	70,340	33,006	1,119,483	1,075,530	139,030	44,390	1,258,950
LATVIA	27,119	2,711	1,733	31,563	16,127	4,744	2,289	23,160
LITHUANIA	45,699	2,905	2,396	51,001	35,599	5,077	3,142	43,819
LUXEMBOURG	14,028	521	535	15,084	16,569	966	712	18,247
MALTA	4,200	254	154	4,608	4,370	438	206	5,015
NETHERLANDS	351,449	9,252	19,567	380,268	400,044	16,805	26,147	442,997
POLAND	425,859	18,613	15,993	460,465	351,427	33,152	21,484	406,063
PORTUGAL	67,742	5,109	3,604	76,455	51,108	9,878	4,815	65,800
ROMANIA	236,217	17,345	8,073	261,634	161,816	30,202	10,862	202,880
SLOVAKIA	71,688	4,698	3,611	79,997	60,428	7,958	4,759	73,146
SLOVENIA	31,241	1,973	1,210	34,423	31,328	3,599	1,592	36,519
SPAIN	484,599	48,304	25,245	558,148	470,519	92,235	33,629	596,383
SWEDEN	265,252	5,262	14,819	285,333	289,671	9,709	19,802	319,183
TOTAL EU-27	**9,699,590**	**490,550**	**413,483**	**10,603,623**	**10,388,056**	**898,896**	**547,335**	**11,834,287**
UK	918,139	47,390	55,735	1,021,264	998,785	88,928	74,784	1,162,497
TOTAL EU-28	**10,746,184**	**538,428**	**474,573**	**11,759,184**	**11,540,000**	**988,654**	**629,433**	**13,158,087**
ICELAND	7,308	154	524	7,987	8,558	276	702	9,536
ISRAEL	28,560	5,689	4,473	38,721	23,473	10,171	5,953	39,597
NORWAY	205,250	3,479	9,602	218,331	244,434	6,237	12,231	262,902
SWITZERLAND	311,617	11,422	16,659	339,698	372,809	20,964	22,126	415,899
TOTAL 32 COUNTRIES	**11,149,276**	**561,263**	**504,965**	**12,215,504**	**12,017,345**	**1,030,157**	**669,443**	**13,716,944**

In terms of average (per-patient) cost savings, when MT was compared to standard care, the countries with the highest savings were Switzerland (€22,488), followed by Norway (€20,908) and Luxembourg (€17,099) compared to an average €5,613 for Europe.

For countries in which MT generated additional costs compared to standard care, we estimated the incremental cost per QALY gained to assess the cost-effectiveness of MT (Table 31). For all countries MT was cost-effective using a €22,727 cost per QALY threshold. Only for Bulgaria, was MT judged not cost-effective when using annual GDP estimates as the cost-effectiveness threshold. For countries not in Table 31, MT was dominant over standard care (i.e. more QALYs and lower costs) under all scenarios.

Table 31. Incremental cost per QALY gained from a health & social care and societal perspectives

	HEALTH AND SOCIAL CARE	COST EFFECTIVE AT €22,727 PER ADDITIONAL QALY?	SOCIETY	COST EFFECTIVE AT €22,727 PER ADDITIONAL QALY?	COST-EFFECTIVE COMPARED TO GDP PER CAPITA?
BULGARIA	11,761	Yes	10,258	Yes	No
CROATIA	10,343	Yes	7,313	Yes	Yes
CYPRUS	7,916	Yes	2,181	Yes	Yes
CZECH REPUBLIC	4,066	Yes	MT dominates	Yes	Yes
ESTONIA	5,533	Yes	2,150	Yes	Yes
GREECE	1,999	Yes	MT dominates	Yes	Yes
HUNGARY	5,042	Yes	2,760	Yes	Yes
ISRAEL	6,967	Yes	MT dominates	Yes	Yes
LATVIA	11,429	Yes	8,738	Yes	Yes
LITHUANIA	8,479	Yes	6,030	Yes	Yes
POLAND	7,636	Yes	5,581	Yes	Yes
PORTUGAL	9,318	Yes	5,968	Yes	Yes
ROMANIA	9,846	Yes	7,776	Yes	Yes
SLOVAKIA	7,276	Yes	4,427	Yes	Yes
SPAIN	2,113	Yes	MT dominates	Yes	Yes

COMMUNITY-BASED REHABILITATION FOLLOWING STROKE

In 2017, across Europe, just over 1.4 million people aged 20 years or over suffered a stroke, with Germany, Italy and France presenting the highest numbers (Table 32). Of these, 855,083 (59%) stroke patients were eligible for community based (CB) rehabilitation.

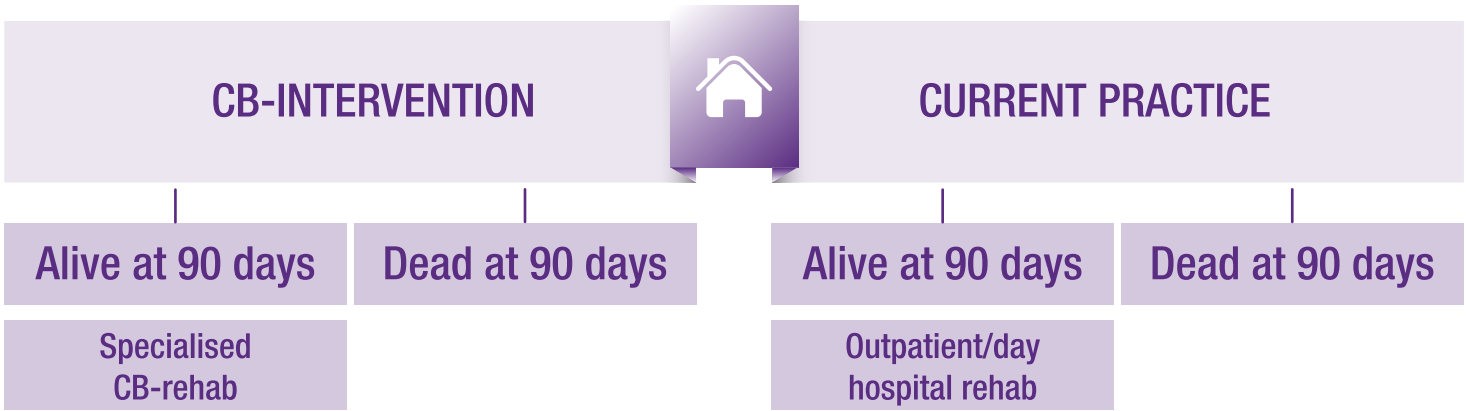
Table 32. Number of strokes in individuals aged 20 years or over

	INCIDENT STROKE CASES	ELIGIBLE INCIDENT STROKE CASES
AUSTRIA	23,555	13,748
BELGIUM	27,893	16,450
BULGARIA	38,269	22,421
CROATIA	20,386	11,974
CYPRUS	1,558	911
CZECH REPUBLIC	38,801	22,586
DENMARK	12,451	7,313
ESTONIA	4,593	2,666
FINLAND	17,331	10,231
FRANCE	130,310	77,262
GERMANY	241,408	142,013
GREECE	34,008	20,315
HUNGARY	39,851	23,204
IRELAND	7,366	4,268
ITALY	165,346	99,085
LATVIA	12,157	7,104
LITHUANIA	14,989	8,714
LUXEMBOURG	1,066	626
MALTA	885	517
NETHERLANDS	35,139	20,622
POLAND	124,003	72,362
PORTUGAL	27,326	16,283
ROMANIA	102,779	60,046
SLOVAKIA	20,468	11,787
SLOVENIA	6,175	3,623

	INCIDENT STROKE CASES	ELIGIBLE INCIDENT STROKE CASES
SPAIN	101,147	59,744
SWEDEN	24,658	14,568
TOTAL EU-27	**1,273,919**	**750,443**
UK	133,888	79,122
TOTAL EU-28	**1,407,807**	**829,565**
ICELAND	598	349
ISRAEL	11,176	6,498
NORWAY	12,159	7,121
SWITZERLAND	19,653	11,550
TOTAL 32 COUNTRIES	**1,451,393**	**855,083**

Evidence and best-practice guidelines now recommend that stroke patients discharged from hospital should continue to have access to specialised CB rehabilitation services.[228 229] Therefore, in our study we compared CB rehabilitation for stroke patients discharged from hospital to current practice (Figure 13). We defined current practice as inpatient care followed by some level of stroke rehabilitation delivered in either out-patient clinics or day hospital.[230 231]

Figure 13. Comparison of CB rehabilitation with current practice



The target population of CB rehabilitation was defined as:

- stroke survivors who had a confirmed diagnosis (intracerebral haemorrhages, ischaemic stroke and strokes of unknown type);
- were aged ≥ 20 years old;
- were admitted to hospital after stroke onset.

- To work out the costs of CB rehabilitation, our model included all types of stroke cases: intracerebral haemorrhages, ischaemic strokes and strokes of unknown type over a one-year cycle. Following stroke, individuals could die from stroke or move to one of six degrees of stroke-disability at three months (i.e. mRS 0 to 5). The simulation was run for the two interventions and computed for 28 age group /gender combinations (two gender and 14 age five-year groups). Country, age, and gender-specific numbers of incident stroke cases were derived from the Global Burden of Disease.[1]

CB rehabilitation was simulated to reduce the severity of stroke-related disability (mRS score 0-5) at three months post stroke. Its effectiveness relative to current practice was derived from a published meta-analysis, which found an improvement in the Barthel Index at six to eight weeks post-intervention.[230] In the meta-analysis, the mean difference in the Barthel Index score between those receiving community- as opposed to centre-based rehabilitation was estimated at 1.00 (95% CI: 0.12 to 1.88). Given that there was a lag between the patient being admitted and receiving the intervention, we assumed that this effect would take place three months after stroke onset. We assumed that the probability of death at 90 days for patients admitted to hospital was the same for both current practice and CB care groups.[232]

We assumed that stroke survivors receiving current practice would have the same mRS distribution at three months as the stroke survivors in OXVASC.[233] To model the effect of CB rehabilitation, we converted the three month distribution of mRS scores in OXVASC[233] into a distribution of Barthel Index scores,[234] and applied the effectiveness of the intervention as derived from the meta-analysis.[230] We then back transformed this new Barthel Index distribution into a new mRS distribution, which included the effect of the intervention. The costs and (quality-adjusted) life expectancy over a five-year time horizon conditional on mRS at three months were then simulated to determine the differences between the two interventions.

The intensity of rehabilitation was assumed to be the same as that studied by Beech et al.,[231] with patients in CB therapy and current practice receiving physiotherapy, occupational therapy and speech therapy (Table 33).

Table 33. Use of rehabilitation services231

	CB THERAPY*	CURRENT PRACTICE*
PHYSIOTHERAPY		
MEAN INPATIENT UNITS	8.0	12.0
MEAN COMMUNITY-BASED UNITS	14.4	3.0
OCCUPATIONAL THERAPY		
MEAN INPATIENT UNITS	8.6	20.0
MEAN COMMUNITY-BASED UNITS	23.3	3.9
SPEECH AND LANGUAGE THERAPY		
MEAN INPATIENT UNITS	2.8	4.6
MEAN COMMUNITY-BASED UNITS	10.9	1.3

**Each unit equalled a 20-minute visit with a therapist*

Intervention costs were estimated by multiplying the therapy-related resource use with the unit costs in Table 34**.** The unit costs for the rehabilitative therapies were based on UK costs obtained from NHS reference costs[3] and converted into Euros (€). To capture country-heterogeneity in intervention costs, we applied weights to the unit costs that were estimated for each of the selected countries. These weights were obtained by dividing the cost for an outpatient care visit in each country by that of the same visit in the UK.

Table 34. Unit costs of rehabilitative therapy

	UNIT COST, 2017
INPATIENT-BASED PHYSIOTHERAPY	€48.22
COMMUNITY-BASED PHYSIOTHERAPY	€65.02
INPATIENT-BASED OCCUPATIONAL THERAPY	€64.00
COMMUNITY-BASED OCCUPATIONAL THERAPY	€91.25
INPATIENT-BASED SPEECH AND LANGUAGE THERAPY	€91.17
COMMUNITY-BASED SPEECH AND LANGUAGE THERAPY	€84.16

For those undergoing CB rehabilitation, the average QALY gain over five years was 1.82, compared with 1.75 for those undergoing current practice. As a result, at the population level, the total QALYs projected for the 32 countries was 1.6 million with CB rehabilitation and 1.5 million with current practice, an increase of 61,890 QALYs (Table 35). For all countries, CB rehabilitation generated more QALYs than current practice.

Table 35. QALYs gained at the population level

	CB REHABILITATION	CURRENT PRACTICE	DIFFERENCE
AUSTRIA	25,804	24,792	1,012
BELGIUM	29,845	28,660	1,186
BULGARIA	41,724	40,071	1,653
CROATIA	22,088	21,209	879
CYPRUS	1,699	1,633	67
CZECH REPUBLIC	42,783	41,102	1,681
DENMARK	13,499	12,966	533
ESTONIA	5,033	4,834	199
FINLAND	18,518	17,779	738
FRANCE	137,375	131,878	5,498
GERMANY	259,599	249,287	10,312
GREECE	35,316	33,889	1,427
HUNGARY	43,805	42,077	1,728
IRELAND	8,211	7,893	318
ITALY	170,443	163,523	6,920
LATVIA	13,095	12,570	525
LITHUANIA	16,378	15,729	649
LUXEMBOURG	1,152	1,107	45
MALTA	973	935	38
NETHERLANDS	38,122	36,617	1,505
POLAND	135,976	130,613	5,363
PORTUGAL	28,518	27,367	1,151
ROMANIA	112,556	108,108	4,449
SLOVAKIA	23,113	22,216	898
SLOVENIA	6,708	6,443	265
SPAIN	107,774	103,491	4,283
SWEDEN	26,358	25,311	1,047

	CB REHABILITATION	CURRENT PRACTICE	DIFFERENCE
TOTAL EU-27	**1,366,225**	**1,311,871**	**54,355**
UK	142,432	136,762	5,670
TOTAL EU-28	**1,508,656**	**1,448,633**	**60,024**
ICELAND	657	631	26
ISRAEL	12,371	11,890	481
NORWAY	13,261	12,740	521
SWITZERLAND	21,269	20,430	839
TOTAL 32 COUNTRIES	**1,556,207**	**1,494,317**	**61,890**

On average, across the 32 countries under study, the intervention costs were €1,270 per patient receiving CB rehabilitation compared with €762 for those in current practice. At the population level, this translated into costs of €1,086 billion as opposed to € 652 million (Table 36). However, inpatient costs following the intervention were lower after CB rehabilitation compared to current practice (€18.8 billion vs. €19.4 billion, respectively).

Table 36. Population-based health and social care costs for patients undergoing CB vs current rehabilitation practice, € thousands

	CB REHABILITATION						CURRENT PRACTICE					
		SUBSEQUENT COSTS						SUBSEQUENT COSTS				
	INTERVENTION	INPATIENT	OUTPATIENT	A&E	SOCIAL CARE	TOTAL COSTS	INTERVENTION	INPATIENT	OUTPATIENT	A&E	SOCIAL CARE	TOTAL COSTS
AUSTRIA	13,588	450,771	13,868	2,101	274,128	754,457	8,152	465,138	13,547	2,122	276,532	765,492
BELGIUM	13,441	486,798	6,270	681	295,353	802,543	8,064	502,025	6,111	686	296,187	813,073
BULGARIA	7,824	83,016	2,543	214	9,465	103,061	4,694	85,187	2,484	216	9,595	102,176
CROATIA	2,525	51,619	1,592	1,322	14,403	71,461	1,515	53,190	1,554	1,334	14,582	72,176
CYPRUS	389	2,010	693	133	4,845	8,070	233	2,088	677	135	4,874	8,007
CZECH REPUBLIC	5,342	308,111	11,218	332	39,713	364,715	3,205	319,368	10,964	336	40,280	374,152
DENMARK	8,930	228,657	2,546	498	189,215	429,846	5,358	235,142	2,485	502	190,815	434,302
ESTONIA	2,048	24,814	2,004	180	10,941	39,988	1,229	25,730	1,960	182	11,117	40,219
FINLAND	54,367	342,206	21,523	2,130	275,913	696,138	32,618	353,679	20,989	2,146	277,251	686,682
FRANCE	157,161	1,382,760	55,911	4,969	749,972	2,350,773	94,290	1,419,039	54,458	5,008	749,423	2,322,218
GERMANY	157,292	7,221,238	202,590	2,317	2,228,011	9,811,447	94,369	7,433,734	197,715	2,336	2,246,039	9,974,192
GREECE	14,071	357,322	1,944	1,466	63,204	438,008	8,442	365,033	1,892	1,475	63,115	439,958
HUNGARY	2,294	196,437	4,172	529	106,417	309,849	1,376	202,831	4,081	535	108,034	316,856
IRELAND	8,414	73,944	3,102	1,184	51,853	138,498	5,048	76,954	3,031	1,197	52,435	138,666
ITALY	120,650	1,809,517	60,833	19,992	952,129	2,963,121	72,385	1,864,844	59,235	20,114	949,464	2,966,042
LATVIA	4,128	23,594	1,752	133	8,616	38,223	2,477	24,334	1,712	134	8,744	37,402
LITHUANIA	3,385	49,079	2,534	102	25,553	80,653	2,031	50,632	2,478	103	25,931	81,175
LUXEMBOURG	579	25,028	716	27	18,592	44,941	347	25,850	698	27	18,661	45,582
MALTA	432	8,269	124	33	4,472	13,329	259	8,608	121	33	4,541	13,562
NETHERLANDS	39,144	545,027	30,784	966	499,404	1,115,325	23,485	563,010	30,036	974	502,502	1,120,008
POLAND	56,670	439,870	43,796	835	284,318	825,489	34,000	454,330	42,788	844	287,559	819,521
PORTUGAL	15,299	106,460	7,108	2,870	19,813	151,550	9,179	110,030	6,924	2,891	19,800	148,824
ROMANIA	11,943	229,712	12,099	447	131,751	385,952	7,165	236,397	11,826	452	133,674	389,513
SLOVAKIA	5,714	85,808	12,011	324	41,428	145,284	3,428	88,810	11,763	328	42,330	146,659
SLOVENIA	1,934	42,342	1,118	168	29,795	75,357	1,160	43,795	1,092	169	30,049	76,266
SPAIN	108,976	862,892	57,620	16,599	324,030	1,370,117	65,381	888,997	56,143	16,720	323,894	1,351,134
SWEDEN	87,675	305,098	30,767	3,650	394,420	821,609	52,601	314,745	30,010	3,680	395,785	796,821
TOTAL EU-27	**913,871**	**16,632,367**	**814,065**	**71,210**	**8,658,091**	**27,089,604**	**548,286**	**17,138,546**	**794,217**	**71,821**	**8,706,461**	**27,259,331**
UK	151,663	1,529,592	59,524	11,512	1,106,657	2,858,948	90,992	1,583,550	58,023	11,587	1,108,367	2,852,518
TOTAL EU-28	**1,030,566**	**18,368,612**	**928,619**	**82,126**	**9,914,020**	**30,323,943**	**618,298**	**18,927,819**	**905,899**	**82,819**	**9,965,336**	**30,500,172**
ICELAND	700	11,077	641	61	9,802	22,281	420	11,508	626	62	9,860	22,477
ISRAEL	6,391	30,736	1,369	841	26,043	65,381	3,835	32,369	1,343	854	26,268	64,669
NORWAY	15,753	312,315	4,891	627	323,999	657,584	9,451	321,812	4,775	632	326,156	662,827
SWITZERLAND	8,084	564,735	2,279	778	434,935	1,010,811	4,850	582,066	2,222	784	437,266	1,027,189
TOTAL 32 COUNTRIES	**1,086,355**	**18,815,722**	**896,454**	**83,099**	**10,706,548**	**31,588,178**	**651,769**	**19,395,989**	**874,583**	**83,818**	**10,762,476**	**31,768,636**

Over the five years, CB rehabilitation was associated with overall health and social care costs of €31.6 billion compared with €31.8 billion for standard rehabilitation (Table 36). CB rehabilitation for eligible stroke patients generated savings in health and social care costs across the 32 countries of around €180 million. The countries with the biggest savings, in terms of health and social care costs if CB rehabilitation was implemented were Germany, with projected five-year savings of €163 million, followed by Switzerland (savings of €16 million) and Austria (savings of €11 million).

With informal care costs and productivity losses included, overall costs were €43.6 billion with CB compared with €43.9 billion for current rehabilitation care. Therefore, from a societal perspective, CB rehabilitation for eligible stroke patients would generate savings across the 32 countries of €295 million over a five-year period (Table 37).

Table 37. Societal costs for patients undergoing CB vs current practice, € thousands

	CB REHABILITATION				CURRENT PRACTICE			
	HEALTH & SOCIAL CARE	INFORMAL CARE	PRODUCTIVITY LOSSES	TOTAL COSTS	HEALTH & SOCIAL CARE	INFORMAL CARE	PRODUCTIVITY LOSSES	TOTAL COSTS
AUSTRIA	754,457	55,819	196,838	1,007,114	765,492	57,663	197,852	1,021,007
BELGIUM	802,543	47,602	212,153	1,062,298	813,073	48,919	213,311	1,075,302
BULGARIA	103,061	16,123	46,222	165,407	102,176	16,705	46,525	165,406
CROATIA	71,461	19,057	31,957	122,474	72,176	19,732	32,200	124,108
CYPRUS	8,070	2,235	7,470	17,776	8,007	2,304	7,516	17,827
CZECH REPUBLIC	364,715	50,382	116,522	531,619	374,152	52,219	117,090	543,461
DENMARK	429,846	32,453	188,739	651,038	434,302	33,494	189,450	657,246
ESTONIA	39,988	4,056	14,850	58,894	40,219	4,214	14,918	59,351
FINLAND	696,138	13,593	160,880	870,611	686,682	13,993	161,451	862,126
FRANCE	2,350,773	189,633	849,960	3,390,365	2,322,218	194,367	853,825	3,370,411
GERMANY	9,811,447	500,573	3,094,716	13,406,736	9,974,192	516,904	3,105,620	13,596,717
GREECE	438,008	44,703	102,330	585,041	439,958	45,769	102,926	588,653
HUNGARY	309,849	24,322	75,297	409,468	316,856	25,240	75,855	417,952
IRELAND	138,498	18,861	69,163	226,521	138,666	19,520	69,629	227,814
ITALY	2,963,121	320,613	1,059,866	4,343,601	2,966,042	328,160	1,063,981	4,358,182
LATVIA	38,223	9,332	27,092	74,648	37,402	9,685	27,240	74,327
LITHUANIA	80,653	9,794	32,063	122,510	81,175	10,165	32,230	123,570
LUXEMBOURG	44,941	2,200	9,302	56,443	45,582	2,263	9,368	57,213
MALTA	13,329	1,123	3,124	17,576	13,562	1,165	3,145	17,871
NETHERLANDS	1,115,325	38,603	382,444	1,536,371	1,120,008	39,784	384,204	1,543,996
POLAND	825,489	64,021	214,887	1,104,397	819,521	66,258	216,863	1,102,642
PORTUGAL	151,550	23,214	103,329	278,093	148,824	23,795	103,724	276,343
ROMANIA	385,952	63,117	125,709	574,778	389,513	65,451	126,762	581,727
SLOVAKIA	145,284	15,820	41,490	202,594	146,659	16,503	41,851	205,012
SLOVENIA	75,357	7,406	20,647	103,410	76,266	7,649	20,795	104,710
SPAIN	1,370,117	209,804	497,752	2,077,673	1,351,134	215,134	500,604	2,066,873
SWEDEN	821,609	21,462	348,374	1,191,446	796,821	22,068	349,453	1,168,342
TOTAL EU-27	**27,089,604**	**1,936,861**	**7,858,606**	**36,885,071**	**27,259,331**	**1,995,309**	**7,898,699**	**37,153,340**
UK	2,858,948	208,089	1,290,328	4,357,365	2,852,518	213,660	1,295,700	4,361,879
TOTAL EU-28	**30,323,943**	**2,146,344**	**9,219,348**	**41,689,635**	**30,500,172**	**2,210,381**	**9,265,236**	**41,975,789**
ICELAND	22,281	595	9,100	31,976	22,477	613	9,134	32,224
ISRAEL	65,381	22,875	72,528	160,783	64,669	23,617	72,903	161,188
NORWAY	657,584	14,075	170,063	841,722	662,827	14,511	170,500	847,838
SWITZERLAND	1,010,811	48,372	356,716	1,415,900	1,027,189	49,813	358,005	1,435,007
TOTAL 32 COUNTRIES	**31,588,178**	**2,239,574**	**9,809,448**	**43,637,200**	**31,768,636**	**2,306,454**	**9,857,625**	**43,932,715**

However, CB rehabilitation did not generate cost savings when compared to current practice for all countries. For these countries, we estimated the incremental cost per QALY gained to assess the cost-effectiveness of CB (Table 38). In these countries, CB was found to be cost-effective both when compared against NICE's willingness-to-pay threshold for an additional QALY and the country's GDP per capita, except for Sweden for which an ICER of above the €22,727 threshold was estimated under a health and social care perspective. For countries not in Table 38, CB rehabilitation was dominant over current practice, i.e. it generated more QALYs and resulted in lower costs.

Table 38. Incremental cost per QALY gained from a health and social care and societal perspectives

	HEALTH AND SOCIAL CARE	COST EFFECTIVE AT € €22,727 PER ADDITIONAL QALY?	SOCIETY	COST EFFECTIVE AT € €22,727 PER ADDITIONAL QALY?	COST-EFFECTIVE COMPARED TO GDP PER CAPITA?
BULGARIA	536	Yes	0.5	Yes	Yes
CYPRUS	946	Yes	CB dominates	Yes	Yes
FINLAND	12,809	Yes	11,494	Yes	Yes
FRANCE	5,194	Yes	3,630	Yes	Yes
LATVIA	1,565	Yes	611	Yes	Yes
POLAND	1,113	Yes	327	Yes	Yes
PORTUGAL	2,369	Yes	1,521	Yes	Yes
SPAIN	4,433	Yes	2,522	Yes	Yes
SWEDEN	23,681	No	22,071	Yes	Yes
UK	1,134	Yes	CB dominates	Yes	Yes
ISRAEL	1,482	Yes	CB dominates	Yes	Yes

In terms of cost savings per patient treated, when CB rehabilitation was compared to current practice, the countries with the largest savings were Switzerland (€1,654), followed by Germany (€1,338), Luxembourg (€1,230) and Austria (€1,011) compared to an average €346 for Europe.

AUTHORS' DISCUSSION

The cost of stroke to Europe's health and social care systems is set to rise, while the productivity losses due to stroke disability and death are set to fall. Much of this can be attributed to the projected aging of the European population – the number of strokes and people living with stroke are set to rise, while the number of people of working age (under 65) is set to fall.

For the 32 European countries under analysis we estimated the total cost of stroke to be €60 billion in 2017, of which €27 billion (45%) were incurred by European healthcare systems and a further €5 billion (8%) were incurred by European social care systems, representing an annual stroke care spend of €59 per capita in Europe. For the EU-28, the estimated total cost of stroke was €57 billion a year, of which €30 billion (52%) were incurred by EU health and social care systems, representing an annual stroke care spend of €57 in the EU. The healthcare spend on stroke care represented 1.65% of the total healthcare budget for European healthcare systems, and 1.64% for those in the EU.

Hospital inpatient care accounted for over 60% (€16 billion) of stroke related healthcare costs, followed by outpatient specialist care (€5 billion, 18%), primary care (€3 billion 13%), pharmaceuticals (€1 billion, 5%) and emergency care (€919 million, 3%). However, these costs varied widely between countries. For example, in Cyprus, hospital care accounted for 11% of total healthcare costs (€1 million), with most stroke-related expenditure devoted to outpatient care and pharmaceuticals. By contrast, in Switzerland, 86% of stroke-related healthcare costs were devoted to hospital care (€482 million), with less than 10% (€43 million) of costs being devoted to primary, outpatient and emergency care.

The results from our regression analyses indicate that per capita stroke-related health and social care costs were significantly associated with increases in a nation's wealth resulting in increased stroke-related costs. However, we found that even for countries with the same levels of national income, health and social care expenditure on stroke varied widely. For example, even though Germany's (€39,600) and Belgium's (€38,700) per capita GDP was similar in 2017,[3] Germany's expenditure on stroke-specific health and social care was nearly twice that for Belgium on a per capita basis (€113 vs. €68, respectively, adjusted for price differentials). We also observed a clear and significant linear trend between increases in overall healthcare expenditure and stroke-related health and social care expenditure, with each additional Euro of overall health expenditure per capita increasing stroke-related care costs by €0.0135.

Although, cost differences between European countries can be partly explained by differences in GDP and system configuration (for example the number of inpatient days in Finland due to stroke was 98 per 1,000 in the population, compared with 17 in Spain), a better understanding is required of variations in health expenditures. Presenting data revealing differences in costs across countries should provide a solid foundation for further research and discussion, but we cannot in this study explain all the patterns revealed. For example, the differences in medication costs across countries could be explained by differences in the prices paid for the same medicines, higher volumes of drug consumption or differences in the types of drugs consumed. In turn, such differences may be related to price setting and reimbursement mechanisms, variations in clinical practice, or other factors. Future research may clarify these possible explanations. More generally, careful evaluation of expenditure decisions, within a clear cost-effectiveness framework, similar to that employed by NICE, might improve value-for-money and strengthen moves towards stronger evidence-based care across the Europe.[235]

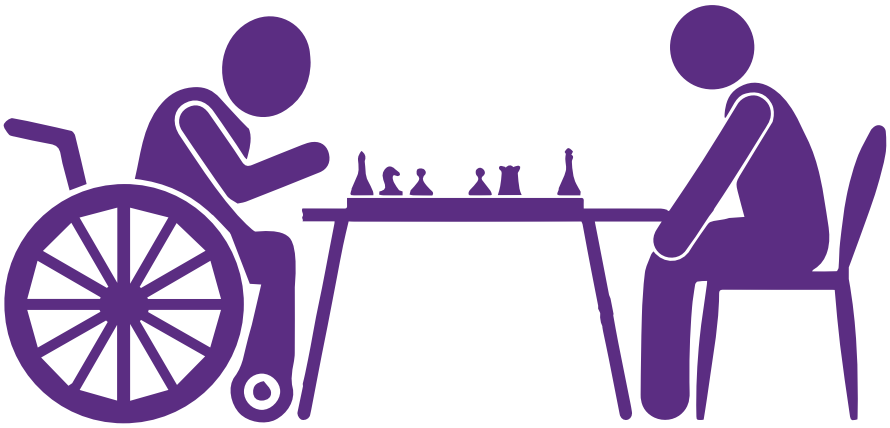
We have estimated the costs of stroke for the EU over the last 15 years. In 2003 we estimated the total care costs of stroke to be €34 billion for the 25 countries forming the EU at that time.[4] These costs rose to €38 billion in 2009 (27 EU countries),[236] and to a further €45 billion in 2015 (28 EU countries).[237] In our current analysis, we found that for the EU-28 total costs of stroke were estimated at €57 billion for 2017. By using the same approach to estimate the costs of stroke over time, it is possible to reliably compare the economic burden of stroke over time, which are useful to decision makers and health policy planners, as they provide evidence that will be helpful when evaluating the impact of public health interventions to decrease the prevalence of stroke risk factors (for example obesity, salt intake, smoking, alcohol consumption, sedentary lifestyles).

It is worth noting, however, that this is the first analysis to include the costs associated with long-term institutionalisation in a nursing/residential care home due to stroke. We have also been better able to fully utilise data in the SHARE database, to better capture the proportion of primary, outpatient and emergency care due to stroke. In previous analyses, in the main, this information was obtained using the assumption that the proportion of visits to primary, outpatient or emergency care would be the same as the proportion of hospital discharges due to stroke. Data from this analysis, does show, that for the great majority of countries, previous assumptions were underestimating the costs of primary, outpatient and emergency care in stroke.

However, these costs are unlikely to remain stable over the next decades. It is undisputed that over the next decades significant demographic change will take place across Europe, as a result of decreasing birth rates for many countries, an ageing population, and, for many countries, a loss in the total population, particularly at a working age.[238] Therefore, the number of people

having a stroke, living with it and dying from it will likely change, and with it, the economic costs associated with stroke.

By 2040, in the 32 European countries under study, the population is projected to fall in 12 countries, and overall, to increase in Europe by just 4%. However, due to demographic change, the number of those aged 85 years and over is projected to increase by 89% by 2040.

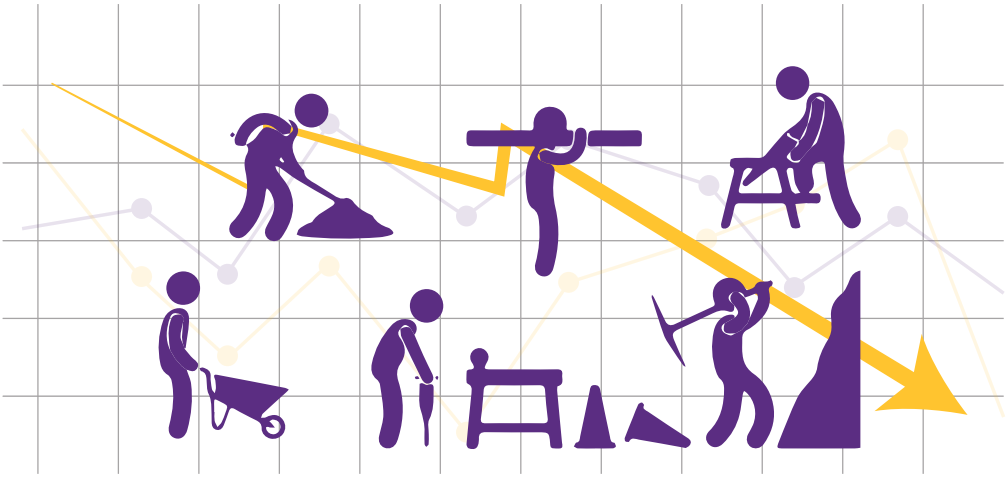


As a result, the projected number of people living with stroke will increase by 35% (from nine million in 2017 to 12 million in 2040), with all countries projected to see the number of prevalent cases increase by at least 10% (Lithuania) and up to a maximum of 94% (Luxembourg). Consequently, we estimated the costs of stroke to increase from €60 billion in 2017 to €75 billion in 2030, €80 billion in 2035 and €86 billion in 2040. This means that, in just 13 years, the cost of strokes are projected to increase by 26%, and by 44% in 23 years' time.

Stroke-related healthcare costs are also projected to rise at a similar rate, increasing from €27 billion in 2017 to €33 billion in 2030, €35 billion in 2035 and €37 billion in 2040. Therefore, stroke-related healthcare costs will increase by 23% in 2030, and by 39% in 2040. However, there is considerable variation on the rate of increase in stroke-related healthcare costs between countries. For example, while healthcare costs associated with stroke are projected to more than double by 2040 in Malta, in Lithuania and Bulgaria, stroke-related healthcare costs are projected to increase by less than 15%. Such differences are explained, in part, by the differing projected demographic change European countries will experience. Whereas the population of Malta is expected to grow by 10% between 2017 and 2040, and the number of those aged 85 years and over by 228%, in Lithuania the population will decrease by a quarter over the same time period, with the population 85 years and over increasing by 51%.

As opposed to other categories of costs, productivity losses due to morbidity or mortality associated with stroke are projected to decrease, especially by 2040. Mortality losses associated with premature death due to stroke will decrease from €6.2 billion in 2017 to €6.1 billion in 2030, and €6.0 billion in

2035 and 2040. This represents a decrease in costs of 4% between 2017 and 2040. For morbidity losses, costs are projected to decrease from €6.3 billion in 2017 to €6.2 billion in 2040 (a decrease of 1%). Such decreases are due to the overall projected reduction in the population aged 65 years or less (i.e. of work age) across the 32 European countries under study by 2040. For example, in the four most populous countries in the EU, once the UK is no longer a member state, there will be considerable falls in the working age population. In Germany, the working age population is projected to decrease from 54 million in 2017 to 49 million in 2040 (9% decrease). In France, the projected decrease will be of 2% (42 million to 41 million, respectively), and in Italy and Spain it will be of 13% (Italy: 39 million to 34 million, and Spain 31 million to 27 million).



With stroke being strongly associated with age, the projected increases in the number of older people in Europe, will result in a higher number of people suffering a stroke and living with stroke in 2040. The resulting increase in the costs of stroke, as well as those of a wide array of conditions, [239] [240] will result in additional costs being placed in already strained health and social care systems across Europe. [241] Therefore, European countries will have to invest in stroke interventions known to be cost-effective in order to halt the expected increase in costs and overall burden, whilst increasing health outcomes for the population. As a result, this study evaluated investments into three different interventions across the stroke pathway, mainly: prevention to reduce the likelihood of people suffering a stroke in the first place; acute treatment in order to minimise stroke damage to the brain and reduce the likelihood of disability; and rehabilitation to improve the quality of life of stroke survivors.

Overall, we found that:

- routinely treating patients with known atrial fibrillation using warfarin or any of the new anticoagulant therapies;
- acutely treating non-minor ischaemic stroke patients with mechanical thrombectomy;
- providing rehabilitation in a community setting once stroke patients were discharged from hospital stroke patients

would all be cost-effective at the European level generating increases in quality-adjusted life expectancy at levels found to be very good value for money. In addition, with the exception of NOACs, interventions would also generate substantial cost savings.

In the case of anticoagulation therapy, we found that warfarin would yield substantial cost savings across Europe when compared to current practice. However, it would generate the lowest total number of QALY gains when compared with the four NOACs under study, with edoxaban and rivaroxaban being at the lower and upper range bound, respectively. On the other hand, routine use of warfarin was the only anticoagulant therapy that was found to be both more effective and less costly than current practice consistently across all the 32 countries under study.

Except in six of the wealthier countries in Europe on a per capita basis (i.e. Germany, Switzerland, Norway, Finland, Luxembourg and Iceland), each of the four NOACs were estimated to be more costly than current practice. Although they were also found to be very cost-effective at the European level, for some Eastern European countries, in particular Bulgaria, full adoption of NOACs was not found to be cost-effective due to their high cost and the relative low national incomes, and therefore smaller healthcare budgets.

Acutely treating non-minor ischaemic patients with mechanical thrombectomy, as opposed to current standard care, was also found to consistently lead to higher quality-adjusted life expectancy across all 32 European countries. In addition, MT was found to generate both health, social care, and overall societal care cost savings across Europe overall. However, the costs of the intervention were not outweighed by savings of similar magnitude in health and social care costs in almost half the countries under study. Adopting NICE's cost-effectiveness threshold (€22,727 per QALY gained), we found that MT was cost-effective when compared to current practice in all 32 countries. Adopting a nation's income as proxy for the cost-effectiveness threshold, we found that MT was cost-effective in all but one country (Bulgaria).

Although the impact of CB rehabilitation was modest on a given stroke patient, CB rehabilitation increased quality-adjusted life expectancy considerably at the population level given the high numbers of eligible patients. In addition, it was found to be cost-effective as opposed to standard care (i.e. rehabilitation in hospital settings) from a health and social care, and societal perspective in European countries, and in Europe overall.

To the best of our knowledge, this is the first study to quantify the current and future projected costs of stroke, and to identify the impact of investing in promising cost-effective interventions to prevent, treat and help stroke patients in their rehabilitation across 32 European countries. We believe that our study will be of use to policy makers when assessing whether or not to make substantial cost commitments in stroke care.

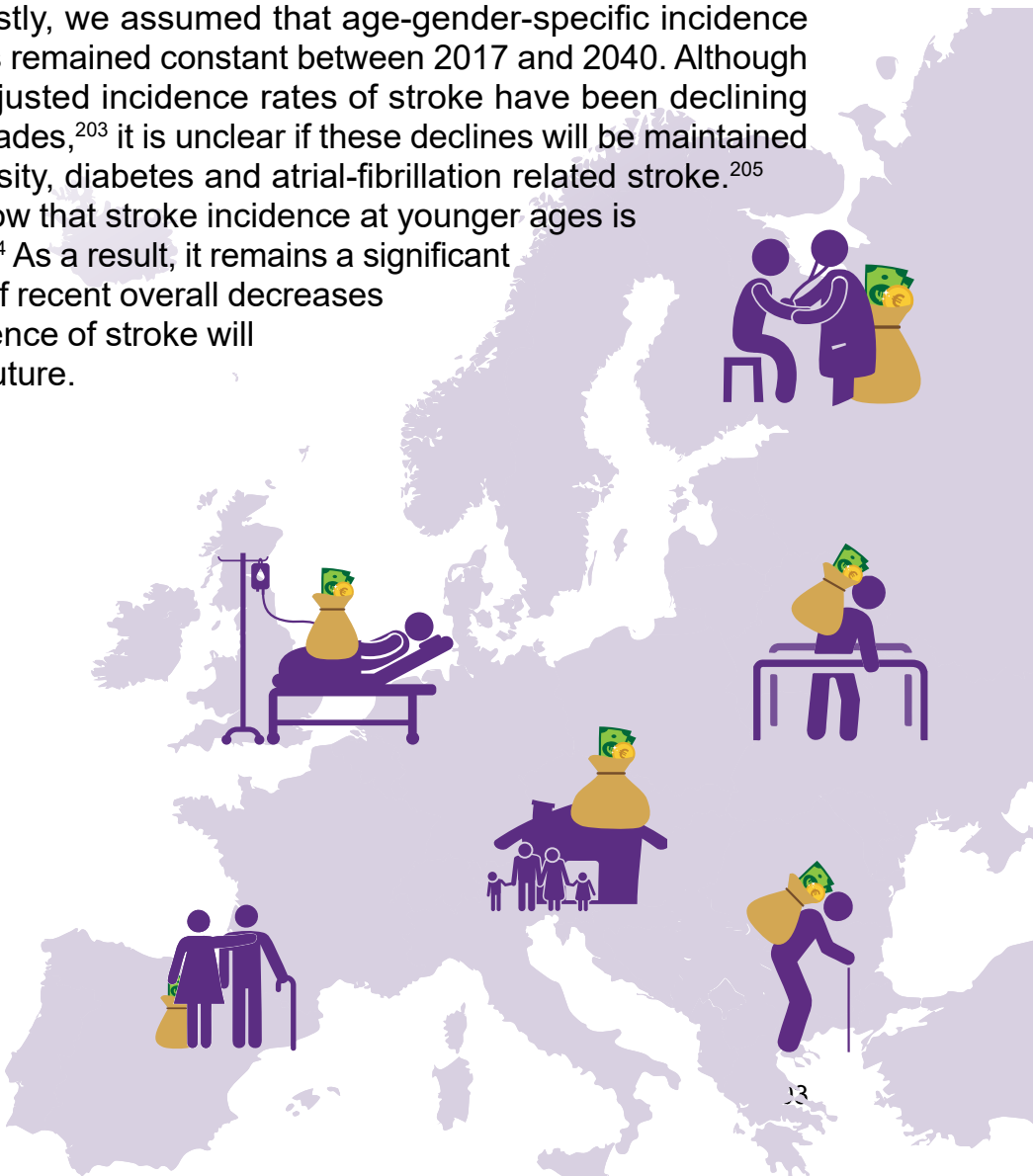
However, our study has a number of limitations. The precision of our study depends on the quality and availability of comparable stroke-related data across countries. Given the 32 countries under analyses, the eight major categories of cost examined, and the unit costs needed to value each resource use type, over 200 sources were consulted and utilised for this study. Our study encountered deficiencies in information on related resource use and unit costs. As stated above, the vast majority of countries report no data on the number of primary, outpatient and emergency care visits due to stroke. As a result, we had to make use of SHARE, a cross-national panel database of micro-data on health, socio-economic status and social and family networks. For this study we used data collected in Wave 2, Wave 4 and Wave 6 which included over 30,000 respondents resident in 21 European countries (Austria, Belgium, Croatia, the Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Israel, Luxembourg, the Netherlands, Poland, Portugal, Slovenia, Spain, Sweden and Switzerland). As a result, for countries not in SHARE, we had to combine data from similar countries that were in SHARE to obtain care estimates for the 11 remaining countries.

The costs for sick leave and early retirement due to incapacity did not include expenditure on sick leave benefits. One of the reasons was to avoid valuing the same spell of leave twice and another was that sick leave benefits are considered to be “transfer payments”. This means that they are neither a cost nor a gain to society as they represent a redistribution of income from the paying government to the stroke patient without any resource consumption (for example there is no exchange of services). Both UK and US guidelines caution against including these transfer payments in any economic analysis.[242 243] Furthermore, our sick leave and early retirement costs were only estimated during the time it takes to replace a worker with another from the pool of unemployed, i.e. the friction period. An alternative would have been to value worker absence in terms of lost earnings without any adjustment, i.e. the human capital approach. However, as there is little consensus as to which approach is best,[242 244] we adjusted for the

'friction period' to be consistent with previous work and allow meaningful comparisons with conditions such as cancer, blood disorders and dementia.[5] [6] [8] Nonetheless, in sensitivity analyses, we estimated that the total costs of cancer increased from €60 billion (using friction-adjusted costs) to €65 billion (using the human capital approach).

Our estimates on the costs of stroke in 2017 are likely to be an underestimate. Some categories of healthcare costs, such as health education, public health activities, supportive treatments (for example anti-depressants, anxiolytics), home adaptations, and care provided outside the healthcare system (for example social worker visits, paid formal care, meals on wheels, and hospice care based outside hospitals) is not recorded in healthcare statistics. These categories of cost were not included because of data limitations and the inability to collect these data for all countries under study. Additional research is also necessary to assess the costs incurred by working people with stroke returning to their post but whose productivity is diminished because of illness.

Although our study projects the likely impact of stroke on healthcare and social care systems, as well as in the wider economy, as a result of demographic change taking place across Europe, a number of assumptions had to be made. Firstly, we assumed that age-gender-specific incidence and prevalence rates remained constant between 2017 and 2040. Although age- and gender-adjusted incidence rates of stroke have been declining over the last two decades,[203] it is unclear if these declines will be maintained given the rise in obesity, diabetes and atrial-fibrillation related stroke.[205] Recent data also show that stroke incidence at younger ages is starting to increase.[204] As a result, it remains a significant challenge to assess if recent overall decreases in age-specific incidence of stroke will be observed in the future.



We also assumed that future mortality rates after stroke would remain the same as those observed in 2017. Although there is some evidence that stroke fatality has been improving over time,[207] it is unclear how increased survival rates will impact functional ability, quality of life and therefore, subsequent care needs both from the health and social care systems, but also from friends and families. For example, it is unclear if future patients surviving a stroke who would have otherwise died, would become disabled and hence require increased levels of healthcare, social care and informal care. In addition, evidence from population-based cohort-studies using multiple methods of stroke ascertainment,[203] the gold-standard when assessing the incidence and health outcomes after stroke,[208] have not found evidence of improved survival one-year after stroke over the last decade.[209]

Another important assumption for this study, is that we assumed that the probability of receiving informal care, and the hours of care received, after stroke will remain the same in the future as that observed in Work package 1 using SHARE data.[2] With predicted declines in the working age population it is unclear how the burden of caring by friends and family would be spread. For example, it might be the case that individuals of working age will have a higher burden of care placed on them. Alternatively, non-working age population could end up providing more care, with more of the burden of care being placed on spouses of relatively older stroke survivors. Or simply put, informal care is displaced by an increase in more formal care, with paid carers providing more of the care.

In terms of the Markov models used to estimate the impact of stroke interventions at the population level, the precision of our findings depends on the quality and availability of data, as well as several assumptions made when building the models. The lack of effectiveness data that were directly applicable to each of the 32 European countries led to the assumption that the relative effects of the interventions were constant across Europe, i.e. no heterogeneity across countries. However, the relative effects of each intervention under evaluation were derived from head-to-head randomised clinical trials and meta-analysis of trials, where the control group represented current practice / standard care. Furthermore, given the lack of data, we assumed that anticoagulant, aspirin and MT (i.e. device, alteplase, consumables and tests) intervention costs were the same across all countries. We also assumed that the type and number of healthcare professionals needed to provide the MT and rehabilitation interventions were the same across all countries but were valued using country specific unit costs.

The benefits and costs of the three interventions under evaluation were estimated over a five-year period which may not be long enough to reflect all important differences compared to current practice. In particular, the costs and benefits of the warfarin intervention are likely to be conservative, as we would expect its effect on the incidence of stroke to go beyond the five

year period. However, the intervention options were assessed each against current practice/standard care, and not against each other, hence limiting the ability to inform an economic decision where all these strategies were to be included as relevant alternative and mutually exclusive alternatives.

Differences in stroke-related healthcare resource use across the 32 European countries were estimated by converting UK data from OXVASC using country-specific weights. The weights were based on aggregate-level national data (for example number of inpatient days per capita for all diagnosis, number of inpatient days by hospital discharge with stroke) and represent only proxy measures for the real healthcare system differences across all European countries. Alternative approaches to estimating the country weights could have resulted in different estimates of costs per country. For example, adopting country weights adjusted by age group resulted in different societal cost savings. However, sensitivity analysis results showed that these alternative approaches were likely to lead to the same cost-effectiveness judgements.

The lack of country-specific cost-effectiveness thresholds across many of the 32 European countries represented an additional challenge to determine the cost-effectiveness of the interventions under evaluation when there were no cost savings. We could expect that the willingness to pay for an additional QALY may vary across countries with values different from those adopted in our analysis. We used two different thresholds, England's NICE threshold (€22,727 per QALY gained) and the country's per capita GDP threshold, to determine the cost-effectiveness of each intervention across the 32 countries. However, the threshold value adopted only changed the cost-effectiveness conclusion in a minority of countries.

Finally, it is relevant to quantify the decision uncertainty associated with each of the three interventions under study. However, we report only point estimates without measures of uncertainty. The quantification of decision uncertainty does presents a set of new challenges, such as how to aggregate the uncertainty about the several assumptions used in the analysis (for example country weights, constant relative effects across countries) with the uncertainty about the precision of the model inputs in a metric that is easily understandable to policy makers. In future work, we plan to undertake a series of scenario and probabilistic sensitivity analysis to better characterise the decision uncertainty across each country.

In conclusion, our study provides a snapshot of the economic consequences posed by stroke to 32 European countries in 2017. It estimates that stroke costs these countries €60 billion a year, and together with the evidence we have gathered over the last 15 years,[4 236 237] it would appear that the costs of stroke are rising over time, partly due to an ageing population, making the absolute number of people living with stroke increase throughout Europe.

This study has also projected that the costs of stroke in the 32 countries under study will increase by 44% between 2017 and 2040, with some countries seeing rises in stroke-related costs of nearly 100%. These projected increases will undoubtedly place a burden in already stretched health and social care systems, but also in the overall economy, with informal carers having to take greater responsibility for the care of stroke survivors. As a result, European countries will have to put interventions and policies in place to try and mitigate these cost increases, whilst also maximising the health outcomes and quality of life for stroke survivors.

Finally, and in conclusion, our study provides an estimate of the costs and outcomes when investing in different interventions across three different points in the stroke pathway. In a context of increasing burden of stroke in Europe, it is recommended that European countries adopt:

- anticoagulant therapy in known atrial fibrillation cases to prevent stroke in the first place;
- mechanical thrombectomy in order to reduce both short- and long-term disability;
- community-based rehabilitation to improve stroke patients' ability to perform activities of daily living.

These three interventions will result, for the vast majority of European countries, in health, social care and societal cost savings as well as increases in quality-adjusted life expectancy. In addition, decisions about the choice of anticoagulant therapy to routinely prescribe, the individual wealth of a country should guide this decision as some therapies were not cost-effective in relatively less affluent Eastern European countries.

SAFE'S CONCLUSION

Accurate predictions about the future are notoriously difficult to make. But our research provides very strong indicators of the overall future costs of stroke and of the component parts of stroke care. We are confident that our findings are actually underestimates of the future cost of stroke, simply because there were areas of expenditure for which there is too little data. And we made sure that the assumptions we had to make in order to provide indicators of future costs were conservative. Those assumptions are fully documented in the full version of this report and in published and soon to be published research papers.

It is clear that the economic burden of stroke across the 32 countries we studied is huge.

The total cost of stroke in these 32 countries was €60 billion in 2017.

And the costs will rise over the next 20 years. Between 2017 and 2030 overall costs of stroke are projected to rise by €25 per citizen. This goes up by €33 per citizen from 2017 to 2035 and €42 per citizen from 2017 to 2040. The costs of stroke in the 32 countries under study are projected to increase by 44% between 2017 and 2040, with some countries seeing rises in stroke-related costs of nearly 100%.

These projected increases will undoubtedly place a burden in already stretched health and social care systems, but also in the overall economy, with informal carers having to take greater responsibility for the care of stroke survivors. As a result, European countries will have to put interventions and policies in place to try and mitigate these cost increases, whilst also maximising the health outcomes and quality of life for stroke survivors.

The results show that the amount of stroke-related health and social care costs in individual countries were significantly associated with that country's wealth – the wealthier the country the more it spent on stroke. But even for countries with the same levels of national income, health and social care expenditure on stroke varied widely. More research is needed so we can better understand the reasons for this. What is clear, however, is that the costs effectiveness of different interventions is key. Careful evaluation of expenditure decisions, within a clear cost-effectiveness framework, similar to that employed by NICE, could improve value-for-money and strengthen moves towards stronger evidence-based care across the Europe.

We studied the economic impact of three specific interventions which already have a strong evidence base for their clinical effectiveness. All three – treating known atrial fibrillation patients with anti-coagulation, providing mechanical

thrombectomy in acute ischaemic stroke and providing community-based rehabilitation – would increase the number of extra years of good health across the population and have been shown to be costs effective in our study. In most cases they would save money. Clearly there is no good reason not to prioritise adopting these three interventions.

Based upon our findings for these three interventions, SAFE believes that improving stroke care at all stages of the pathway, from prevention to life after stroke, would not only improve outcomes for people, but would also reduce the overall economic burden of stroke. Risk factors for stroke, such as high blood pressure and diabetes, are too often undetected; many stroke patients across Europe are still not getting access to acute stroke units, (let alone mechanical thrombectomy); and the economic impact of stroke on individuals and families can be devastating.

We call on all countries across Europe to invest in better stroke care, believing this will be not just improve outcomes, but will be cost effective and will reduce the economic burden of stroke.

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ABOUT SAFE

The Stroke Alliance for Europe (SAFE) an international non-profit-making organisation formed in 2004 in Brussels, Belgium. It is the voice of stroke patients in Europe, representing a range of stroke support organisation from more than 30 European countries.

SAFE's goal is to decrease the number of strokes in Europe by advocating for better prevention, access to adequate treatment, post-stroke care and rehabilitation.

For more information about SAFE, please visit **www.safestroke.eu**.

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