

Economic burden of non-malignant blood disorders across Europe: a population-based cost study



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Summary

Background Blood disorders comprise a wide range of diseases including anaemia, malignant blood disorders, and haemorrhagic disorders. Although they are a common cause of disease, no systematic cost-of-illness studies have been done to assess the economic effect of non-malignant blood disorders in Europe. We aimed to assess the economic burden of non-malignant blood disorders across the 28 countries of the European Union (EU), Iceland, Norway, and Switzerland.

Methods Non-malignant blood disorder-related costs (WHO International Classification of Diseases, 10th revision [ICD] D50–89) were estimated for 28 EU countries, Iceland, Norway, and Switzerland for 2012. Country-specific costs were estimated with aggregate data on morbidity, mortality, and health-care resource use obtained from international and national sources. Health-care costs were estimated from expenditure on primary care, outpatient care, emergency care, hospital inpatient care, and drugs. Costs of informal care and productivity losses due to morbidity and early death were also included. To these costs we added those due to malignant blood disorders (ICD-10 C81–96 and D47) as estimated in a Burns and colleagues' companion Article to obtain the total costs of blood disorders.

Findings Non-malignant disorders of the blood cost the 31 European countries €11 billion in 2012. Health-care costs accounted for €8 billion (75% of total costs), productivity losses for €2 billion (19%), and informal care for less than €1 billion (6%). Averaged across the European population studied, non-malignant disorders of the blood represented an annual health-care cost of €159 per ten citizens. Combining malignant and non-malignant blood disorders, the total cost of blood disorders was €23 billion in 2012.

Interpretation Our study highlights the economic burden that non-malignant blood disorders place on European health-care systems and societies. Our study also shows that blood disorder costs were evenly distributed between malignant and non-malignant blood disorders. Our results should be of use to decision makers and research-funding authorities charged with allocating health-care resources and research funds.

Funding European Hematology Association.

Introduction

Blood disorders comprise a wide range of diseases including anaemia (eg, nutritional, haemolytic, or aplastic), malignant blood disorders (eg, Hodgkin's lymphoma, non-Hodgkin lymphoma, multiple myeloma, or leukaemia), haemorrhagic disorders (eg, haemophilia or purpura), blood cell disorders (eg, agranulocytosis), and disorders involving blood-forming organs (eg, spleen) or the immune mechanism (eg, hypogammaglobulinaemia or sarcoidosis). The most common blood disorder is anaemia, which reduces the number of red blood cells therefore hampering the ability of blood to carry oxygen. Approximately 1.6 billion people worldwide are affected by anaemia, roughly one in every four people,¹ and anaemia is particularly prevalent in people with other diseases, such as cancer, with prevalence surveys showing that more than 60% of patients with cancer have anaemia.²

Malignant blood disorders are also one of the ten most common forms of cancer both in terms of incidence and mortality. According to the International Agency for Research on Cancer,³ in 2012, 188 000 people (36 per

100 000) were diagnosed with malignant blood disorders in the European Union (EU), Norway, Iceland, and Switzerland, and 483 000 people were alive with the disorders (93 per 100 000). Although early detection, diagnostic approaches, and treatments have improved survival, approximately 100 000 people in the EU die of blood cancers each year.³

In this study, we aimed to assess the economic burden of non-malignant blood disorders across the 28 countries of the EU, Iceland, Norway, and Switzerland, including direct health-care costs, informal care costs, and productivity losses for the most recent year for which data were available (2012). As part of this study, we also combined the costs of malignant and non-malignant disorders to obtain the total costs of all blood disorders in 2012 and for purposes of comparison.

Methods

Analysis framework and data sources

Costs of non-malignant blood disorders were estimated for all 28 countries in the EU, Iceland, Norway, and Switzerland. Non-malignant blood disorders were

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Research in context

Evidence before this study

We searched MEDLINE and the UK National Health Service Economic Evaluation Database for studies published in English between Jan 1, 2000, and Dec 31, 2015. We used the search terms “costs*”, “economic burden”, “cost of illness”, or “burden of illness”, and “blood disorder”. Health-care costs for anaemia associated with particular disease groups have been assessed in several countries. The economic burden of less common non-malignant blood disorders—namely, haemophilia, neutropenia, and thrombocytopenia—has also been assessed in some European countries. However, the focus and methodology of these studies vary considerably. We did not identify any studies that estimated the economic burden associated with the full range of non-malignant blood disorders in any country.

Added value of this study

To our knowledge, our study is the first to assess the economic burden of all non-malignant blood disorders for

31 European countries. We estimated the total costs of non-malignant blood disorders to be €11 billion in 2012 to the 28 EU countries, Iceland, Norway, and Switzerland. Total health-care costs represented 75% of the €11 billion and productivity losses due to illness represented 19%. Non-malignant blood disorders accounted for nearly half of the overall economic burden associated with all blood disorders.

Implications of all the available evidence

Our results highlight that non-malignant blood disorders equate to nearly half of the overall economic burden of all blood disorders and therefore have a substantial effect on health-care budgets. These findings provide new evidence that can aid decision makers and research-funding authorities charged with allocating health-care resources and research funds.

defined by the WHO International Classification of Diseases, 10th revision (ICD-10), codes D50–89 (diseases of the blood and blood-forming organs and some disorders involving the immune mechanism). The costs of malignant blood disorders (ICD 10 C81–96 and D47) have been published in a companion Article in *The Lancet Haematology* (see Burns and colleagues⁴). Therefore, for this study, we estimated the costs of non-malignant blood disorders, to which we added the costs for malignant blood disorders.

For all countries we used the same methodological framework to obtain data and value non-malignant blood disorder-related resource use.^{5–7} An annual time-frame was adopted whereby resource use attributable to non-malignant blood disorders within the most recent year for which data were available was measured, irrespective of disease onset. Resource use was valued by applying country-specific unit costs. Costs were, where applicable, updated to 2012 prices⁸ and national currencies were converted to euros using 2012 exchange rates.⁹ To allow comparisons between countries, we also adjusted for cost of living with the purchasing power parity method.¹⁰

An extensive range of international and national sources were consulted for country-specific aggregate data, including WHO, the Organisation for Economic Co-operation and Development, the Statistical Office of the European Communities (EUROSTAT), and national ministries of health and statistical institutes (appendix pp 2–8). We also consulted peer-reviewed published studies or national reports from governmental or professional bodies. Data availability was presented using a grading system of A (national non-malignant blood disorder-specific data), B (non-malignant blood disorder-specific data from a survey or sample), C (national data,

but not disease specific), D (no national data available). For example, inpatient care was graded A for all countries. If no data were found, extrapolations were done from similar countries (eg, similar health-care expenditure per person, life expectancy, and geographical location).

Health-care expenditure

Non-malignant blood disorder-related health-care service included: primary care, accident and emergency (A&E) care, hospital inpatient care, outpatient care, and drugs (appendix pp 2–5). For eight countries, national data were missing (grade D level of evidence) for A&E attendance for any cause (Croatia, Czech Republic, Greece, Iceland, Lithuania, Luxembourg, Slovenia, and Sweden). All-cause A&E attendance was estimated using attendance rates from similar countries and applying these to the population size¹¹ of the countries without data (appendix p 3).

Drug expenditure for non-malignant blood disorders consisted of sales for medicinal products under the Anatomical Therapeutic Chemical (ATC) Classification System for blood and blood-forming organs (code B), which were obtained for all countries. However, ATC B will include medicinal products for the treatment of other conditions. In Europe, the proportion of ATC B drug expenditure due to non-malignant blood disorders was reported for the Netherlands (23%)¹² and Germany (17%).¹³ In the absence of other data, the drug expenditure due to non-malignant blood disorders was estimated by multiplying the average proportion from Germany and the Netherlands (20%) by the ATC B expenditure in each of the remaining countries.

Country-specific population size data obtained from EUROSTAT¹¹ were used to estimate health-care costs per capita.

See Online for appendix

Informal care costs

Informal care costs were equivalent to the opportunity cost of unpaid care (ie, the time [work or leisure] that carers forego), valued in monetary terms, to provide unpaid care for relatives with non-malignant blood disorders. The number of hours of informal care that patients received across European countries were obtained from the Survey of Health, Ageing and Retirement in Europe (SHARE).¹⁴ SHARE is a multidisciplinary and cross-national panel database of micro data for health, socioeconomic status, and social and family networks of approximately 123 000 individuals across 20 European countries.¹⁴ We used waves 2 and 4 of the SHARE survey, which collected data on more than 30 000 individuals resident in 17 EU countries in 2006 and 2010. For the remaining 14 countries, we estimated the hours of informal care by combining data from similar countries in waves 2 and 4 (appendix p 6). For patients who had died during the previous 12 months, estimates of the hours of informal care as reported by caregivers in SHARE were applied to the numbers of people dying of a malignant blood disorder.¹⁵ For patients alive with a non-malignant blood disorder, estimates were obtained from SHARE on the number of hours of informal care required by individuals severely limited in daily activities. Given the absence of prevalence estimates for non-malignant blood disorders, we used estimates on the prevalence of malignant blood disorders³, and to these apply country-specific ratios of the number of hospital bed-days due to malignant and non-malignant blood disorders out of all hospital stays. These estimated prevalence figures for non-malignant blood disorders were then combined with the average number of hours of informal care (appendix p 5).

Productivity losses

Productivity costs included the foregone earnings related to non-malignant disorders-attributable mortality and were estimated using the number of disease-related deaths,¹⁵ national annual earnings,¹⁶ and employment rates.¹⁷ Future earnings lost because of mortality were discounted to present values using a 3·5% annual rate (ie, the value society attaches to present as opposed to future costs).¹⁸

Costs due to non-malignant blood disorder-related morbidity comprised both the costs associated with individuals being declared incapacitated or disabled because of the disease (permanent absence), and the costs due to individuals taking sickness leave for a defined time period (temporary absence; appendix p 7). Costs were estimated by multiplying the total working time lost owing to non-malignant blood disorders by mean earnings.¹⁶ Furthermore, we used the friction period approach whereby costs for temporary and permanent absence were counted only during the time taken to replace a worker (first 90 days of work absence).¹⁹

All health and non-health-care resource use was valued using country-specific unit costs (appendix pp 10, 17–24).

Statistical analysis

We estimated the effects on the total costs of non-malignant blood disorders of changes in health-care resource use (all categories) and earnings (men and women) across all countries (adopting a sensitivity range of +20% to –20%), proportion of ATC B-related pharmaceutical expenditure due to non-malignant blood disorders (adopting a sensitivity range of 17% and 23%), discount rate for productivity losses due to early mortality (adopting 10%, 3·5%, and 0% rates), and adoption of no friction period for costs due to disease-related morbidity.

We report costs for non-malignant blood disorders, which were then combined with the costs of malignant blood disorders from Burns and colleagues' companion Article⁴ to obtain the costs of all blood disorders that are also presented here. To investigate correlations in non-malignant blood disorder-related health-care expenditure between countries, we undertook ordinary least-squares univariate regression analyses, using national income (as measured using gross domestic product [GDP] per capita), and crude blood disorders mortality per 1000 people in the population, respectively, as explanatory variables. 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 14.1).

Role of the funding source

The funder of the study, the European Hematology Association (EHA), is the European society of medical professionals for haematology. EHA commissioned the University of Oxford to do an independent study of the costs of blood disorders. EHA had no role in study design, data collection, data analysis, and data interpretation. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Non-malignant blood disorders cost the 31 European countries being studied €11 billion in 2012 (table 1), of which, €10·6 billion (97%) were accrued in the 28 EU countries alone. This figure represents a total cost of €211 per ten European citizens (table 2). The five most populous countries (France, Germany, Italy, Spain, and the UK) accounted for €7 billion (68% of all costs). Non-malignant blood disorders cost European health-care systems €8 billion in 2012, representing 75% of the total economic burden for the disorders. Inpatient care was the major cost component at €4 billion, accounting for 43% of health-care costs, followed by expenditure on drugs at €2 billion (28% of total health-care costs).

Informal care accounted for more than 55 million h with a cost of €618 million (6% of total costs, table 1). More than 31 000 working-years were lost due to mortality, which were valued at €602 million (5% of

	Health-care costs						Productivity losses		Informal care costs (€)	Total costs (€)
	Primary care (€)	Outpatient care (€)	Accident and emergency (€)	Inpatient care (€)	Drugs (€)	Total health care (€)	Mortality (€)	Morbidity (€)		
Austria	3604	6043	2466	58534	33614	104261	15981	14727	7045	142015
Belgium	11178	22232	2964	109612	91907	237893	15872	19272	22123	295161
Bulgaria	1924	2283	280	8599	9660	22746	1763	29528	539	54575
Croatia	3865	2159	7490	10392	7657	31564	1553	11083	756	44956
Cyprus	441	1172	319	508	2626	5067	614	1093	1202	7975
Czech Republic	3536	8655	1671	25868	49627	89357	2547	11669	3747	107319
Denmark	6057	16084	3702	41529	36830	104203	14317	23108	16894	158522
Estonia	584	856	468	2323	2672	6902	304	20299	205	27710
Finland	5919	17206	2483	40108	31084	96801	5732	10250	2613	115395
France	23455	37184	4518	886580	434223	1385959	90354	106517	74404	1657233
Germany	250147	205853	3686	606986	304900	1371572	128768	271415	111284	1883038
Greece	10632	23763	4702	72898	104002	215998	6940	12032	7864	242834
Hungary	4370	6772	1128	31875	27550	71696	3458	51227	3394	129775
Iceland	1567	1189	331	3624	1682	8393	586	510	139	9628
Ireland	11045	11532	6094	47760	18683	95114	6982	5127	3134	110357
Italy	79758	89214	59585	415328	396795	1040680	79150	11035	164541	1295405
Latvia	448	1035	91	1451	3587	6611	883	11253	231	18979
Lithuania	845	828	243	2279	3235	7432	697	20573	342	29044
Luxembourg	666	1205	83	3961	1978	7894	9	1586	880	10370
Malta	168	277	102	1335	1077	2959	356	86	311	3712
Netherlands	11891	13318	1585	202399	56000	285193	18981	40831	27194	372199
Norway	14508	7873	3583	49369	34762	110096	10141	34003	8783	163024
Poland	27152	84125	3106	80795	89004	284183	8715	376554	10395	679847
Portugal	5463	7169	2194	13524	18051	46401	10923	15210	12289	84824
Romania	2732	9068	451	16199	26569	55018	3017	84465	1017	143516
Slovakia	5044	12259	617	11895	21804	51618	1252	5654	1760	60285
Slovenia	832	647	418	10494	5242	17632	1713	5026	640	25012
Spain	384954	224631	129407	231225	102330	1072547	38636	87024	68882	1267089
Sweden	24261	48214	11395	57977	74403	216249	12169	28921	10539	267878
Switzerland	7970	5905	1136	57734	37568	110314	25286	36496	3175	175271
UK	142023	235242	35215	427241	262273	1101993	94570	138276	51595	1386434
Total for 28 EU countries	1022994	1089026	286463	3419676	2217384	8035543	566255	1413839	605821	10621459
Total for 31 European countries	1047039	1103993	291514	3530404	2291396	8264346	602269	1484848	617918	10969381

Data are thousands of euros. No adjustment for price differentials. Totals do not match sum of costs because of rounding. EU=European Union.

Table 1: Costs of non-malignant blood disorders in 31 European countries in 2012

total costs). We estimated that 19 million working days were lost in 2012 owing to non-malignant blood disorder-related morbidity, which, when adjusted using the friction period, accounted for more than €1 billion (14% of the total economic burden).

Health-care costs of blood disorders were equivalent to €159 per every ten European citizens (table 2), but varied widely between countries, with an 11-times difference between the lowest cost per capita (Lithuania, €25 for every ten citizens) and highest cost per capita (Iceland,

€263 for every ten citizens; figure A, table 2). Although these differences decreased after adjusting for price differentials between countries, considerable differences persisted between countries (table 2, figure B). For example, a six-times difference between the highest spender (Spain, €253 for every ten citizens after adjustment) and the lowest spender (Lithuania, €41 for every ten citizens after adjustment) remained. The results after the ordinary least-squares regression showed a strong positive association between per capita blood

disorder-related health-care expenditure and per capita national income, with a €1 increase in national income per head being associated with an increase of €0·002 in health-care costs of non-malignant blood disorders per European citizen ($p=0\cdot0010$; appendix p 15). However, no significant statistical association was found between health-care expenditure per capita on non-malignant blood disorders (adjusted for price differentials) and respective mortality rates ($p=0\cdot277$; appendix p 16).

Sensitivity analysis showed that health-care resource use, the use of the friction period, and earnings were main drivers of total costs of non-malignant disorders. A 20% variation in health-care resource use had the biggest effect on total non-malignant blood disorder costs (11% change), with the resulting total costs varying between €9·77 billion and €12·16 billion (appendix p 13). Also, not adjusting morbidity losses using the friction period had a substantial effect on total costs (9% increase to €12·0 billion). Finally, a 20% variation in earnings resulted in a 5% change on total costs, with these varying between €10·27 billion and €11·51 billion.

After combining the economic burden of malignant and non-malignant blood disorders, the economic burden of blood disorders in 2012 was €23 billion (appendix p 11). Costs were evenly distributed between malignant (€12 billion, 52% of total costs) and non-malignant blood disorders (€11 billion, 48%; table 3). Although for most countries the cost of malignant blood disorders ranged from 40% to 60% of the total costs of blood disorders, these proportions varied considerably for several countries. For Poland and Lithuania, approximately 70% of the total costs of blood disorders were due to non-malignant blood disorders, whereas in Austria and Slovenia this proportion fell to around 30%.

All blood disorders cost the European health-care systems €16 billion in 2012 (table 3), representing 68% of the total costs due to blood disorders (appendix p 14). Inpatient care was the major cost component at €7 billion, accounting for 48% of health-care costs, followed by expenditure on drugs at €4 billion (28% of total health-care costs). As with total costs, health-care costs of malignant and non-malignant blood disorders accounted for approximately the same proportion of health-care costs due to blood disorders (47% vs 53%, respectively; table 3, appendix p 14).

Informal care (ie, unpaid care) of people with blood disorders cost €1·6 billion (14% of total costs, table 3), with €1 billion (61%) of these costs due to malignant blood disorders. Productivity losses due to mortality were valued at €2·5 billion (11% of total costs; appendix p 11). €2 billion (75%) of mortality losses due to blood disorders were due to malignant blood disorders, and in no country were the losses due to malignant blood disorders lower than for non-malignancies. Finally, we estimated that blood disorder-related morbidity, when adjusted using the friction period, cost €3 billion in 2012 (14% of the total economic burden).

	Health-care costs		Total costs	
	Cost per ten citizens in the population (€)	Cost per ten citizens in the population PPP* (€)	Cost per ten citizens in the population (€)	Cost per ten citizens in the population PPP* (€)
Austria	124	113	169	153
Belgium	214	194	266	240
Bulgaria	31	66	74	159
Croatia	74	116	105	165
Cyprus	59	65	93	102
Czech Republic	85	121	102	145
Denmark	187	138	284	210
Estonia	52	73	209	295
Finland	179	149	214	177
France	212	189	254	226
Germany	168	162	230	223
Greece	194	217	218	244
Hungary	72	125	131	226
Iceland	263	243	301	279
Ireland	208	189	241	220
Italy	175	174	218	217
Latvia	32	48	93	137
Lithuania	25	41	97	159
Luxembourg	150	127	198	167
Malta	71	92	89	116
Netherlands	170	156	222	204
Norway	221	140	327	208
Poland	74	125	176	298
Portugal	44	55	80	101
Romania	27	57	71	149
Slovakia	96	140	112	163
Slovenia	86	106	122	150
Spain	229	253	271	299
Sweden	228	169	282	209
Switzerland	139	91	220	144
UK	174	154	218	194
Total for 31 European countries	159	159	211	211

PPP=purchasing power parity method. *Adjusted for price differentials with the PPP.

Table 2: Health-care and total costs of non-malignant blood disorders per ten citizens in 31 European countries in 2012, by country, adjusted and non-adjusted for price differentials

Discussion

To our knowledge, our study is the first to provide cost estimates for non-malignant blood disorders in 31 European countries using a common methodological approach. We estimated the total costs of non-malignant blood disorders to be €11 billion in 2012 to the 28 EU countries, Iceland, Norway, and Switzerland. However, we also identified large variation in total costs and health-care costs per ten citizens across the 31 European countries. Combining the costs of malignant and non-malignant

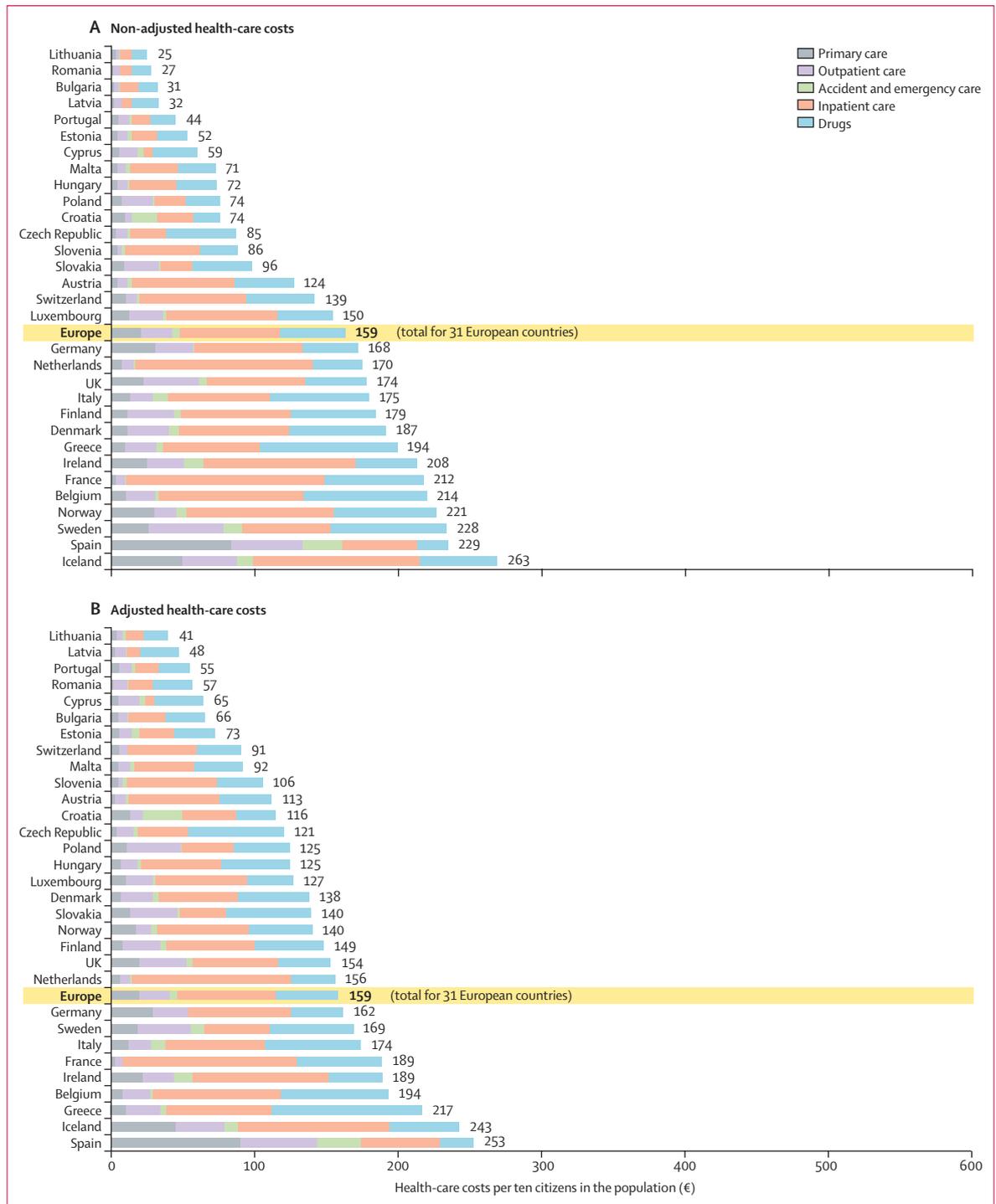


Figure: Health-care costs of non-malignant blood disorders per ten citizens in 31 European countries in 2012, by health-care service category (A) Cost data not adjusted for price differentials. (B) Cost data adjusted for price differentials.

disorders, the total cost of blood disorders across 31 European countries was €23 billion in 2012, of which €16 billion were due to health-care costs. Our study also permitted a comparison of the costs of non-malignant and malignant blood disorders. Overall, malignant and

non-malignant blood disorders accounted for a similar proportion of overall costs. However, because of the higher prevalence of non-malignant blood disorders (eg, anaemia) than of malignant blood disorders, the costs per prevalent case are higher for malignant blood disorders.

The results of our regression analyses found that, in the same way as for similar exercises for cancer⁷ and malignant blood disorders (Burns and colleagues⁴), the higher the national income of a country (as measured using GDP per capita), the higher the health expenditure on blood disorders. Similarly to malignant blood disorders, no statistical association was found between mortality rates due to non-malignant blood disorders and respective per capita health-care expenditure. Our data for the variation of health-care costs across countries provide a basis for further research and discussion. They highlight the need for setting up benchmarks concerning the most effective and efficient public policy initiatives and health-care systems in Europe. For this, we need to address intelligence gaps about the effectiveness and cost-effectiveness of existing care options for non-malignant blood disorders as well as factors affecting access to treatment and diagnosis. With the continuous introduction of innovative but more expensive management options²⁰ (gene therapy, in-vitro blood production, diagnostic tests for iron deficiency anaemia, etc), it is important to assess, in a systematic and explicit manner, whether the implementation of these options represent value for money in terms of patient benefit relative to present clinical practice.

Our results are similar to national estimates for the health-care costs of non-malignant blood disorders. For example, €1.34 billion in Germany in 2008 versus €1.39 billion in our study,¹³ €202 million in the Netherlands in 2011 versus €285 million in our study,¹² and €1.1 billion in England (accounting for 84% of the UK population) in 2012 versus €1.1 billion in the UK in our study.²¹ In France, costs were estimated for the year 1998, therefore estimates will now be out of date.²²

Because the same framework was used to estimate the economic burden of all cancers (including malignant blood cancers), cardiovascular disease, and dementia across the EU alone, we can reliably compare these data with costs we calculated due to blood disorders.^{5-7,23,24} By these estimates, cancer and cardiovascular disease pose a higher economic burden on the EU alone than do blood disorders (€143 billion for cancer and €195 billion for cardiovascular disease in 2009 vs €22 billion for blood disorders). The higher economic burden for these diseases relative to blood disorders was also true for all the costs assessed, including health care, productivity losses, and informal care. Costs of dementia were estimated for 2007 and only for the 15 countries who were members of the EU before 2004. For these 15 countries, the economic burden of dementia was €189 billion compared with €20 billion for blood disorders in 2012. Much of the burden of dementia was due to long-term institutionalisation (€49 billion) and informal care costs (€129 billion). Dementia-related health-care costs accounted for €10 billion in 2007, lower than those estimated for blood disorders in these same 15 countries (€14 billion). Such comparisons of the economic burden of different diseases are important and useful to decision

	Non-malignant blood disorders	Malignant blood disorders*	Total blood disorders	Proportion of costs due to non-malignant blood disorders
Health-care costs	8264	7309	15 574	53%
Mortality costs	602	1882	2485	25%
Morbidity costs	1485	1698	3183	48%
Informal care costs	618	979	1597	39%
Total costs	10 969	11 869	22 722	48%

Data are millions of euros unless otherwise stated. *Malignant blood disorders estimates obtained from Burns and colleagues.⁴

Table 3: Non-malignant blood disorders as a proportion of all blood disorder costs in 31 European countries

makers and health-policy planners. They can help inform and plan decisions about the allocation of resources to service provision, prevention interventions, and research funding.²⁵

The limitations of our study should be highlighted. First, as with previous work on the economic burden of cardiovascular disease, cancer, and dementia, the precision of our estimates depended on the quality and availability of similar disease-related data across Europe. For this study, we obtained and used data from more than 170 different sources, all of which varied in terms of quality, scope, and reliability. Despite calls to improve and standardise health data across Europe,^{26,27} we encountered important limitations in epidemiological data. For example, prevalence data for non-malignant blood disorders were unavailable except for anaemia.¹ However, the available estimates for anaemia did not cover the 31 European countries or refer to the general population. Furthermore, the prevalence of anaemia is age related and there are ongoing debates on which haemoglobin threshold should be used to define anaemia in a general population, creating further obstacles in estimating prevalence across countries.^{28,29} Hence, we could not compare health-care costs per prevalent case across countries. As with previous work, disease-related use of primary, outpatient, and emergency care were, on the whole, largely absent. Therefore, we had to make assumptions and extrapolations to estimate these numbers.

Secondly, estimates of the informal care needs of patients with non-malignant blood disorders were estimated from SHARE. Given that we were unable to obtain prevalence estimates for the number of people with a non-malignant blood disorder, some simplifying assumptions had to be made. As a result, informal care costs associated with non-malignant blood disorders might not be as reliable as those for malignant blood disorders, where prevalence information was obtained from GLOBOCAN.³ In addition, we used information from more than 30 000 individuals in waves 2 and 4 of SHARE, which included only residents of 17 EU countries, albeit in diverse geographical regions. As a result, for the 14 remaining countries not in SHARE, we had to combine data from similar countries that were included in order to obtain informal care estimates.

To estimate productivity losses due to mortality, we accounted for age-specific and sex-specific employment rates in our analysis. Therefore, wider economic trends will affect estimates of productivity losses and hamper comparisons across time. For example, in 2007, when we estimated the economic burden of dementia, the unemployment rate in Greece was 7·8% as opposed to 24·5% in 2012,¹⁷ resulting in decreased productivity losses in more recent years.

Finally, our estimates are likely to be underestimates. Some categories of health-care and social-care costs, such as supportive treatments (eg, antiemetic drugs and antibiotics), institutionalisation in nursing and residential care homes, and care provided in palliative settings outside hospitals are not recorded in health statistics. These categories of cost were not included because of data limitations and the inability to obtain these data for all countries being studied.

Despite these limitations, our study highlights the economic burden that non-malignant blood disorders place on European health-care systems and societies. Our study also shows that blood disorder costs were evenly distributed between malignant and non-malignant blood disorders. Our results should be of use to decision makers and research funding authorities charged with allocating health-care resources and research funds.

Contributors

RL-F and JL designed the study. All authors contributed to the literature search, data collection, data analysis, data interpretation, and wrote the manuscript. All authors approved the final version of the manuscript.

Declaration of interests

We declare no competing interests.

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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Online Appendix

In this online appendix, we provide detailed methodology and data sources used for the estimation of the costs of non-malignant blood disorders in 31 European countries. We also provide additional results of the costs of non-malignant blood disorders and all blood disorders in the EU-28, Iceland, Norway and Switzerland.

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Methods and data sources

Healthcare expenditure

Five categories of healthcare service associated with care for non-malignant blood disorders were included: primary care, accident and emergency (A&E) care, hospital inpatient care, outpatient care, and drugs.

The methods used and respective data sources are reported in **Table 1** and are discussed in greater detail in the following sections.

Table 1. Sources used to obtain healthcare resource use, by category and country.

Country	Primary care	Outpatient care	A&E	Inpatient care
Austria	C ¹	C ¹	C ¹	A ^{2,3}
Belgium	C ⁴	C ⁵	C ⁶	A ^{2,3}
Bulgaria	C ⁷	C ⁷	C ⁸	A ^{2,3}
Croatia	C ⁹	C ¹⁰	D	A ^{2,3}
Cyprus	A ^{11,12}	A ^{11,12}	C ^{11,12}	A ^{2,3}
Czech Rep.	C ¹³	C ¹³	D	A ^{2,3}
Denmark	C ^{14,15}	A ^{14,15}	A ^{14,16}	A ^{2,3}
Estonia	C ¹⁷	C ¹⁷	C ¹⁷	A ^{2,3}
Finland	B ^{18,19}	C ²⁰	C ²⁰	A ^{2,3}
France	B ^{21,22}	B ^{22,23}	C ^{22,24}	A ^{2,3}
Germany	A ^{25,26}	A ^{25,26}	C ²⁷	A ^{2,3}
Greece	C ²⁸	C ²⁸	D	A ²⁹
Hungary	C ³⁰	C ³¹	C ³²	A ^{2,3}
Iceland	C ³³	C ³³	D	A ^{2,3}
Ireland	C ³⁴	C ³⁵	C ³⁵	A ^{2,3}
Italy	C ²⁵	C ²⁵	C ³⁶	A ^{2,3}
Latvia	C ³⁷	C ³⁷	C ³⁷	A ^{2,3}
Lithuania	C ³⁸	C ³⁸	D	A ^{2,3}
Luxembourg	C ³⁹	C ³⁹	D	A ^{2,3}
Malta	C ⁴⁰	C ⁴⁰	C ⁴⁰	A ^{2,3}
Netherlands	A ^{41,42}	A ^{41,42}	C ^{42,43}	A ^{2,3}
Norway	C ⁴⁴	A ⁴⁵	C ⁴⁴	A ^{2,3}
Poland	C ⁴⁶	C ⁴⁷	C ⁴⁸	A ^{2,3}
Portugal	C ⁴⁹	C ⁴⁹	C ⁵⁰	A ^{2,3}
Romania	C ⁵¹	C ⁵¹	C ⁵²	A ^{2,3}
Slovakia	C ⁵³	C ⁵³	C ⁵⁴	A ^{2,3}
Slovenia	A ^{55,56}	A ^{55,56}	D	A ^{2,3}
Spain	C ^{57,58}	B ^{58,59}	B ^{58,59}	A ^{2,3}
Sweden	C ⁶⁰	C ⁶⁰	D	A ^{2,3}
Switzerland	C ⁶¹	C ⁶¹	C ⁶²	A ^{2,3}
UK	A ⁶³⁻⁶⁵	C ⁶⁶⁻⁶⁹	C ^{67,68,70,71}	A ^{2,3}

Dependant on the availability of data, the methods used to estimate disease-related healthcare resource use fell in one of the following categories, in order of priority:

A. National non-malignant blood disorders-specific data: Blood disorders-specific healthcare data were available for the whole population;

B. Survey/sample non-malignant blood disorders-specific data: Blood disorders-specific healthcare data were available for a representative sample of the population either as the proportion of overall healthcare utilisation that was due to non-malignant blood disorders or as healthcare utilisation rates per patient with the condition, e.g. annual outpatient visits per patient;

C. National data but not disease-specific: All-cause healthcare resource use data were available but not due to non-malignant blood disorders. For non-inpatient categories, we estimated disease-specific resource use by multiplying all-cause national data by the proportion of ambulatory visits due to non-malignant blood disorders out of all ambulatory visits, if available. If disease-related ambulatory information was not available, we used the proportion of hospital discharges due to non-malignant blood disorders out of all discharges to allocate national healthcare utilisation;

D. No national data: we derived national utilisation data for all diseases from similar countries and allocated it into non-malignant blood disorders using the approach defined in (C).

Primary care

Primary care activities consisted of visits to or from general practitioners (GPs). Country-specific overall visits to primary care due to all conditions were obtained for all countries.^{1,4,7,9,11,13,14,17,18,21,25,28,30,33,34,37-41,44,46,49,51,53,55,57,60,61,63,65}

To the total number of primary care visits we applied the proportion of primary care that was attributable to non-malignant blood disorders using the following:

- 1) In Finland,¹⁹ data were available for a published study evaluating the reasons for primary care attendance in a cohort of Finnish citizens.
- 2) In Cyprus,¹² Slovenia,⁵⁶ and the UK⁶⁴ published data were available on the proportion of primary consultations due to non-malignant blood disorders.
- 3) In France,²² Germany,²⁶ and the Netherlands,⁴² data on ambulatory care expenditure by disease group were used to derive the number of visits due to non-malignant blood disorders by applying the respective proportion of expenditure, out of all ambulatory expenditure, to the total number of primary care visits.
- 4) In Denmark and Spain,^{15,58} the proportion of disease-related outpatient visits out of all outpatient visits was available and was applied to the total number of primary care visits.
- 5) In the remaining 22 countries, the proportion of hospital discharges (including day cases) due to non-malignant blood disorders out of all discharges was applied to the total number of primary care visits.

Outpatient care

Outpatient care comprised specialist consultations and treatments taking place in outpatient wards, clinics, or patients' homes. Country-specific overall visits to outpatient care due to all conditions were obtained for all countries.^{1,5,7,10,11,13,14,17,20,23,25,28,31,33,35,37-41,45,47,49,51,53,55,59-61,66-69} To the total number of outpatient care visits we applied the proportion of care that was attributable to non-malignant blood disorders using the following:

- 1) In Cyprus,¹² Denmark,¹⁵ Norway,⁴⁵ Slovenia,⁵⁶ and Spain⁵⁸ published data were available on the proportion of outpatient care consultations due to non-malignant blood disorders.
- 2) In France,²² Germany,²⁶ and the Netherlands,⁴² data on ambulatory care expenditure by disease group were used to derive the number of visits due to non-malignant blood disorders by applying the respective proportion of expenditure, out of all ambulatory expenditure, to the total number of outpatient care visits.
- 3) In the remaining 24 countries, the proportion of overall hospital discharges due to non-malignant blood disorders was applied to the total number of outpatient visits.

Accident & Emergency care

A&E care consisted of all non-malignant blood disorders-related hospital emergency visits. Country-specific overall visits to A&E due to all conditions were obtained for 23 countries.^{1,6,8,11,14,17,20,24,27,32,35-37,40,43,44,48,50,52,54,59,62,67,68,70,71}

All-cause attendance figures were not available in 7 countries (Croatia, Czech Republic, Greece, Lithuania, Luxembourg, Slovenia, and Sweden) and A&E rates were derived from similar countries and applied to them. Therefore, for: 1) Czech Republic we used estimates from Slovakia;⁵⁴ 2) Lithuania we used estimates from Estonia;¹⁷ 3) Luxembourg we used estimates from Belgium;⁶ 4) Sweden we used estimates from Denmark;¹⁴ and 5) Croatia, Greece and Slovenia we used estimates from a previous multicountry regression.⁷²

To the total number of emergency care visits we applied the proportion of care that was attributable to non-malignant blood disorders using the following:

- 1) In Denmark published data were available on the proportion of A&E consultations due to non-malignant blood disorders.¹⁶
- 2) In Cyprus,¹² Norway,⁴⁵ Slovenia,⁵⁶ and Spain⁵⁸ data on the proportion of all outpatient care visits due to non-malignant blood disorders were applied to the total number of A&E visits.
- 3) In France,²² and the Netherlands,⁴² data on outpatient expenditure by disease group were used to derive the number of A&E visits due to non-malignant blood disorders, by applying the respective proportions of expenditure to the overall number of A&E visits.
- 4) For the remaining 26 countries, all-cause A&E visits were obtained and allocated into non-malignant blood disorders using the proportion of overall hospital discharges due to non-malignant blood disorders.

Hospital inpatient care

National data were available on non-malignant blood disorders-related days in hospital and day-cases in all countries. Except for Greece, where these data were obtained from the OECD,²⁹ data was obtained from EUROSTAT.^{2,3}

Healthcare unit costs

For all countries, health care resource use was valued using country-specific unit costs (**Table 2**).

Table 2. Sources used to obtain healthcare unit costs, by category and country.

Country	Primary care	Outpatient care	A&E	Inpatient care
Austria	A ⁷³	A ⁷³	A ⁷⁴	B ⁷⁵
Belgium	A ⁷⁶	A ⁷⁶	A ⁷⁶	A ⁷⁷
Bulgaria	B ⁷⁵	B ⁷⁵	D ⁷²	B ⁷⁵
Croatia	A ⁷⁸	A ⁷⁸	A ⁷⁸	A ⁷⁸
Cyprus	A ⁷⁹	A ⁸⁰	D ⁷²	A ⁸⁰
Czech Rep.	B ⁸¹	B ⁸¹	D ⁷²	B ⁸¹
Denmark	A ¹⁴	A ¹⁵	A ⁸²	A ⁸³
Estonia	B ¹⁷	A ¹⁷	B ¹⁷	A ¹⁷
Finland	A ⁸⁴	A ⁸⁵	A ⁸²	A ⁸⁵
France	B ⁸⁶	B ⁸⁷	A ⁸⁸	B ⁷⁵
Germany	A ⁸⁹	A ⁸⁹	A ⁸⁹	B ²⁶
Greece	A ⁹⁰	A ⁹⁰	A ⁹⁰	A ⁹⁰
Hungary	B ³²	B ³²	A ³²	A ³²
Iceland	A ⁹¹	A ⁹¹	B ⁹²	B ⁹²
Ireland	A ⁹³	A ⁹³	A ⁹³	A ⁹⁴
Italy	A ⁸⁹	A ⁹⁵	A ⁸⁹	A ⁹⁶
Latvia	B ⁹⁷	B ⁹⁷	D ⁷²	A ⁹⁸
Lithuania	B ³⁸	B ³⁸	A ⁸⁹	B ³⁸
Luxembourg	A ⁹⁹	A ⁹⁹	A ⁹⁹	B ⁷⁵
Malta	B ⁴⁰	C ¹⁰⁰	A ¹⁰¹	A ¹⁰¹
Netherlands	B ⁴¹	A ¹⁰²	A ¹⁰²	B ⁴²
Norway	A ¹⁰³	A ¹⁰³	C ¹⁰⁰	A ¹⁰³
Poland	A ¹⁰⁴	A ¹⁰⁵	D ⁷²	A ¹⁰⁴
Portugal	A ¹⁰⁶	A ¹⁰⁷	A ¹⁰⁷	A ¹⁰⁷
Romania	C ¹⁰⁰	C ¹⁰⁰	D ⁷²	B ⁷⁵
Slovakia	C ¹⁰⁰	C ¹⁰⁰	D ⁷²	B ⁷⁵
Slovenia	C ¹⁰⁰	C ¹⁰⁰	A ¹⁰¹	B ⁷⁵
Spain	A ¹⁰⁸	A ¹⁰⁸	A ¹⁰⁸	A ¹⁰⁸
Sweden	A ¹⁰⁹	A ¹⁰⁹	A ¹¹⁰	A ¹¹¹
Switzerland	A ¹¹²	A ¹¹³	A ¹¹⁴	A ¹¹²
UK	A ¹¹⁵	A ¹¹⁶	A ¹¹⁶	A ¹¹⁶

Dependant on the availability of data, sources were qualified in order of priority:

- A. Directly obtained from sources such as national fee schedules, published studies, national reports, etc.;
- B. Derived from national expenditure figures (e.g. primary care, outpatient care, inpatient care) using the respective total activity levels. For example, cost per inpatient day was estimated by dividing the total inpatient expenditure by the total number of inpatient days;
- C. Estimates derived costs and prices used in the WHO-CHOICE analysis;¹⁰⁰ and
- D. Derived from the predictions of linear regression analyses of the unit costs of countries with available data.⁷²

Drug expenditure

Drug expenditure for non-malignant blood disorders consisted of sales for medicinal products under the Anatomical Therapeutic Chemical Classification System for Blood and Blood Forming Organs (ATC B).

Information on the expenditure on ATC B drugs was obtained from the OECD Health data for: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Luxembourg, Netherlands, Norway, Portugal, Slovakia, Slovenia, Spain, Sweden and Switzerland.¹¹⁷

For Bulgaria,¹¹⁸ Croatia,¹¹⁹ and Cyprus,^{120,121} information on the expenditure on ATC B drugs was obtained from country-specific national estimates.

For the 6 countries (Latvia,¹²² Lithuania,¹²² Malta,¹²⁰ Poland,¹²⁰ Romania,¹²⁰ and the UK¹¹⁷) where we could not determine the overall expenditure on ATC B drugs, we obtained overall country specific national expenditure on drugs. To that we applied the proportion that was due to ATC B drugs, which we obtained from similar countries. Therefore, for: Latvia and Lithuania we used data from Estonia; Malta we used data from Italy; Poland we used data from Hungary; Romania we used data from Bulgaria; and the UK we used data from France.

However, ATC B will include medicinal products for the treatment of other conditions. Therefore, we obtained the proportion of ATC B drugs relevant for blood disorders from reports from Germany and the Netherlands,^{26,42} and applied this to all other countries.

Non-health care utilisation

Informal care

We conservatively assumed that only patients severely limited in daily activities or who were terminally ill would receive informal care. We used country-specific data from the Survey of Health, Ageing and Retirement in Europe (SHARE) to assess the informal care needs of patients.¹²³ Hence, we estimated the hours of informal care provided due to patients severely limited in daily activities using Wave 2 and Wave 4 of the SHARE survey which collected data on more than 30,000 individuals resident in 17 EU countries in 2006 and 2010 (Austria, Belgium, Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Netherlands, Poland, Portugal, Slovenia, Spain and Sweden). Residents from Ireland and Greece were not included in WAVE 4 and the data collected in WAVE 2 in these countries were combined with WAVE 4 data on the remaining 15 EU countries.

For countries not in SHARE, we combined data from similar countries that were in SHARE to obtain estimates for the 14 remaining countries. Therefore, for: 1) Bulgaria, Croatia, Latvia, Lithuania, Romania, and Slovakia, we pooled data from the Czech Republic, Estonia, Hungary, Slovenia and Poland; 2) For Finland, Iceland and Norway, we pooled data from Denmark and Sweden; 3) for Cyprus and Malta, we pooled data from Greece, Italy, Portugal and Spain; and 4) for Luxembourg, Switzerland and the UK, we pooled data from Austria, Belgium, France, Germany, Ireland, and the Netherlands.

Informal care to patients severely limited in daily activities due to non-malignant blood disorders

Hours of informal care for severely limited patients were estimated by adding the age and sex-specific products of:

- 1) Population estimates.¹²⁴
- 2) Probability of being severely limited in daily activities due to a health condition.

Using data from SHARE, we undertook logistic regressions adjusting for age, gender, presence of health conditions, and country of residence, in order to obtain country-specific estimates of the probability of being severely limited in daily activities due to illness or a health condition.

- 3) Probability of receiving informal care given the patient was severely limited in daily activities.

Using data from SHARE, we performed two logistic regressions (one for care from inside household and another for care outside the household) to evaluate the probability that patients received informal care after adjusting for age, gender, presence of a health condition, and country of residence.

- 4) Hours of informal care received

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 received after adjusting for age, gender, limitations in daily living, presence of health conditions, 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 received.

5) Estimates of the prevalence of non-malignant blood disorders

Given the lack of prevalence estimates for non-malignant blood disorders, we estimated these using the reported -5-year prevalence figures of malignant blood disorders from IARC¹²⁵. Hence, we started with the prevalence of malignant blood disorders, and applied country-specific ratios of the number of hospital bed-days due to malignant and non-malignant blood disorders out of all hospital stays to obtain the prevalence of non-malignant blood disorders..

Informal care to terminally ill patients with non-malignant blood disorders

Hours of informal care for terminally ill patients with non-malignant blood disorders were estimated by adding the age and sex-specific products of:

1) Number of non-malignant blood disorders-related deaths.¹²⁶

2) Probability of receiving informal care in the year before dying

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 patient was estimated using a logistic regression analysis and adjusting for age, gender and country.

3) Hours of informal care received

Using data from 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 terminally-ill patient after adjusting for age, gender, presence of cancer, 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 cancer patients.

Valuing informal care hours

Participants in SHARE were asked about the relationship between carer and person being cared (e.g. spouse, sibling, offspring, parent friend etc...). 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, we then determined the proportion of these carers who were employed or unemployed/economically inactive.¹²⁷

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 8 hours of work. For those carers in retirement, unemployed, or economically inactive, the national hourly minimum wage was applied.¹²⁸ 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.

Mortality losses

For all countries we assumed an initial working age of 15. Age and gender specific deaths due to non-malignant blood disorders, were obtained for all countries from EUROSTAT.¹²⁶ 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, obtained from EUROSTAT,¹²⁷ for each of the 31 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.¹²⁹

Morbidity losses

The costs associated with lost productivity due to morbidity were the costs associated with absence of work due to non-malignant blood disorders. 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 disabled due to their condition, and therefore leaving the labour market. **Table 3** details all the sources used to obtain temporary and permanent absence from work due to non-malignant blood disorders.

Table 3. Sources used to obtain morbidity losses, by country

Country	Temporary absence from work	Permanent absence from work
Austria	130	130
Belgium	131	131
Bulgaria	132	133
Croatia	9	9
Cyprus	134	134
Czech Rep.	135	13,135
Denmark	136,137	137,138
Estonia	17	139
Finland	140,141	141
France	142,143	143,144
Germany	145,146	147
Greece	134	134
Hungary	148	148
Iceland	149	149
Ireland	150	151
Italy	152,153	154,155
Latvia	156	157
Lithuania	158	159
Luxembourg	160	39
Malta	161	40
Netherlands	162	163
Norway	164,165	165,166
Poland	167	167,168
Portugal	169	170
Romania	171	133
Slovakia	172	172
Slovenia	56	55,173
Spain	142,174	174,175
Sweden	60,137	60,137
Switzerland	176	177
UK	178,179	180

Temporary absence from work due to sickness

Country-specific overall annual days of sickness leave due to all conditions was obtained for all countries,^{9,17,56,60,130-132,134-136,140,142,145,148-150,152,156,158,160-162,164,167,169,171,172,176,178} To this we applied the proportion of sickness leave that was attributable to non-malignant blood disorders, which was available in Austria,¹³⁰ the Czech Republic,¹³⁵ Denmark,¹³⁷ France,¹⁴³ Germany,¹⁴⁶ Italy,¹⁵³ Norway,¹⁶⁵ Poland,¹⁶⁷ Slovenia,⁵⁶ Spain,¹⁷⁴ Sweden,¹³⁷ and the UK.¹⁷⁹ For Belgium¹³¹ and Finland¹⁴¹ we used the proportion of overall permanent absence from work due to non-malignant blood disorders.

For countries where we could not establish the proportion of sickness leave attributable to non-malignant blood disorders, we used proportions from other countries. Therefore, for:

- 1) Bulgaria, Estonia, Hungary, Latvia, Lithuania and Romania we used estimates from Poland;¹⁶⁷
- 2) Croatia we used estimates from Slovenia;⁵⁶
- 3) Cyprus, Greece and Portugal we used estimates from Spain;¹⁷⁴
- 4) Iceland we used estimates from Denmark;¹³⁷
- 5) Ireland we used estimates from the UK;¹⁷⁹
- 6) Luxembourg and the Netherlands we used estimates from Belgium;¹³¹
- 7) Malta we used estimates from Italy;¹⁵³
- 8) Slovakia we used estimates from the Czech Republic;¹³⁵ and
- 9) Switzerland we used estimates from Germany.¹⁴⁶

Permanent absence from work due to incapacity or disability

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.^{9,13,39,40,55,60,130,131,133,134,138,139,141,144,147-149,151,155,157,159,163,166,168,170,172,175,177,180} To this we applied the proportion that was attributable to non-malignant blood disorders, which was available in Austria,¹³⁰ Belgium,¹³¹ Finland,¹⁴¹ Germany,¹⁴⁷ Italy¹⁵⁴ Slovenia,¹⁷³ and the UK.¹⁸⁰ For the Czech Republic,¹³⁵ Denmark,¹³⁷ France,¹⁴³ Norway,¹⁶⁵ Poland,¹⁶⁷ Spain,¹⁷⁴ and Sweden,¹³⁷ we used the proportion of overall temporary absence from work due to non-malignant blood disorders.

For countries where we could not establish the proportion of permanent absence from work due to incapacity or disability attributable to non-malignant blood disorders, we used proportions from other countries using the methodology to estimate temporary absence from work due to sickness.

Valuing absence from work

The mean annual earnings identified when estimating informal care and mortality costs were converted to mean daily earnings.¹²⁹ The product of working days lost and mean daily earnings provided the productivity losses associated with non-malignant blood disorders, after adjusting for the ‘friction period’.

Results

Table 4. Unit costs (€) used to value health and non-healthcare resource use, by country, 2012

Country	Mortality losses		Morbidity losses	Informal care		Health care unit costs			
	Yearly earnings		Daily earnings	Hourly earnings		GP visit	Outpatient visit	A&E visit	Inpatient day
	Males	Females		Carers in employment	Carers not in employment				
Austria	€47,247	€34,448	€180	€22	€10	€48	€62	€133	€495
Belgium	€48,926	€41,935	€199	€25	€8	€27	€55	€73	€697
Bulgaria	€6,006	€5,197	€24	€3	€1	€8	€23	€32	€111
Croatia	€13,748	€13,073	€58	€7	€2	€17	€14	€230	€97
Cyprus	€30,331	€24,059	€119	€15	€6	€15	€40	€46	€135
Czech Rep.	€14,715	€11,302	€58	€7	€2	€11	€15	€78	€227
Denmark	€64,616	€50,814	€252	€32	€12	€25	€83	€134	€691
Estonia	€12,559	€9,018	€47	€6	€2	€16	€52	€105	€187
Finland	€48,662	€38,001	€189	€24	€12	€100	€286	€311	€782
France	€38,281	€31,079	€152	€19	€9	€34	€131	€91	€949
Germany	€45,940	€35,594	€179	€22	€7	€50	€63	€82	€573
Greece	€25,252	€20,488	€101	€13	€4	€23	€54	€58	€383
Hungary	€12,109	€10,152	€49	€6	€2	€6	€11	€123	€173
Iceland	€35,239	€27,564	€137	€17	€6	€66	€110	€264	€996
Ireland	€48,333	€38,794	€191	€24	€10	€52	€167	€286	€862
Italy	€35,466	€29,911	€144	€18	€9	€22	€83	€227	€707
Latvia	€10,396	€8,394	€41	€5	€2	€9	€41	€37	€101
Lithuania	€8,620	€7,182	€34	€4	€2	€10	€22	€24	€79
Luxembourg	€56,892	€50,716	€236	€29	€12	€38	€61	€75	€1,038
Malta	€20,985	€18,015	€87	€11	€4	€28	€53	€103	€389
Netherlands	€47,270	€37,814	€186	€23	€9	€42	€126	€176	€1,426
Norway	€61,376	€51,978	€248	€31	€25	€124	€270	€308	€1,487
Poland	€12,091	€10,282	€49	€6	€2	€16	€61	€34	€206
Portugal	€20,097	€16,538	€80	€10	€4	€31	€94	€89	€200
Romania	€7,230	€6,655	€30	€4	€1	€8	€12	€67	€67
Slovakia	€12,351	€9,470	€48	€6	€2	€20	€29	€38	€171
Slovenia	€22,839	€21,481	€97	€12	€5	€25	€37	€98	€344
Spain	€31,074	€25,170	€123	€15	€5	€38	€93	€185	€630
Sweden	€41,766	€35,259	€168	€21	€15	€166	€357	€336	€904
Switzerland	€67,546	€52,566	€264	€33	€12	€70	€318	€142	€1,012
UK	€42,440	€29,348	€158	€20	€8	€53	€156	€135	€614

Table 5. Non-malignant blood disorders-related resource units per 1,000 population, by country 2012

Country	Mortality losses				Morbidity losses	Informal care		Healthcare contacts			
	Deaths		Working years lost		Working days lost	Care hours		GP visits	Outpatient visits	A&E visits	Inpatient days
	M	F	M	F		Carers in employment	Carers not in employment				
Austria	0.01	0.01	0.06	0.02	10	24	30	9	12	2	14
Belgium	0.01	0.02	0.02	0.03	9	47	99	38	36	4	14
Bulgaria	0.01	0.01	0.06	0.02	165	17	47	32	13	1	11
Croatia	0.00	0.01	0.04	0.01	44	15	28	54	36	8	25
Cyprus	0.02	0.03	0.02	0.02	11	61	81	35	34	8	4
Czech Rep.	0.01	0.01	0.02	0.01	19	37	42	31	54	2	11
Denmark	0.02	0.03	0.04	0.03	16	73	60	43	35	5	11
Estonia	0.00	0.01	0.03	0.01	327	19	22	28	12	3	9
Finland	0.01	0.00	0.02	0.02	10	12	17	11	11	1	9
France	0.02	0.02	0.04	0.03	11	29	64	11	4	1	14
Germany	0.01	0.02	0.04	0.02	19	41	68	61	40	1	13
Greece	0.02	0.02	0.03	0.01	11	32	67	41	39	7	17
Hungary	0.01	0.01	0.03	0.02	106	37	56	78	62	1	19
Iceland	0.00	0.01	0.14	0.00	12	19	18	74	34	4	11
Ireland	0.01	0.01	0.36	0.03	6	18	26	46	15	5	12
Italy	0.02	0.03	0.04	0.03	1	85	142	62	18	4	10
Latvia	0.00	0.01	0.04	0.03	135	15	20	25	12	1	7
Lithuania	0.01	0.00	0.04	0.00	200	17	27	29	12	3	10
Luxembourg	0.01	0.03	0.00	0.00	13	37	51	33	38	2	7
Malta	0.01	0.02	0.06	0.00	2	43	64	15	13	2	8
Netherlands	0.01	0.02	0.02	0.02	13	42	68	17	6	1	8
Norway	0.01	0.02	0.03	0.04	28	32	31	23	6	2	7
Poland	0.00	0.00	0.02	0.01	199	29	41	45	36	2	10
Portugal	0.02	0.02	0.06	0.03	18	79	102	17	7	2	6
Romania	0.00	0.00	0.02	0.02	139	10	12	16	37	0	12
Slovakia	0.01	0.01	0.01	0.03	22	37	48	47	77	3	13
Slovenia	0.01	0.01	0.07	0.01	25	17	22	16	9	2	15
Spain	0.01	0.02	0.04	0.02	15	64	100	218	51	15	8
Sweden	0.01	0.02	0.04	0.03	18	29	34	15	14	4	7
Switzerland	0.01	0.01	0.05	0.04	17	9	10	14	2	1	7
UK	0.01	0.01	0.04	0.03	14	27	35	42	24	4	11
EU-28	0.01	0.02	0.04	0.02	39	42	67	56	28	4	12
Europe 31	0.01	0.02	0.04	0.02	38	41	66	55	28	4	11

Table 6. Costs of all blood disorders (malignant and non-malignant) in 31 European countries, by country, 2012

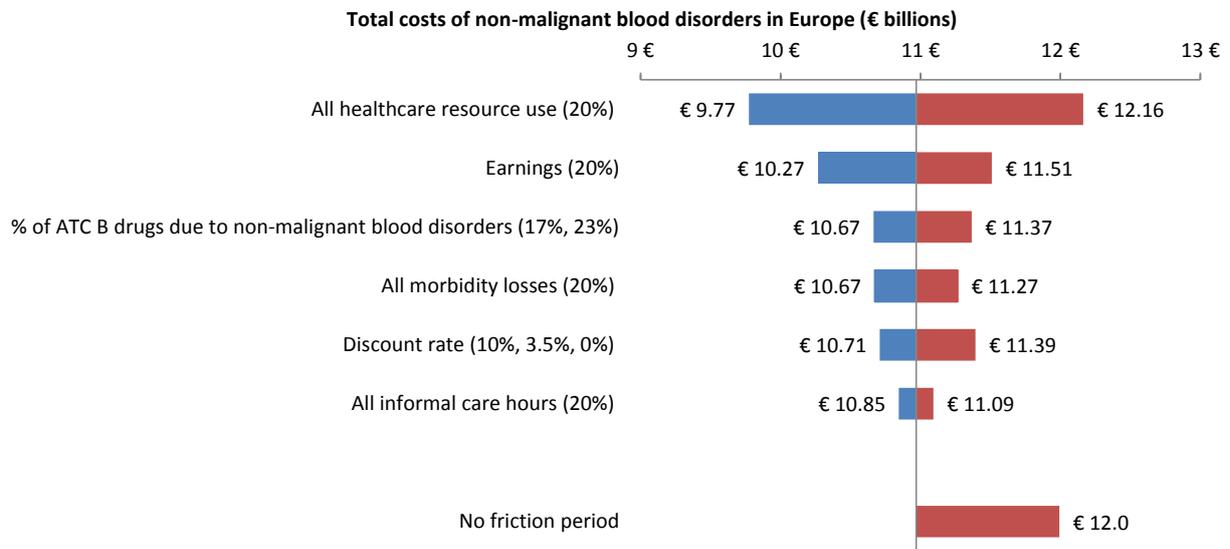
Country	Healthcare costs						Productivity losses		Informal care costs	TOTAL costs	% total cost of non-malignant blood disorders
	Primary care	Outpatient care	A&E	Inpatient care	Drugs	Total healthcare	Mortality	Morbidity			
Austria	9,373	15,717	2,823	152,021	86,666	266,599	112,655	44,115	37,261	460,630	31%
Belgium	14,814	29,462	3,928	177,956	145,423	371,583	107,943	89,201	71,136	639,862	46%
Bulgaria	3,525	4,183	514	17,331	16,391	41,944	10,870	33,875	2,637	89,326	61%
Croatia	11,294	6,309	21,885	20,027	15,397	74,912	20,689	34,832	6,729	137,162	33%
Cyprus	827	2,201	599	1,881	5,971	11,479	5,924	2,392	3,658	23,453	34%
Czech Rep.	6,149	15,051	2,906	49,959	81,069	155,133	14,732	26,113	9,326	205,305	52%
Denmark	6,909	44,684	5,204	92,311	68,532	217,641	48,979	75,310	35,250	261,207	61%
Estonia	1,570	2,299	1,256	7,043	4,279	16,447	2,552	24,262	853	44,114	63%
Finland	6,684	36,953	5,315	120,260	55,292	224,506	36,084	26,689	16,671	303,949	38%
France	31,680	50,223	6,102	1,436,061	901,698	2,425,765	274,523	285,872	189,934	3,176,094	52%
Germany	342,533	281,880	5,783	1,481,863	546,787	2,658,845	487,093	952,637	292,760	4,391,334	43%
Greece	29,074	64,979	12,856	229,178	173,967	510,055	18,645	20,556	12,653	561,909	43%
Hungary	10,425	16,154	2,692	55,196	59,488	143,955	13,176	56,407	7,326	220,865	59%
Iceland	3,270	2,480	691	8,089	3,485	18,015	5,374	1,397	1,557	26,344	37%
Ireland	21,713	22,672	11,980	114,001	38,270	208,637	30,312	13,205	10,583	262,737	42%
Italy	141,219	157,963	105,501	915,214	653,916	1,973,813	301,543	31,670	368,417	2,675,443	48%
Latvia	1,463	3,383	297	5,544	5,082	15,768	3,942	13,450	1,097	34,257	55%
Lithuania	1,923	1,884	554	6,479	4,092	14,933	3,518	23,756	1,247	43,454	67%
Luxembourg	1,340	2,425	167	12,125	5,953	22,009	2,038	5,598	1,939	31,585	33%
Malta	218	360	133	2,551	2,604	5,865	1,055	313	733	7,965	47%
Netherlands	24,404	32,493	3,253	402,174	111,438	573,762	106,004	97,278	64,028	841,072	44%
Norway	16,898	23,786	7,020	155,689	57,869	261,262	40,104	58,173	25,692	385,232	42%
Poland	47,346	146,694	5,417	129,328	129,754	458,539	56,000	410,661	23,903	949,104	72%
Portugal	9,330	12,242	2,937	29,825	56,171	110,505	47,710	25,913	26,329	210,457	40%
Romania	6,504	21,590	1,073	37,631	56,531	123,330	24,863	96,900	4,681	249,773	57%
Slovakia	8,437	20,507	1,033	21,767	39,043	90,788	8,748	12,282	3,658	115,475	52%
Slovenia	1,358	1,679	1,085	37,031	12,473	53,626	5,043	31,101	2,734	92,504	27%
Spain	499,959	291,739	168,067	463,308	336,472	1,759,545	159,887	149,659	154,386	2,223,477	57%
Sweden	31,801	72,957	17,242	153,901	116,981	392,882	48,788	108,580	29,938	580,188	46%
Switzerland	16,666	12,348	2,375	148,637	99,065	279,091	83,339	107,151	22,647	492,228	36%
UK	154,959	464,644	47,524	982,624	442,773	2,092,524	402,547	323,143	167,514	2,985,728	46%
EU-28	1,426,833	1,823,327	438,127	7,154,592	4,172,516	15,015,394	2,355,864	3,015,771	1,547,379	21,818,434	49%
Europe 31	1,463,667	1,861,942	448,213	7,467,006	4,332,935	15,573,763	2,484,682	3,182,491	1,597,275	22,722,237	48%

Table 7. Healthcare costs of all blood disorders in 31 European countries in 2012, by country

Country	All blood disorders	
	Cost per 10 in population (€)	Cost per 10 in population (€) PPP*
Austria	317	288
Belgium	335	302
Bulgaria	57	122
Croatia	175	275
Cyprus	133	147
Czech Rep.	148	210
Denmark	390	289
Estonia	124	175
Finland	416	344
France	372	331
Germany	325	314
Greece	459	513
Hungary	145	251
Iceland	564	522
Ireland	455	415
Italy	332	331
Latvia	77	114
Lithuania	50	82
Luxembourg	419	355
Malta	140	183
Netherlands	343	314
Norway	524	333
Poland	119	201
Portugal	105	132
Romania	61	128
Slovakia	168	246
Slovenia	261	322
Spain	376	415
Sweden	414	307
Switzerland	351	230
UK	330	292
Europe 31	300	300

*Adjusted for price differentials with the purchasing power parity method.

Figure 1. Tornado plot of the results of the sensitivity analysis on the total costs of non-malignant blood disorders in 31 European countries, € billions, 2012



The horizontal axis represent the total costs of non-malignant blood disorders in 31 European countries. The categories/parameters being changed are displayed along the vertical axis. The horizontal bars represent the range in total costs associated with the specified change for each category/parameter, e.g. $\pm 20\%$ change in earnings across all countries. Blue bars represent reductions and red bars represent increases in total costs of non-malignant blood disorders associated with the value of the category being changed. The labels represent the upper and lower bounds of total costs of non-malignant blood disorders for a given category parameter. The base-case total costs of non-malignant blood disorders (€11 billion) are indicated by a vertical line cutting through the horizontal bars.

Figure 2. Total costs by blood disorder type, € millions, 2012

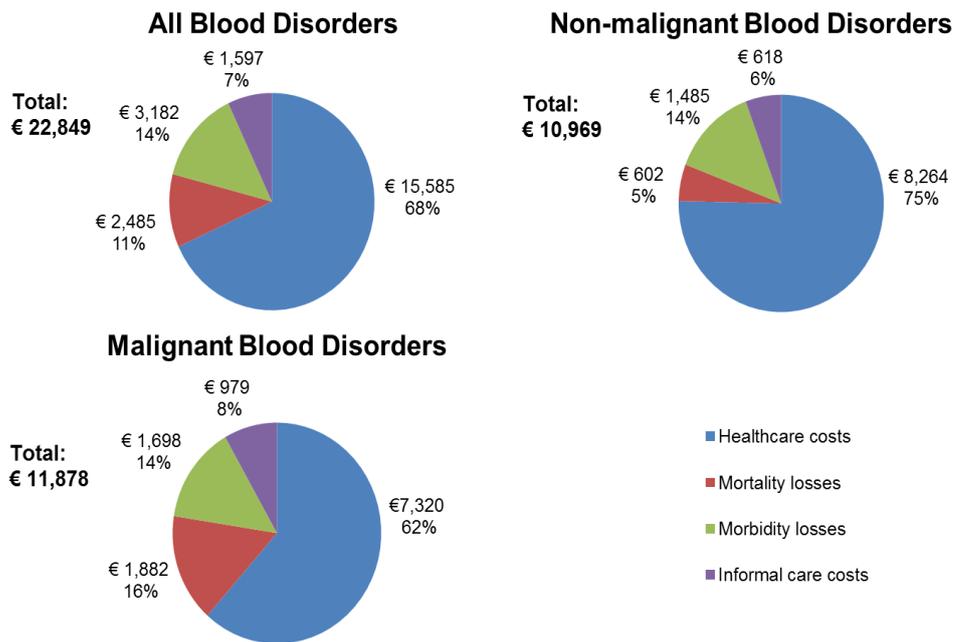


Figure 3. Proportion of healthcare expenditure by category and blood disorder type, 2012

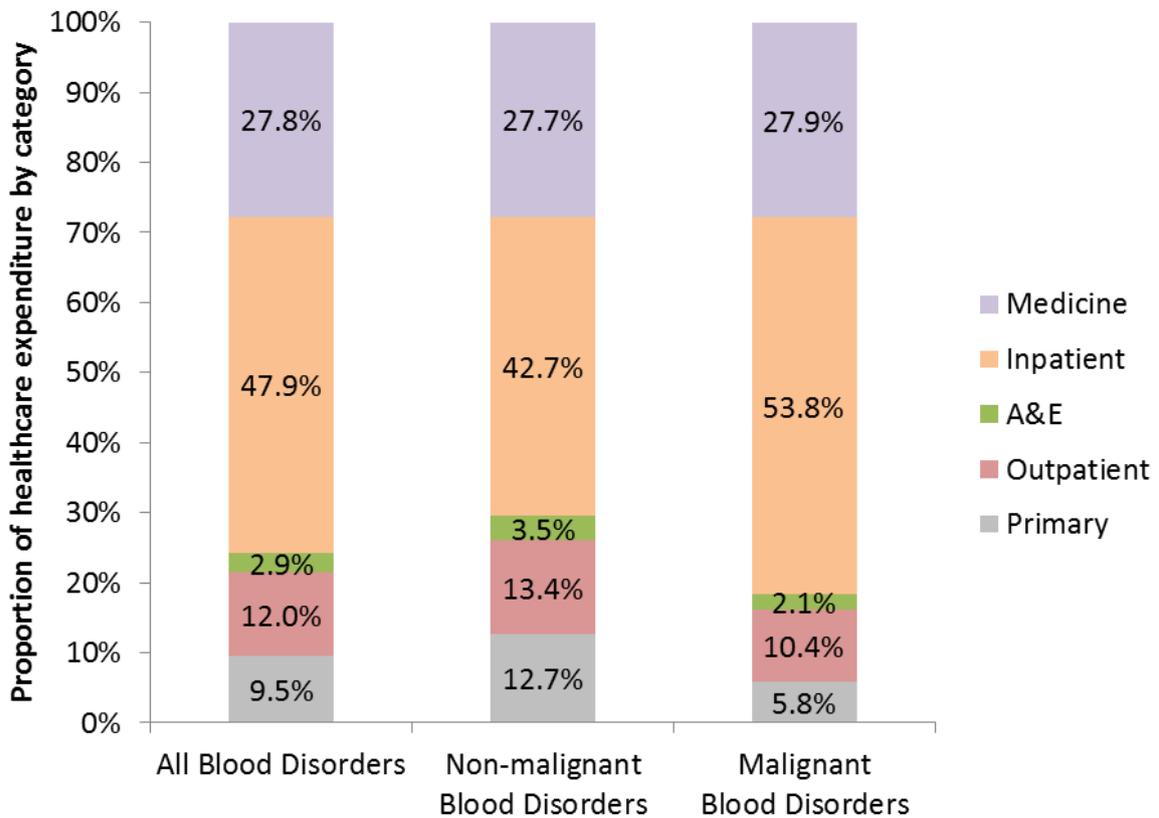
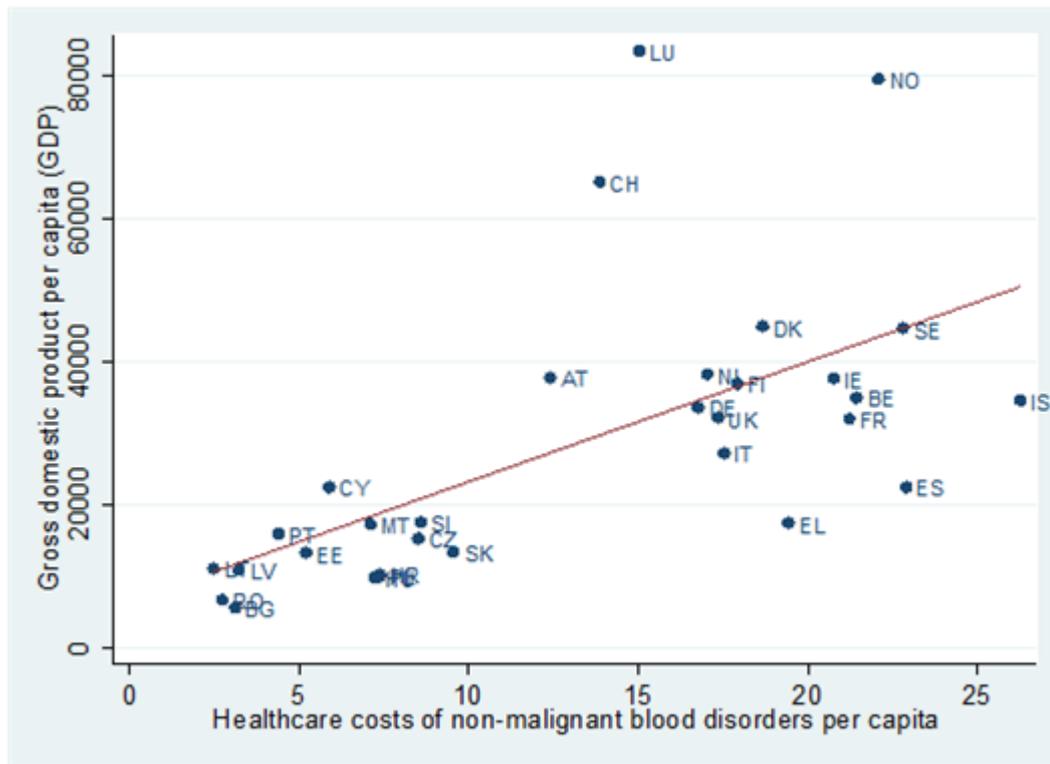


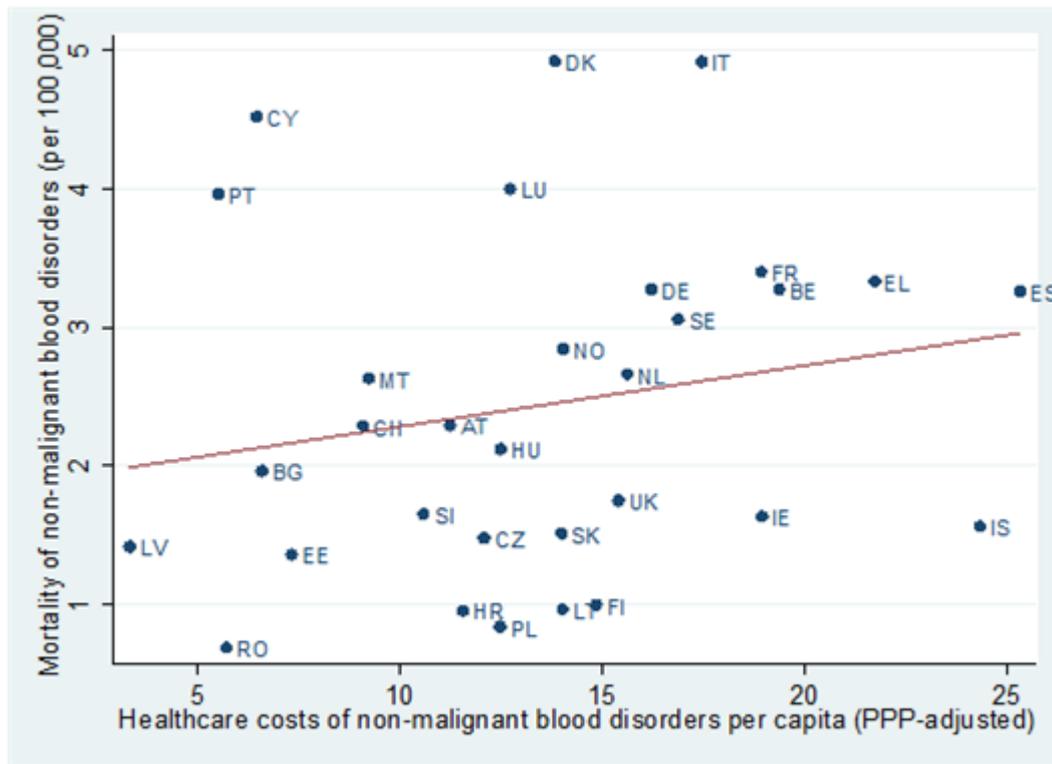
Figure 4. Association between healthcare expenditure due to non-malignant blood disorders per capita (€) and gross domestic product per capita (€)



The table below reports the output from the OLS regression:

Healthcare expenditure due to non-malignant blood disorders per capita	Coefficient	95% CI	P-value
GDP per capita	0.0002	(0.00001 to 0.0004)	0.001
Constant	6.64	(2.83 to 10.46)	0.001
R-squared	0.38		
Prob > F	0.001		

Figure 5. Association between healthcare expenditure due to non-malignant blood disorders per capita (€) and mortality (crude) per 100,000, adjusting for price differentials



The table below reports the output from the OLS regression:

Healthcare expenditure due to non-malignant blood disorders per capita	Coefficient	95% CI	P-value
Mortality per 100,000	0.874	(-0.740 to 2.487)	0.277
Constant	11.332	(7.185 to 15.480)	<0.0001
R-squared	0.039		
Prob > F	0.277		

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