Henderson RH, French D, Maughan T, Adams R, Allemani C, Minicozzi P, Coleman MP, McFerran E, Sullivan R, Lawler M. The economic burden of colorectal cancer across Europe: a population-based cost-of-illness study. The Lancet Gastroenterology & Hepatology. 2021 Jul 28. https://www.thelancet.com/journals/langas/home

Defining the economic burden of colorectal cancer across Europe

Supplementary Appendix

A1 Supplementary Methods

A1·1 Health care utilization

Colorectal cancer (CRC) healthcare resources included were: primary healthcare, outpatient care, accident and emergency (A&E) care, hospital care (Table A1), and medications. The methodology employed to evaluate CRC-related healthcare resource use was dependent on the data source. Aggregate activity and costing data were derived from global and national sources including World Health Organization (WHO), the Organization for Economic Co-operation and Development (OECD), the Statistical Office of the European Communities (Eurostat), national ministries of health, and national statistics institutes. Where no national reports were available, department heads at health institutes were contacted by email. Data were also accessed from peer-reviewed published studies or national reports from governmental/professional bodies.

Country	Primary care	Outpatient care	A&E care	Hospital care	SACT
Austria	B[1–3]	B[1,2,4]	B[1,2,5]	A[+1,6,7]	A[+8]
Belgium	B[1,2,9]	B[1,2,4]	B[1,2,10]	A[+1,6,7]	A[+8]
Bulgaria	B[1,2,11]	B[1,2,4]	B[1,2,12]	A[+1,6,7]	A[+8]
Croatia	B[13]	B[1,2,4]	C[1,2]	A[+1,6,7]	A[+8]
Cyprus	B[1,2,14]	A[15]	B[1,2,16]	A[+1,6,7]	C[17]
Czech Rep.	B[1,2,18]	A[19]	B[1,2,10]	A[+1,6,7]	A[+8]
Denmark	B[1,2,20]	A[+21]	A[+22]	A[+1,6,7]	C[23]
Estonia	B[1,2,24]	A[25]	B[24,26]	C[1,6]	A[+8]
Finland	B[1,2,27]	A[28]	B[1,2,29]	A[+1,6,7]	A[+8]
France	B[1,2,30]	B[1,2,4]	B[1,2,10]	A[+1,6,7]	A[+8]
Germany	B[1,2,31]	A[32]	B[1,2,10]	A[+1,6,7]	A[+8]
Greece	B[1,2,33]	B[1,2,4]	B[1,2,10]	A[+1,6,7]	A[+8]
Hungary	B[1,2,34]	B[1,2,4]	B[1,2,35]	A[+1,6,7]	A[+8]
Iceland	B[1,2,36]	A[37]	B[1,2,38]	A[+1,6,7]	C[23]
Ireland	B[1,2,39]	B[1,2,4]	B[1,2,10]	A[+1,6,7]	A[+8]
Italy	B[1,2,40]	B[1,2,4]	B[1,2,40]	A[+1,6,7]	A[+8]
Latvia	A[+41]	A[+41]	B[1,2,42]	A[+1,6,7]	A[+8]
Lithuania	B[1,2,43]	B[1,2,4]	C[1,2]	A[+1,6,7]	A[+8]
Luxembourg	B[1,2,44]	B[1,2,4]	C[1,2]	A[+1,6,7]	A[+8]
Malta	B[1,2,45]	B[1,2,45]	B[1,2,45]	A[+1,6,7]	C[46]
Netherlands	B[1,2,47]	A[+48]	B[1,2,10]	A[+1,6,7]	C[23]
Norway	B[1,2,49]	A[50]	B[1,2,49]	A[+1,6,7]	A[+8]
Poland	B[1,2,51]	B[1,2,4]	B[1,2,10]	A[+1,6,7]	A[+8]
Portugal	B[1,2,52]	B[1,2,4]	B[1,2,10]	A[+1,6,7]	A[+8]
Romania	B[1,2,53]	B[1,2,4]	C[1,2]	A[+1,6,7]	A[+8]
Serbia	B[54]	B[1,2,4]	C[1,2]	A[+1,6,7]	A[+8]
Slovakia	B[1,2,55]	A[1,2,56]	B[1,2,55]	A[+1,6,7]	A[+8]
Slovenia	B[1,2,57]	A[58]	B[1,2,59]	A[+1,6,7]	A[+8]
Spain	B[1,2,60]	A[61]	B[1,2,10]	A[+1,6,7]	A[+8]
Sweden	B[1,2,62]	A[63]	B[1,2,64]	A[+1,6,7]	A[+8]
Switzerland	B[1,2,65]	B[1,2,4]	B[1,2,10]	A+[1,6,7]	A[+8]
Turkey	B[66]	B[1,2,4]	B[67]	A[+1,6,7]	A[+8]
UK	B[1,2,68]	A+[69]	B[1,2,70]	A[+1,6,7]	A[+8]

Table A1 Sources employed to obtain healthcare resource use, by category and country.

SACT – systemic anti-cancer therapy

Numbers refer to supplementary reference numbers

Data are ranked into the following domains.

A^+. National CRC data: CRC-specific healthcare data are obtained for that country's population;

A. National cancer-specific data: Cancer-specific healthcare data are obtained for that country's population;

B. National data but not CRC-specific: All-cause healthcare resource use data are obtained, but not specifically related to CRC. CRC-specific resource use was determined by multiplying all-cause national data by the percentage of ambulatory visits due to CRC as a proportion of total ambulatory visits, if available. If CRC-related ambulatory information was not available, the percentage of hospital discharges due to CRC was used as a proportion of all discharges, in order to assign that country's healthcare utilisation;

C. No national data: the country's activity data are obtained for all diseases from similar countries and that data are assigned as CRC data for the particular country, using the approach defined in (B).

A1·1·1 Primary care

Primary care contacts include the number of GP consultations. Country-specific total visits to primary care due to all conditions were obtained for all countries (Supplementary references), except for Czech Republic, Denmark, Estonia, Luxembourg, Malta, and Slovakia, where the total healthcare expenditure on GP visits for all conditions were obtained.[1-3,9,11,13,14,18,20,24,27,30,31,33,34,36,39,40,41,43-45,47,49,51-55,57,60,62,65,66,68] To the total number of primary care visits or costs, we applied the percentage of primary care that was ascribed to CRC, using the discharge proportion of CRC from the 'all diseases' discharge total.[1]

The exact healthcare expenditure for the number of GP and outpatient visits for CRC was given for Latvia.[41]

A1·1·2 Outpatient care

Outpatient care activities included 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 most (n=23) countries.[1,2,4] Total expenditure on outpatient activity was available for Germany and Netherlands.[32,48] To the total number of outpatient care visits or costs, we applied the percentage of care that was ascribed to CRC, using the discharge proportion of CRC from the 'all diseases' discharge total.[1] In the case of Cyprus, Czech Republic, Estonia, Finland, Iceland, Norway, Slovakia, Slovenia, Spain, and Sweden, the number of outpatient visits to an oncologist were captured and the prevalence rate of CRC amongst all cancers was used to calculate CRC outpatient visits.[15,19,25,28,37,41,45,50,56,58,61,63] For Denmark and the UK, CRC outpatient visits were directly stated.[21,69]

A1·1·3 Accident and Emergency care

Emergency care consisted of all CRC-related hospital emergency visits. Country-specific overall visits to A&E due to all diseases were obtained for 32 countries.[1,2,5,10,12,16,24,26,29,35,38,40,42,45,49,55,59,64,67,70] To the total number of A&E visits, we applied the percentage of A&E care that was ascribed to CRC, using the discharge proportion of CRC from all diseases discharge total.[1] Denmark was the notable exception, where the number of A&E visits for CRC were directly reported.[22]

In 5 countries (Croatia, Lithuania, Luxembourg, Romania, and Serbia), attendance figures could not be obtained and A&E rates had to be derived from similar countries. Therefore, for 1) Croatia and Serbia, we used estimates from Slovenia;[59] 2) Lithuania, we used estimates from Estonia;[26] 3) Luxembourg, we used estimates from Belgium;[10] 4) Romania, we used estimates from Bulgaria.[12] For all of the A&E visits to each country, we applied the percentage of care that was attributable to CRC.

A1·1·4 Hospital care

With the exception of Estonia, national data were available on CRC-related days in hospital and day-cases. For all countries, this information was obtained from Eurostat.[1,6,7] For Estonia, age- and gender-standardised rates of hospital bed-days and day cases due to CRC in Latvia were applied to Estonian population estimates in 2015.[2]

A1·2 Healthcare unit costs

For all countries, health care resource use was evaluated using country-specific unit costs (Table A2).

A1·2·1 Primary care costs

All costs for GP visits in 30 countries were stated directly; [20,24,41,75,79,83,84,86,90,92,94,98,100,104,106,107,110,112,114-116,119,122,126,128,132,135,138,141,143] Denmark, Estonia, and Malta were exceptions;[20,24,45] here the total healthcare expenditure for primary care was listed and we applied the percentage of primary care that was ascribed to CRC, using the discharge proportion of CRC from all diseases discharge total.

A1·2·2 Outpatient care costs

All costs for outpatient visits in most (n=29) countries were stated directly.[41,48,76,80,83,85,87,90,91,101,105,108,110,113-115,120,123,127,128,133,136,139,142,143] Oncology budgets for outpatient care ,were available for all countries except - Estonia, Finland, Germany, and Iceland, and the prevalence rate of CRC amongst all cancers was used to calculate CRC outpatient care costs. [24,32,37] For Slovakia, the total healthcare expenditure for outpatient care was listed and we applied the percentage of outpatient care that was ascribed to CRC, using the discharge proportion of CRC from all diseases discharge total [1,71].

A1·2·3 Accident & Emergency care costs

All costs for A&E visits in 30 countries were stated directly; Bulgaria, the Czech Republic, and Romania were exceptions: here similar countries costs were used.[77,81,84,88,91,93,96,102,108,110,111,117,124,126,129,130,133,140,141,144] For Estonia, the total healthcare expenditure for A&E care was listed, and we applied the percentage of A&E care that was ascribed to CRC, using the discharge proportion of CRC from all diseases discharge total.[1,24] The exact healthcare expenditure per A&E visit was acquired for Hungary and Iceland.[72,73]

A1·2·4 Hospital care costs

For 31 countries, their hospital care costs were directly stated;[7,17,41,78,82,89,91,97,99,103,105,109,110,111,113,118,121,125,128,131,134,137,139,141,145] Two countries listed their oncology budgets for hospital cancer care - Estonia and Iceland – their prevalence rate of CRC amongst all cancers was used to calculate CRC outpatient care costs. [24,37]

All costs were expressed in local currency units and inflated/deflated to 2015 employing, harmonised indices of consumer prices to balance inflation for hospital services in the euro area, the EU, the European Economic Area and for other countries, including accession and candidate countries.[74]

A1·3 Medication expenditure

Medication expenditure consisted of the sum of sales of chemotherapy and targeted therapy for CRC, identified by country of sale; these data were obtained from the IQVIA oncology database.[8] For Denmark, Iceland, and the Netherlands, total expenditure on medications was obtained from the OECD, for Cyprus total expenditure on medications was obtained from Eurostat and for Malta total expenditure on medication was obtained from a government report.[17,23,46] The proportions of chemotherapy and targeted therapy for CRC medications were applied as follows:

1) Greek estimates were used for Cyprus;

2) German estimates were used for Denmark and the Netherlands;

3) Swedish estimates were used for Iceland;

4) Italian estimates were used for Malta.

Country	Primary care	Outpatient care	A&E care	Hospital care	SACT
Austria	B[75]	A[76]	B[77]	A[+78]	A[+8]
Belgium	B[79]	A[80]	B[81]	A[82]	A[+8]
Bulgaria	B[83]	B[83]	E	C[7,17]	A[+8]
Croatia	B[84]	B[85]	B[84]	C[7,17]	A[+8]
Cyprus	B[86]	A[87]	B[88]	A[89]	C[17]
Czech Rep.	B[90]	B[90]	E	C[7,17]	A[+8]
Denmark	C[20]	A[91]	A[91]	A[91]	C[23]
Estonia	C[24]	B[24]	C[24]	B[24]	A[+8]
Finland	B[92]	A[37]	B[93]	A[37]	A[+8]
France	B[94]	A[95]	B[96]	A[97]	A[+8]
Germany	B[98]	A[32]	B[77]	A[99]	A[+8]
Greece	B[100]	B[101]	B[102]	A[+103]	A[+8]
Hungary	B[104]	A[+105]	B[72]	A[+105]	A[+8]
Iceland	B[106]	A[37]	B[73]	A[37]	C[23]
Ireland	B[107]	A[+108]	A[+108]	A[109]	A[+8]
Italy	A[110]	A[110]	A[110]	A[110]	A[+8]
Latvia	A[+41]	A[+41]	B[111]	A[+41]	A[+8]
Lithuania	B[112]	A[113]	B[77]	A[113]	A[+8]
Luxembourg	B[114]	A[114]	B[77]	C[7,17]	A[+8]
Malta	C[45]	D[115]	B[111]	B[111]	C[46]
Netherlands	B[116]	A[+48]	A[+117]	A[+118]	C[23]
Norway	B[119]	B[120]	B[93]	A[+121]	A[+8]
Poland	B[122]	A[123]	B[124]	A[+125]	A[+8]
Portugal	B[126]	A[127]	B[126]	C[7,17]	A[+8]
Romania	D[115]	D[115]	E	C[7,17]	A[+8]
Serbia	B[128]	B[128]	B[129]	B[128]	A[+8]
Slovakia	D[115]	B[71]	B[130]	C[7,17]	A[+8]
Slovenia	D[115]	D[115]	B[111]	A[+131]	A[+8]
Spain	B[132]	A[133]	A[133]	A[134]	A[+8]
Sweden	B[135]	A[136]	B[93]	A[+137]	A[+8]
Switzerland	B[138]	A[+139]	C[1,2,140]	A[+139]	A[+8]
Turkey	B[141]	B[142]	B[141]	B[141]	A[+8]
UK	A[+143]	A[+143]	A[+144]	B[145]	A[+8]

Table A2 Sources used to obtain healthcare unit costs, by category and country.

SACT – systemtic anti-cancer therapy

Numbers refer to supplementary references

For all countries, health care resource use is determined using country-specific unit costs.

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

A^{+}. CRC-specific expenditure data.

A. Cancer-specific expenditure data.

B. Directly obtained from sources such as national fee schedules, national reports, published studies, etc;

C. Acquired from national expenditure figures (e.g. primary care, outpatient care, emergency care, hospital care), using the respective total activity levels. For example, cost per hospital day is estimated by dividing the total hospital expenditure by the total number of hospital days;

D. Estimates derived costs and prices used in the WHO-CHOICE (**CHO**osing **I**nterventions that are **C**ost-**E**ffective) analysis;

E. Derived from the predictions of linear regression analyses of the unit costs of countries with available data.

A1·4 Non-health care utilisation

A1·4·1 Prevalence

Prevalence figures were used to calculate informal care and morbidity losses. Country-specific data for total prevalence of cancer and CRC were obtained for Bulgaria (2011, prevalence population extrapolated to 2015), Czech Republic (2015), Denmark (2015), Finland (2015), France (2008, prevalence population extrapolated to 2015) Italy (2015) Iceland (2015), Ireland (2015), Latvia (2015), Norway (2015), Slovenia (2014, prevalence population extrapolated to 2015), Sweden (2015), and Switzerland (2015).[146–154] German 10-year prevalence figures for 2013-2014 were obtained and extrapolated to actual prevalence for the German population in 2015, using estimates for England on the basis of similar socio-economic development between the Germany and UK. [155,156] The actual prevalence in England (2015) was extrapolated to cover all of the UK population.[156] For the remaining 21 countries, 5-year prevalence estimates at the end of 2012 from IARC were used and extrapolated to actual prevalence for each country as follows:[157]

1) German estimates were used for Austria and Luxembourg;

2) Bulgarian estimates were used for Romania and Turkey;

3) Czech estimates were used for Hungary, Poland, and Slovakia;

3) Danish estimates were used for Belgium and the Netherlands;

4) Italian estimates were used for Cyprus, Greece, Malta, Portugal, and Spain;

4) Slovenian estimates were used for Croatia and Serbia;

5) Latvian estimates were used for Estonia and Lithuania.

A1·4·2 Survival

Country-specific age-standardised five-year net survival estimates for CRC patients were obtained based on data from the CONCORD programme.[158] Cyprus, Greece, Hungary, Luxembourg, Serbia and Turkey did not have CRC survival estimates published, so estimates from similar countries were used as follows:

1) Bulgarian estimates were used for Turkey;

2) Croatian estimates were used for Serbia

3) Czech Republic estimates were used for Hungary;

4) German estimates were used for Luxembourg;

5) Italian estimates were used for Greece and Cyprus.

A1·4·3 Mathematical proofs for permanent earnings lost using conditional probability of survival :

Annuity formula assumes stream of payments from next year

$$PV = \frac{X}{1+i} + \frac{X}{(1+i)^2} + \cdots \frac{X}{(1+i)^n} = X\left(\frac{1}{i} - \frac{1}{i(1+i)^n}\right)$$

Amending this for survival

$$let\ a = \frac{\varphi X}{1+i} + \frac{\varphi^2 X}{(1+i)^2 +} + \cdots$$
$$=> \ \frac{\varphi}{1+i}a = \frac{\varphi^2 X}{(1+i)^2 +} + \cdots$$
$$=> \ a\left(1 - \frac{\varphi}{1+i}\right) = \frac{\varphi X}{1+i}$$
$$=> \ a\left(\frac{i+\delta}{1+i}\right) = \frac{\varphi X}{1+i}$$
$$=> \ a = \frac{\varphi X}{i+\delta}$$

$$PV = \frac{\varphi X}{1+i} + \frac{\varphi^2 X}{(1+i)^2 +} + \cdots \frac{\varphi^n X}{(1+i)^n}$$
$$= \frac{\varphi X}{i+\delta} - \frac{\varphi^n}{(1+i)^n}\frac{\varphi X}{i+\delta}$$
$$= \varphi X\left(\frac{1}{i+\delta} - \frac{\varphi^n}{(i+\delta)(1+i)^n}\right)$$

Where: a = present value of an annuity

PV = Present Value (€)

X = Annual earnings lost (€)

i = discount rate (%)

n = years lost

φ = conditional probability of survival

δ = conditional probability of not surviving

A1·4·4 High Resolution Hospital Care Data

Data were ranked (in order from highest to lowest per country) for: CRC hospital care costs as a proportion of CRC healthcare expenditure; CRC pharmaceutical costs as a proportion of CRC healthcare expenditure; CRC healthcare costs as a proportion of total healthcare expenditure; CRC 5-year net survival, number of oncologists, number of computer tomography (CT) scans performed, number of CT scanners, numbers of radiotherapy equipment, number of radiologists, and number of surgical oncologists (personal communication, Nancy Anderson, European Society of Surgical Oncology).[158–162]

A1·4·5 Informal care

We were cautious in our selection of the numbers of patients who would potentially receive informal care, either those severely limited in daily activities, or those who were terminally ill. Prevalence figures for all cancer patients were calculated as detailed above and employed, along with data from Survey of Health, Ageing and Retirement in Europe (SHARE) to evaluate the informal care needs of CRC patients (Table A3).[163] Therefore,

we estimated the hours of informal care provided due to CRC using Wave 6 of the SHARE survey, which collected data on more than 60,000 individuals' resident in 17 European countries in 2015 (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, France, Germany, Greece, Italy, Luxembourg, Poland, Portugal, Spain, Sweden, Switzerland and Slovenia). To obtain estimates for the 16 countries who were not in SHARE, data were combined from similar countries that were in SHARE. Therefore, for: 1) Bulgaria, Hungary, Latvia, Lithuania, Romania, Serbia, Slovakia, and Turkey, data were pooled from the Czech Republic, Estonia, Slovenia and Poland; 2) For Finland, Iceland and Norway data were pooled from Denmark and Sweden; 3) for Cyprus and Malta, data were pooled from Greece, Italy, Portugal and Spain and 4) for Luxembourg, Ireland and the UK, data were pooled from Austria, Belgium, France, Germany and the Netherlands.

A1·4·5·1 Informal care for patients severely limited in daily activities due to CRC

Hours of informal care for severely limited cancer patients were estimated by multiplying number of cancer cases, by the probability of being severely limited by cancer, by the probability of receiving care with cancer, by the fraction of CRC patients amongst all cancer patients.

1) Prevalence of cancer in the population was calculated as detailed in section 1·4·1.

2) Probability of being severely limited in daily activities due to cancer.

SHARE data were used to undertake logistic regressions, calibrating for the presence of cancer, presence of other health conditions and country of residence, to determine country-specific estimates of the probability of being severely limited in daily activities due to cancer.

3) Probability of receiving informal care due to cancer.

SHARE data were used to perform two logistic regressions (one for internal household caregiving and one for external household caregiving), to assess the probability that cancer patients received informal care, after calibrating for the presence of cancer, presence of other health conditions, and country of residence.

4) Hours of informal care received due to cancer.

SHARE data were used to perform an ordered logistic regression (OLR) to evaluate the amount of informal care time from caregivers (approximately per day, per week, per month or less often) that cancer patients received, after calibrating for the presence of cancer, limitations in daily living, presence of other health conditions, and country of residence. Using information from SHARE, data from the OLR was converted into unpaid care hours (either daily, weekly, monthly or annually) that patients with cancer received. Informal care hours were then transformed to CRC-specific care hours by multiplying by CRC prevalence rate amongst all cancers.

Calculations from Stataa based on SHARE Wave 6 data						**Hours of care provided, based on CRC prevalence and probability of CRC patient receiving care**								
Severely Limited		**Hours**	**Marginal effects**	**Hours**	**Country**	**Total cases of cancer**	**Probability of limited by cancer**	**Probability of receiving care**	**CRC proportion of cancer**	**Severely Limited (hrs)**	**CRC deaths (2015)**	**Terminally Ill (hrs)**	**Total Informal Care (hrs)**	**Hrs provided by under 65s**
Caregiver 1	daily	1840	0.061922	113.94	**Austria**	388,376	0.0760	0.0366	0.1223	52,424	2,062	1,968,155	2,020,580	1,503,807
	weekly	368	0.030672	11.29	**Belgium**	508,880	0.0971	0.0486	0.1325	126,091	2,874	2,743,200	2,869,291	2,135,457
	monthly	96	-0.008441	-0.81	**Bulgaria**	264,739	0.1002	0.0489	0.1544	79,462	2,512	2,397,675	2,477,138	1,843,599
	annually	8	-0.084153	-0.67	**Croatia**	201,408	0.1521	0.0645	0.1490	116,699	2,063	1,969,110	2,085,809	1,552,354
	Total			123.74	**Cyprus**	40,374	0.1119	0.0401	0.1223	8,778	115	109,766	118,544	88,226
Care giver 2	daily	1840	0.046148	84.91	**Czech Rep.**	387,367	0.0968	0.0472	0.1395	97,802	3,592	3,428,523	3,526,325	2,624,452
	weekly	368	0.041146	15.14	**Denmark**	299,108	0.0988	0.0411	0.1356	65,296	1,836	1,752,441	1,817,737	1,352,843
	monthly	96	-0.009895	-0.95	**Estonia**	49,681	0.0823	0.0467	0.1227	9,272	473	451,473	460,745	342,908
	annually	8	-0.077399	-0.62	**Finland**	259,102	0.1070	0.0442	0.1022	49,609	1,213	1,157,795	1,207,403	898,604
	Total			98.48	**France**	2,982,000	0.1095	0.0450	0.1190	692,952	17,700	16,894,447	17,587,399	13,089,343
Caregiver 3	daily	1840	0.066247	121.89	**Germany**	3,677,028	0.1297	0.0591	0.1321	1,476,435	25,466	24,307,005	25,783,440	19,189,211
	weekly	368	0.082579	30.39	**Greece**	517,569	0.1187	0.0302	0.1078	79,154	2,805	2,677,340	2,756,495	2,051,509
	monthly	96	-0.004146	-0.40	**Hungary**	362,272	0.1002	0.0489	0.1762	124,134	5,008	4,780,079	4,904,212	3,649,938
	annually	8	-0.14468	-1.16	**Iceland**	13,799	0.1070	0.0442	0.1032	2,669	69	65,860	68,529	51,002
	Total			150.73	**Ireland**	167,715	0.1031	0.0473	0.1222	39,626	1,013	966,897	1,006,523	749,100
	Grand Total			**396.36**	**Italy**	3,000,000	0.1019	0.0370	0.1380	618,745	18,979	18,115,238	18,733,984	13,942,684
					Country	**Total cases of cancer**	**Probability of being limited by cancer**	**Probability of receiving care**	**CRC proportion of cancer**	**Severely limited (hrs)**	**CRC deaths (2015)**	**Terminally ill (hrs)**	**Total informal care**	**Hrs provided By under 65s**
Terminally Ill					**Latvia**	75,042	0.1002	0.0489	0.1086	15,841	703	671,005	686,847	511,183
Help Time	**Hours**	**Marginal effects**	**Hours**		**Lithuania**	110,376	0.1002	0.0489	0.1037	22,259	979	934,444	956,703	712,022

Under a month	153.34	0.08765	13.44	**Luxembourg**	25,494	0.1348	0.0619	0.1273	10,736	115	109,766	120,503	89,684
1 to 3 months	306.67	0.15139	46.43	**Malta**	20,466	0.1119	0.0401	0.1450	5,277	122	116,448	121,724	90,593
3 to 6 months	690.01	0.19721	136.08	**Netherlands**	765,349	0.1031	0.0473	0.1508	223,188	5,176	4,940,433	5,163,621	3,843,002
6 to 11 months	1303.36	0.18725	244.05	**Norway**	250,832	0.1070	0.0442	0.1409	66,231	1,595	1,522,409	1,588,640	1,182,338
1 year	1840	0.37649	692.75	**Poland**	1,397,014	0.0736	0.0347	0.1275	180,501	12,163	11,609,444	11,789,945	8,774,614
Total			**1132.75**	**Portugal**	494,537	0.1417	0.0595	0.1461	241,381	3,847	3,671,917	3,913,298	2,912,455
				Romania	730,407	0.1002	0.0489	0.1355	192,381	6,123	5,844,333	6,036,714	4,492,798
Probability of providing unpaid care				**Serbia**	339,122	0.0878	0.0468	0.1413	78,038	2,594	2,475,943	2,553,981	1,900,789
to terminally ill cancer patient =			84%	**Slovakia**	199,278	0.1002	0.0489	0.1672	64,777	2,036	1,943,339	2,008,115	1,494,531
Probability of receiving unpaid care				**Slovenia**	98,331	0.0965	0.0516	0.1376	26,683	784	748,319	775,002	576,792
if patient has CRC =			74%	**Spain**	2,214,111	0.0852	0.0338	0.1053	265,841	15,380	14,680,034	14,945,874	11,123,400
				Sweden	495,420	0.1152	0.0473	0.1236	132,083	2,782	2,655,387	2,787,470	2,074,562
				Switzerland	316,500	0.0691	0.0321	0.1166	32,444	1,794	1,712,352	1,744,796	1,298,557
				Turkey	3,703,530	0.0878	0.0468	0.0837	504,980	6,967	6,649,922	7,154,902	5,325,004
				UK	2,128,923	0.1031	0.0473	0.1258	517,813	16,423	15,675,565	16,193,379	12,051,850

Table A3 Data used to calculate CRC informal care hours in 2015 for 33 European countries.

a- Stata software v·14·2 (StataCorp, College Station, TX, USA); b - Probability of being limited by cancer, and thus requiring informal care; c- hours provided by caregivers under the age of 65, and subsequently valued with hourly wages.

Severely limited (hrs) = Total hrs x No. of cancer patients x Probability of being limited by cancer x Probability of receiving care x CRC proportion

Terminally ill (hrs) = Total hrs x CRC deaths x Probability of providing unpaid care to terminally ill cancer patient

A1·4·5·2 Informal care to terminally ill patients with CRC.

Hours of informal care for terminally ill CRC patients were estimated by multiplying the products of:

1) Number of CRC deaths, derived from Eurostat.[164]

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

The end-of-life questionnaire from SHARE was employed. Participants were asked whether they had provided unpaid care for anyone who had died in the last year. Information provided included indicating the age of the person to whom care was provided and any health conditions from which that person was suffering. The probability of providing informal care for a cancer patient was estimated using logistic regression analysis and calibrating for the individual country.

3) Hours of informal care received due to cancer.

Data from the end-of-life questionnaire were used in SHARE; we performed an OLR to assess the amount of informal care time (about daily, about weekly, about monthly or less often) that caregivers provided to a terminally-ill cancer patient, after calibrating for the presence of cancer, and country of residence. These were transformed into informal care 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.

Informal care hours were then transformed to CRC-specific care hours by multiplying by CRC prevalence rate amongst all cancers.

A1·4·5·3 Valuing informal care hours

SHARE participants were asked about the relationship between the person being cared for and caregiver (e.g. spouse, sibling, offspring, parent, friend etc.). Spouses, siblings and friends providing the care were inferred to be of similar age to the patient, therefore carers of patients aged 65 years or more were reasoned to be retired and those carers of patients aged less than 65 years were reasoned to be of working age. The probability of receiving informal care for a CRC patient was estimated using logistic regression, calibrating for relationship status and age. If the caregiver was 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 estimated the percentage of those carers who were employed or unemployed/economically inactive.

Caregivers of working age, economically active, and in employment, had their mean net hourly wage rate applied to informal care hours. Yearly earnings were calibrated to hourly wage rates, surmising that there were 230 working days each year and each day comprised of 8 hours of work. For caregivers in retirement, unemployed or economically inactive, the national hourly minimum wage was applied.[165] For countries with no official minimum wage rate (Austria, Cyprus, Denmark, Finland, Iceland, Italy, Norway, Sweden, and Switzerland), the lowest-paid sector in the economy was used as a surrogate for the minimum wage.[166–174]

A1·4·6 Mortality losses

The OECD defines that working-age begins at 15. Eurostat provided age and gender-specific deaths for CRC in all countries.[164] Prospective working years lost for the human capital approach (HCA) were determined as the difference between the age at death and the effective age of retirement (individualised for each country).[175,176] The number of working years lost was then multiplied by gender-specific average yearly earnings transformed into mean daily earnings.[177] As not everyone will be active economically (i.e. either working or actively searching for work) or employed, we had to avoid overestimation of the working years lost. Therefore, age- and gender-specific employment and activity rates were obtained from Eurostat, for each of the 33 countries and applied to the prospective lost earnings due to premature mortality.[178,179]

$$Annual\ earnings\ lost\ (CRC\ death) = 230\ days \times Daily\ wage \times Employment\ rate \times Activity\ rate = X$$

Potential future earnings were estimated by using 3.5% and 10% discount rates, with the following formula:[177]

$$Total\ earnings\ lost\ (HCA)\ = X\left(\frac{1}{i} - \frac{1}{i(1+i)^n}\right)$$

$$discount\ rate = i$$

$$years\ lost = n$$

$$\sum_{j=1}^{33}(Total\ male\ earnings\ lost + Total\ female\ earnings\ lost) = Total\ mortality\ losses\ (HCA)$$

A1·4·7 Morbidity losses

Absence of work due to CRC is associated with productivity losses due to morbidity. Morbidity losses would occur when: individuals take leave of absence for a defined period of time or when individuals are declared incapacitated or disabled due to CRC, therefore leaving the labour market. Table A4 describes all the sources used to obtain temporary and permanent absence from work due to CRC.

Temporary absence from work due to sickness

Total sick days were reported for 31 countries. Cyprus and Iceland were the exceptions, for these countries we used Greece and Sweden sick days as surrogates, based on Cyprus and Iceland's population estimates respectively.[24,29,50,182-210] The number of sick days due to cancer were either reported directly or derived from permanent absence due to cancer. The number of cancer sick days was then multiplied by the CRC proportion of hospital bed days [7].

For countries where we could not establish the proportion of sickness leave attributable to cancer, we used proportions from other countries. Therefore, for:

1) Denmark and Iceland, estimates were used from Sweden;[62]

2) Bulgaria, Estonia, Hungary, Latvia, Lithuania, Romania, Serbia, and Turkey, estimates were used from Poland;[180]

3) Cyprus, Greece and Portugal, estimates were used from Spain;[181]

4) Ireland and the UK, estimates were used from France;[182]

5) Malta, Croatia and Slovenia, estimates were used from Italy;[183]

6) Slovakia, estimates were used from the Czech Republic;[184]

7) Switzerland, estimates were used from Germany.[185]

For all countries, the proportion of cancer-specific absent days from work due to CRC was obtained by assuming that this would be the same as the percentage of countrywide days in hospital due to CRC in the working age population. We postulated that the higher the number of days spent in hospital, the higher the number of working days that would be lost due to illness. Therefore, the number of CRC sick days were calculated using the formulae:

1. $CRC\ sick\ days = Cancer\ sick\ days\ \times \frac{CRC\ inpatient\ days}{Cancer\ inpatient\ days}$
2. $CRC\ sick\ days \times Average\ daily\ wage = earnings\ lost$
3. $\sum_{j=1}^{33}(Total\ earnings\ lost) = Total\ temporary\ morbidity\ losses$

Permanent absence from work due to incapacity or disability

Eurostat provided country-specific information on the numbers of working-age individuals receiving incapacity or disability benefits and not being able to work.[186] To this, we applied the percentage that was allotted to cancer.[180,181,184,187–191]

For Austria, the Czech Republic, Luxembourg, the Netherlands, Norway, Poland, Spain, and Sweden, we used the percentage of overall temporary absence from work due to cancer.

Potential working years lost to permanent disability for HCA were determined as the difference between the age at death and the maximum effective age of retirement (individualised by country). Permanent absence was determined by the following steps:

- The number of patients with a CRC disability was ascertained by calculating the product of all patients claiming disability, by the fraction of CRC patients discharged from the number of all healthcare discharges.
- The number of disabled patients in each age band from 15-years (5-year bands) to the effective retirement age (individualised for each country) was multiplied by the proportion of patients with a CRC diagnosis in that age band.
- The annual wage for each country was determined by the product of 230 working days per year multiplied by the daily wage and by the employment rate.
- Finally, the present value of the potential earnings lost over the working life of the CRC patient was the product of annual earnings lost multiplied by the conditional probability of survival multiplied by the present value formula, discounting at 0%, and then discounted at 3·5%, and 10% using the human capital approach.

Where we could not establish the percentage of permanent absence from work due to incapacity or disability attributable to cancer, percentages from other countries were used by the same methodology to estimate temporary absence from work due to sickness. As with temporary absence from work, for all countries the percentage of cancer-specific permanent absence from work due to CRC was obtained by presuming that this would be the same as the percentage of overall days in hospital due to the condition in the working-age population. We postulated that the higher the number of days spent in hospital, the higher the number of working days that would be lost due to permanent absence due to illness.[192]

$$Annual\ earnings\ lost\ (CRC\ disablement) = 230\ days \times Daily\ wage \times Employment\ rate = Y$$

$$Permanent\ earnings\ lost = \varphi Y\left(\frac{1}{i+\delta} - \frac{\varphi^n}{(i+\delta)(1+i)^n}\right)$$

$$conditional\ probability\ of\ survival = \ \varphi = 1 - \ \delta$$

$$discount\ rate = i$$

$$years\ lost = n$$

Temporary morbidity losses were calculated to be the product of CRC sick days multiplied by the average daily wage.

$$\sum_{j=1}^{33}(Permanent\ morbidity\ losses + Temporary\ morbidity\ losses) = Total\ morbidity\ losses$$

Country	Temporary absence from work	Permanent absence from work
Austria	188	186
Belgium	193	186,193
Bulgaria	194	186
Croatia	13	186
Cyprus	195	186
Czech Rep.	184	186
Denmark	196	186
Estonia	197	186
Finland	198,199	186,200
France	182,201	186,202
Germany	185,203	186,204
Greece	195	186
Hungary	34	186
Iceland	20	186,205
Ireland	206	186
Italy	183,207	186,208
Latvia	209	186
Lithuania	210	186
Luxembourg	189	186
Malta	97	186
Netherlands	190,211	186
Norway	191,212	186
Poland	180,213	186
Portugal	214	186
Romania	215	186
Serbia	216	186
Slovakia	217	186
Slovenia	218	186
Spain	181	186
Sweden	62,187	186
Switzerland	219	186
Turkey	220	186
UK	221,222	186

Table A4 Sources used to obtain morbidity losses, by country.

Numbers refer to references

A2 Supplementary Results

Morbidity costs were initially calculated based on one survival estimate per country to give a total of €5·97B. When more granualar survival data (split into 5 age bands per country) was employed to determine costs, there was a rise of 6% (€355M) to €6·325B

A3 Supplementary Tables and Figures

Country	Mortality losses		Morbidity losses	Informal Care		Health care unit costs				
	Yearly earnings		daily earnings	Hourly earnings						
	Males	Females		Carers in employment	Carers not in employment	GP visit	Outpatient visit	A&E visit	Hospital day	Total healthcare
Austria	29,915	22,953	122	15	5	39	11[b]	827	602[a]	1,480
Belgium	37,904	34,488	160	22	8	24	44[b]	394	518[b]	980
Bulgaria	36,611	30,483	146	20	7	26	56	281	513	876
Croatia	33,964	31,121	142	20	6	49	75	683	225	1,032
Cyprus	25,207	20,474	99	12	5	14	38[b]	15	127[b]	193
Czech Rep.	27,874	20,882	108	14	4	21	30	105	209	365
Denmark	56,399	44,331	219	30	10	12	386[b]	88[b]	688[b]	1,174
Estonia	31,737	21,924	115	15	5	39	132	1,195	390[b]	1,755
Finland	43,650	33,924	168	22	12	72	69[b]	313	533[b]	986
France	34,220	28,295	138	20	8	20	26[b]	79	434[b]	559
Germany	41,146	32,358	167	21	8	28	73[b]	77	188[b]	365
Greece	24,570	20,654	99	11	4	11	35	66	290[a]	402
Hungary	49,555	40,817	198	27	10	91	1,095[a]	1,511	1,119[a]	3,816
Iceland	29,766	23,523	117	4	2	57	187[b]	20	513[b]	777
Ireland	33,486	28,105	135	17	6	70	133[a]	257[a]	546[b]	1,007
Italy	37,530	31,293	153	20	9	15[b]	20[b]	286[b]	783[b]	1,104
Latvia	41,844	32,621	159	20	8	5[a]	32[a]	500	385[a]	922
Lithuania	34,961	27,949	136	17	7	13	39[b]	70	150[b]	272
Luxembourg	26,427	24,752	113	14	6	18	18[b]	44	518	598
Malta	26,945	22,551	110	14	5	56	40	127	480	703
Netherlands	38,299	31,341	159	19	7	16	101[a]	101[a]	306[a]	523
Norway	29,589	25,520	122	19	5	12	117	21	186[a]	335
Poland	34,626	28,872	139	19	7	15	30[b]	144	1,032[a]	1,221
Portugal	27,458	22,894	109	15	6	45	44[b]	161	607	857
Romania	44,613	41,957	189	26	9	115	168	212	418	913
Serbia	41,025	36,786	170	26	9	39	16	148	475[a]	677
Slovakia	36,032	27,917	140	19	7	71	99	577	483	1,230
Slovenia	30,514	27,911	127	17	7	35	52	97	699[a]	883
Spain	25,227	21,877	104	13	4	31	61[b]	107	225[b]	424
Sweden	28,818	24,780	118	15	10	101	128[b]	188	293[a]	710
Switzerland	29,184	23,839	121	15	6	29	35[a]	150	537[a]	751
Turkey	24,400	24,670	106	12	7	58	34	101	1,158	1,351
UK	37,790	28,686	148	20	7	42[a]	197[a]	158[a]	178[a]	576
Mean	34,281	28,501	138	18	7	39	110	276	479	904
Upper CI	36,960	30,712	149	20	8	49	178	397	573	1,130
Lower CI	31,603	26,291	128	16	6	29	42	155	385	677

Table A5. Average unit costs (€) in 33 European countries, by country, in 2015.
Adjusted for purchasing power parity (PPP). a - CRC costs, b – other cancer costs. CI – confidence interval.

Country	Mortality				Morbidity	Informal care		Healthcare contacts			
	Deaths		Working years lost			Care hours					
	Males	Females	Males	Females	Working days lost	Carers in employment	Carers not in employment	GP visit	Outpatient visit	A&E visit	Hospital day
Austria	0·03	0·02	0·3	0·1	16	130	105	83	39	4	19[a]
Belgium	0·03	0·02	0·2	0·2	33	128	128	30	49	1	12[a]
Bulgaria	0·06	0·03	0·6	0·2	7	172	172	19	27	1	10[a]
Croatia	0·08	0·05	0·7	0·5	8	223	271	63	34	6	22[a]
Cyprus	0·02	0·01	0·3	0·1	2	71	69	5	12[b]	1	5[a]
Czech Rep·	0·05	0·03	0·5	0·3	29	186	148	23	23[b]	0.5	16[a]
Denmark	0·04	0·03	0·4	0·3	15	183	138	87	15[a]	0.01[a]	9[a]
Estonia	0·07	0·04	0·7	0·4	8	200	151	44	8[b]	5	17[a]
Finland	0·03	0·02	0·3	0·2	20	120	101	10	0.3[b]	2	14[a]
France	0·02	0·02	0·2	0·2	59	137	128	19	33	2	10[a]
Germany	0·04	0·03	0·4	0·3	7	184	133	31	41[b]	1	26[a]
Greece	0·03	0·02	0·3	0·1	1	104	150	51	21	4	12[a]
Hungary	0·11	0·04	1·0	0·4	9	255	242	78	25.5	1	22[a]
Iceland	0·07	0·05	0·6	0·8	4	134	74	22	9[b]	2	13[a]
Ireland	0·07	0·03	0·8	0·3	1	111	106	13	22	1	8[a]
Italy	0·03	0·02	0·4	0·2	4	139	169	56	53	5	12[a]
Latvia	0·05	0·03	0·4	0·2	13	187	159	82	78[a]	3	17[a]
Lithuania	0·06	0·03	0·5	0·3	9	179	149	60	89	28	16[a]
Luxembourg	0·04	0·002	0·4	0·003	115	113	101	24	48	1	15[a]
Malta	0·04	0·03	0·3	0·2	59	143	140	9	12	2	10[a]
Netherlands	0·05	0·03	0·5	0·3	49	174	132	49	80[a]	1	10[a]
Norway	0·06	0·04	0·6	0·4	234	181	126	24	8[b]	2	11[a]
Poland	0·06	0·03	0·6	0·2	58	157	154	25	43	1	8[a]
Portugal	0·11	0·05	1·1	0·6	0·1	194	183	23	20	8	11[a]
Romania	0·10	0·05	1·1	0·5	4	149	155	69	43	1	14[a]
Serbia	0·11	0·04	1·0	0·3	3	139	220	72	147	2	20[a]
Slovakia	0·06	0·03	0·5	0·3	65	187	184	39	105[b]	1	16[a]
Slovenia	0·08	0·03	0·8	0·3	8	193	182	31	11[b]	2	14[a]
Spain	0·05	0·03	0·4	0·3	16	148	173	51	1[b]	6	12[a]
Sweden	0·04	0·04	0·5	0·4	23	171	115	10	4[b]	1	9[a]
Switzerland	0·04	0·03	0·4	0·3	11	129	83	24	25	1	13[a]
Turkey	0·03	0·02	0·4	0·3	9	37	55	6	9	2	3[a]
UK	0·05	0·03	0·5	0·3	43	143	107	19	1	2	8[a]
Mean	0·05	0·03	0·5	0·3	29	154	143	38	34	3	13
Upper CI						170	159	47	46	5	15
Lower CI						139	126	29	23	1	11

Table A6. Colorectal cancer-related resource units per 1,000 population in 33 European countries, by country, 2015.

Mortality losses are CRC deaths (15-years to effective retirement age), for both males and females, and consequential working years lost after adjusting for employment rate. Morbidity losses list the number of CRC sick days taken and are a measure of temporary morbidity. Informal care hours are a measure of voluntary caregiver hours expended on CRC patients. Healthcare contacts are the number of visits for a CRC patient. a - CRC activity, b – General cancer activity. CI – confidence interval

Rank	CRC hospital care 2015 (%)		CRC pharma-ceuticals 2015 (%)		CRC healthcare costs per case 2015 (€)		CRC survival 2009-2014 (%)		Number per 100,000 of population (Eurostat 2015 data)[a]											
									Oncologists		CT scanners		CT scans		Radiologists		Radiotherapy equipment		Surgical Oncologists	
1	LU	84·8	BG	62·0	HU	36,295	BE	67·7	IT	7·1	IS	3·9	BE	19,844·9	EL	31·0	CH	1·7	IS	5·2
2	PL	72·2	FR	45·8	RO	7,388	CH	67·7	PL	5·7	DK	3·8	IS	19,094·7	LT	20·9	FR	*1·7*	FI	4·2
3	MT	69·6	UK	41·8	SK	7,289	IS	66·7	SE	5·7	NO	*3·8*	FR	18,870·2	HR	19·6	DK	1·4	NL	4·0
4	CH	65·5	ES	34·6	BG	4,872	NO	66·1	IS	4·8	LV	3·7	CH	*18,870·2*	AT	18·2	NL	*1·4*	AT	3·0
5	FI	64·9	CZ	32·1	EE	4,865	SE	65·1	EE	4·6	CH	3·6	LU	18,795·7	CZ	18·1	SK	1·2	CY	2·1
6	SI	64·6	SK	26·7	AT	4,054	FI	65·0	NO	4·2	DE	3·5	AT	17,519·6	HU	*18·1*	FI	1·0	SI	2·5
7	EL	64·4	BE	25·0	LV	3,764	DE	64·1	BE	4·0	EL	3·5	TR	17,484·0	SK	*18·1*	IE	1·0	LU	2·3
8	IS	62·9	IE	24·9	HR	3,568	LU	*64·1*	CH	3·9	CY	3·4	LV	16,851·7	EE	17·8	IS	0·9	LT	2·0
9	RS	57·6	FI	24·3	RS	3,145	AT	64·0	ES	3·9	BG	3·4	DE	16,179·3	ES	16·1	NO	0·9	EL	1·8
10	IT	56·1	RO	24·1	LT	2,931	NL	64·0	IE	3·9	IT	3·3	SI	15,620·2	FR	15·5	BE	*0·9*	EE	1·7
11	LV	55·3	IT	24·0	IS	2,902	CY	*63·5*	UK	3·8	AT	2·9	EL	14,601·4	SE	15·3	LU	0·9	BE	1·3
12	PT	54·9	DK	23·7	SI	2,870	EL	*63·5*	AT	*3·5*	FI	2·2	DK	14,310·4	BG	14·5	CZ	0·9	IT	1·2
13	AT	52·0	SI	23·1	PL	2,868	IT	63·5	CY	3·5	SE	*2·2*	CY	13,994·7	LU	13·9	BG	0·8	IE	1·1
14	NO	50·1	HR	22·7	IE	2,619	FR	63·1	DE	3·5	LT	2·1	EE	12,716·9	NO	13·5	HR	0·8	PT	1·0
15	CZ	50·0	HU	21·6	FI	2,597	DK	63·0	EL	3·3	MT	1·9	IE	*10,487·1*	BE	13·5	LT	0·8	RS	0·8
16	BE	49·9	TR	21·3	CH	2,590	ES	62·4	FI	3·2	ES	1·8	NO	*10,487·1*	CY	13·5	MT	0·7	PL	0·7
17	TR	49·1	SE	20·2	DK	2,491	SI	61·4	RO	3·1	PT	1·8	UK	*10,487·1*	LV	13·2	IT	0·7	HR	0·7
18	CY	48·8	PT	19·5	IT	2,345	IE	61·0	LV	3·1	SK	1·8	SE	10,487·0	SI	12·8	SI	0·6	LV	0·6
19	SE	48·7	NO	19·1	PT	2,335	UK	61·0	DK	3·0	IE	1·78	HU	10,442·1	FI	12·7	UK	0·6	NO	0·6
20	DE	44·9	CH	18·7	BE	2,335	PT	60·6	NL	3·0	BE	*1·8*	CZ	10,190·6	RS	12·6	EL	0·6	BG	0·6
21	DK	42·2	AT	18·0	NL	2,314	EE	57·3	CZ	2·9	LU	1·8	LT	9,476·2	PT	12·6	AT	0·5	ES	0·5
22	EE	41·6	MT	12·7	DE	1,964	MT	57·1	HU	*2·9*	PL	1·7	IT	8,844·4	NL	12·4	DE	*0·5*	UK	0·5
23	FR	41·4	PL	12·5	CZ	1,759	LT	55·3	SK	*2·9*	EE	1·7	NL	8,080·8	CH	12·0	ES	0·5	MT	0·5
24	IE	40·3	CY	12·3	FR	1,712	CZ	55·1	PT	2·8	FR	1·7	MT	8,061·1	DE	12·0	PT	*0·5*	RO	0·5
25	ES	36·3	LV	11·8	LU	1,651	HU	*55·1*	LT	2·3	CZ	1·6	HR	7,741·8	DK	11·1	SE	0·5	FR	0·4
26	UK	32·4	LT	10·7	ES	1,461	RO	54·2	BG	2·0	HR	1·5	PL	7,015·5	IS	10·3	CY	0·5	SE	0·4
27	HU	31·0	RS	10·7	UK	1,404	PL	51·3	MT	1·9	TR	1·4	PT	*6,184·4*	RO	10·1	HU	0·5	SK	0·4
28	HR	27·4	IS	10·0	MT	1,299	SK	51·0	HR	*1·7*	NL	1·4	ES	6,184·4	MT	9·0	PL	0·4	DK	0·3
29	BG	26·9	NL	8·2	TR	1,294	BG	50·1	SI	1·7	SI	1·3	BG	5,137·4	PL	8·1	LV	0·4	CH	0·3
30	SK	26·6	DE	8·2	SE	1,090	HR	50·1	FR	1·5	RO	1·2	RO	*5,137·4*	IE	7·8	EE	0·4	DE	0·3
31	LT	25·2	EL	6·6	EL	1,009	RS	*50·1*	RS	0·8	RS	1·0	SK	4,458·2	TR	7·8	RO	0·4	HU	0·3
32	NL	25·0	EE	6·1	NO	696	TR	*50·1*	TR	0·7	UK	1·0	FI	3,908·1	UK	7·5	RS	0·3	CZ	0·3
33	RO	24·1	LU	1·3	CY	259	LV	49·0	LU	0·4	HU	0·9	RS	2,592·7	IT	3·3	TR	0·3	TR	0·1

Table A7. Ranking of hospital related resources and their association with colorectal cancer survival and expenditure for 33 European countries.

a – 2018 data from European Society of Surgical Oncologists (ESSO) members only, some countries may be underrepresented. SACT – systemic anti-cancer therapy; SACT and hospital care costs as a percentage of all CRC healthcare costs; CT – computer tomography. *Exercise caution when figures are underlined as this indicates extrapolation from similar geo-cultural data.

Northern Europe Western Europe Southern Europe Central and Eastern Europe

	Hospital care			SACT		
Country	2009	2015	Change	2009	2015	Change
Austria	56,821	104,808	84.5%	7,723	36,240	369.2%
Belgium	76,342	75,941	-0.5%	10,478	38,088	263.5%
Bulgaria	33,633	38,194	13.6%	9,610	88,194	817.8%
Cyprus	1,747	575	-67.1%	873	145	-83.4%
Czech Rep.	102,390	36,140	-64.7%	16,717	23,190	38.7%
Denmark	33,312	36,841	10.6%	5,793	6,738	16.3%
Estonia	7,467	8,767	17.4%	498	1,286	158.3%
Finland	38,112	39,815	4.5%	4,158	14,906	258.5%
France	373,728	295,779	-20.9%	91,961	326,844	255.4%
Germany	1,052,073	389,986	-62.9%	87,417	219,530	151.1%
Greece	41,608	37,835	-9.1%	15,501	3,878	-75.0%
Hungary	74,544	240,126	222.1%	33,545	167,137	398.2%
Ireland	26,193	22,092	-15.7%	2,381	13,646	473.1%
Italy	535,780	561,445	4.8%	61,615	240,355	290.1%
Latvia	17,034	13,618	-20.1%	2,129	2,910	36.7%
Lithuania	11,686	7,101	-39.2%	1,169	3,026	158.9%
Luxembourg	2,702	4,571	69.2%	338	69	-79.6%
Malta	1,059	2,081	96.4%	318	380	19.7%
Netherlands	196,024	56,882	-71.0%	12,945	18,757	44.9%
Poland	187,808	319,045	69.9%	25,505	55,262	116.7%
Portugal	28,008	71,326	154.7%	9,035	25,265	179.6%
Romania	106,420	143,408	34.8%	47,298	143,178	202.7%
Slovakia	56,222	42,608	-24.2%	20,079	42,832	113.3%
Slovenia	15,558	20,493	31.7%	2,829	7,340	159.5%
Spain	193,202	132,213	-31.6%	53,857	125,704	133.4%
Sweden	19,705	25,817	31.0%	5,971	10,718	79.5%
UK	320,473	116,957	-63.5%	33,414	150,946	351.7%
EU-27	3,609,652	2,844,463	-21.2%	563,156	1,766,564	213.7%

Table A8. Comparison of 2009 to 2015 colorectal cancer costs (x£1,000s) of hospital care and pharmaceutical medicines.

Adjusted for purchasing power parity (PPP). 2009 prices inflated to 2015. SACT – systemic anti-cancer therapy. Green font - CRC activity and costs, Red font – CRC activity and other cancer costs

	Ln(CRC costs)	
Variables	**per capita**	**per case**
CRC incidence per 1000 (2015)	1·78*	1·72
	(2·38)	(1·96)
CRC 5-year net survival (2010-2014)	-3·26	-4·92*
	(-1·77)	(-2·27)
Constant	3.24	9·62
	(2·81)	(7·09)
Observations	33	33
F statistic (p value)	0·029	0·028
R^2	0·21	0·21
t statistics in parentheses, * p<0·05, ** p<0·01, *** p<0·001		

Table A5 Co-efficients from multiple regression of CRC costs per capita and per case against incidence and survival of CRC.

R^2– strength of association

Variables	CRC 5-year net survival
Oncologists	0·00997
	1·56
CT Scanners	-0·00527
	(-0·56)
CT scans	0·00000354
	2·03
Radiologists	-0·000222
	(-0·12)
Radiotherapy machines	0·0516*
	2·09
Surgical oncologists	0·0172*
	2·49
Constant	0·475***
	11·26
Observations	33
F statistic (p value)	0·0053
R^2	0·48
t statistics in parentheses, * p<0·05, ** p<0·01, *** p<0·001	

Table A10 Co-efficients from multiple regression of 5-year net survival for CRC patients against hospital personnel, resources, and activities.

CT – computer tomography; R^2 – strength of association

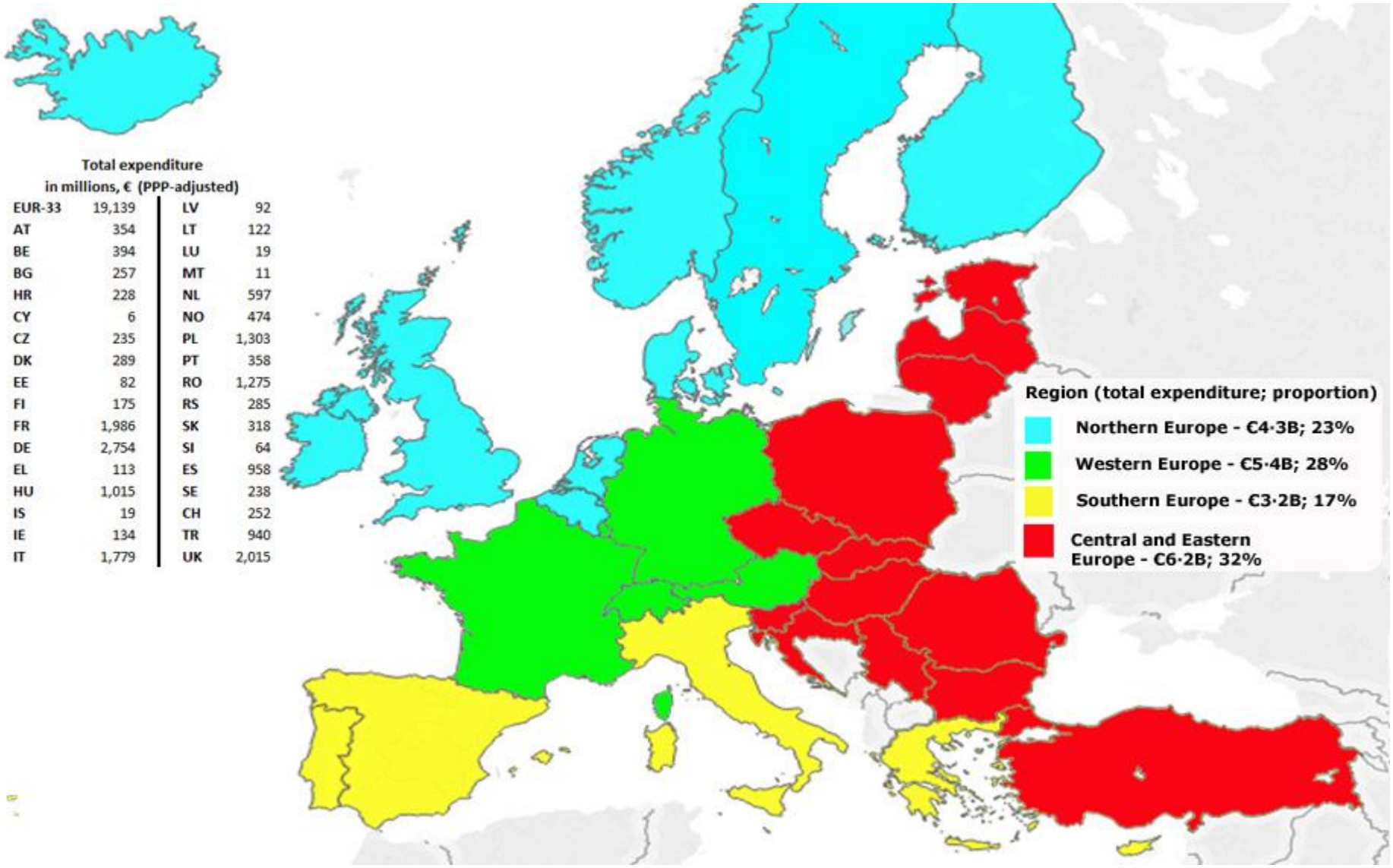

Figure A1. Geographical spread of colorectal cancer costs across 33 European countries in 2015.

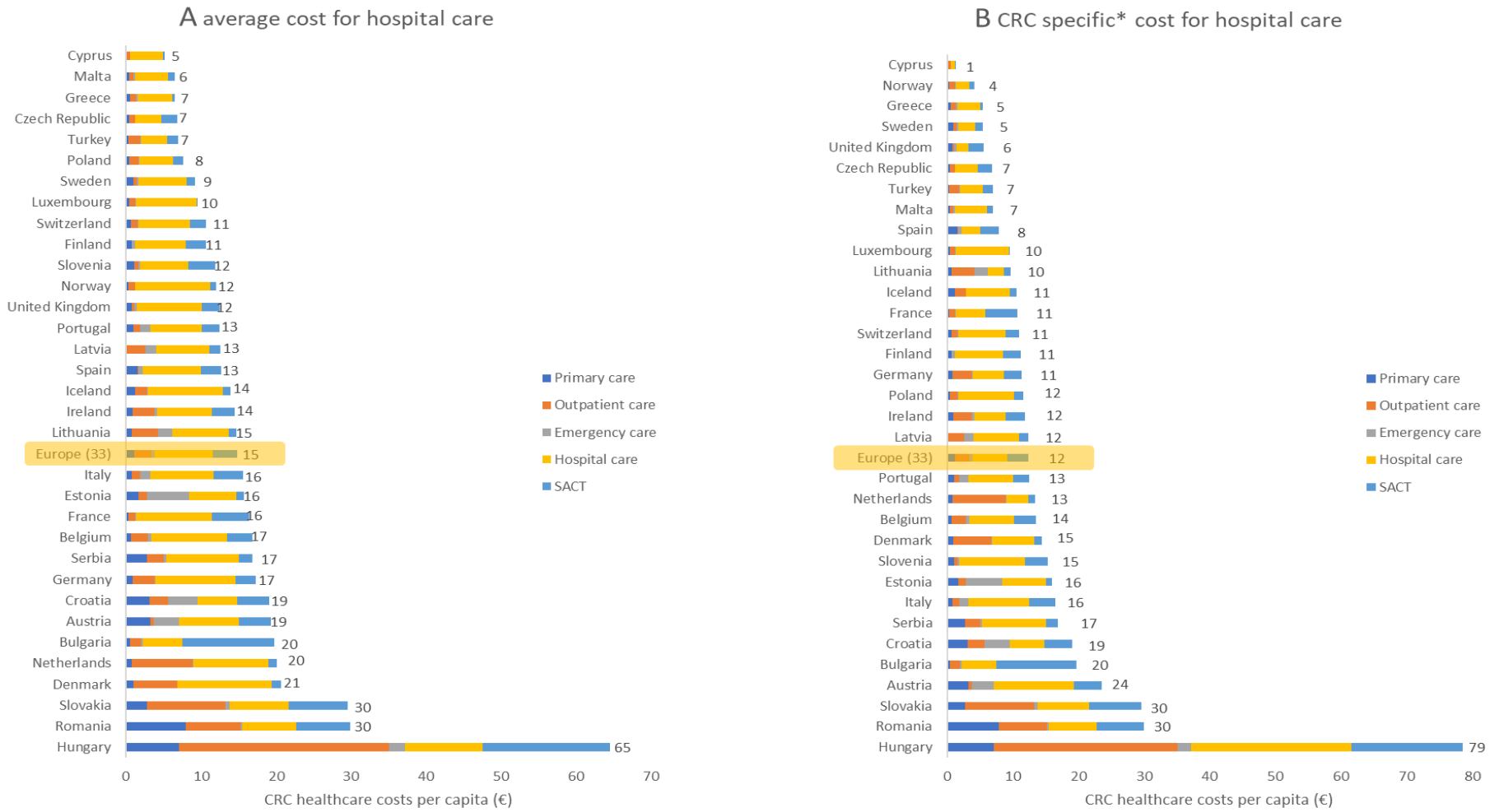

Figure A2 Healthcare costs of colorectal cancer (CRC) per capita in EUR-33 in 2015, by healthcare service category.

(A) Average cost of hospital day adjusted by purchasing power parity (PPP); (B) CRC specific (*where possible) cost of hospital day data adjusted by PPP. SACT – systemic anti-cancer therapy

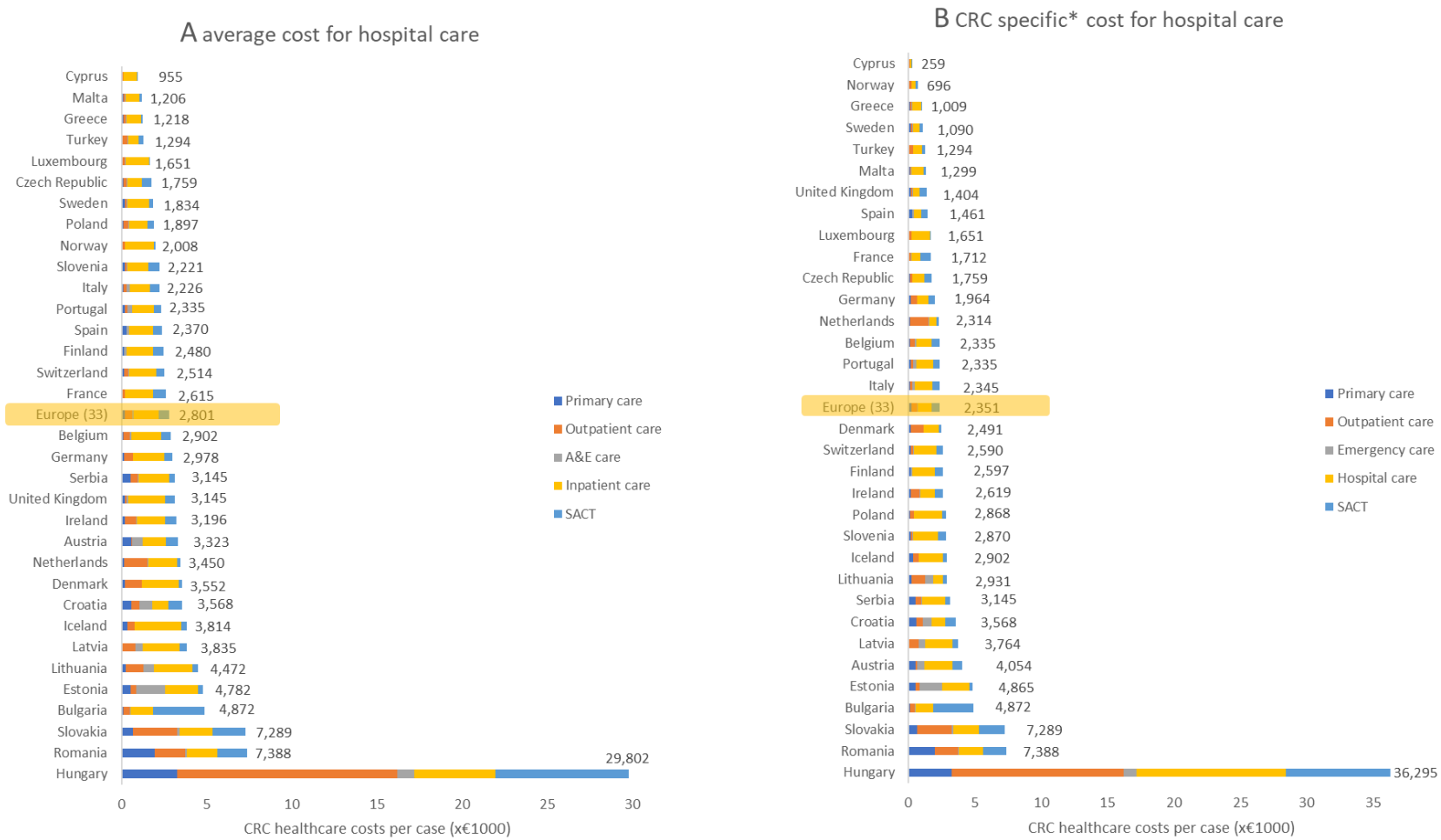

Figure A3 Healthcare costs of CRC per prevalent case in EUR-33 in 2015, by healthcare service category.

(A) Average cost of hospital day adjusted by purchasing power parity (PPP); (B) CRC specific (*where possible) cost of hospital day data adjusted by PPP. SACT – systemic anti-cancer therapy

Scatterplots whose correlations have a p-value > 0·05

Log of CRC costs per capita (€) versus Total Healthcare Expenditure (THE) [17] per capita (€), purchasing power parity (PPP) adjusted. p-value < 0·148, data not shown

Log of CRC costs per case (€) versus THE per case (€), PPP adjusted. p-value < 0·249, data not shown

Log of CRC costs per case (€) (PPP adjusted) versus CRC incidence (per 1,000). p-value < 0·115, data not shown

Log of CRC costs per capita (€) (PPP adjusted) versus 5-year net survival for CRC.[158] p-value < 0·167 data not shown

Log of CRC costs per case (€) (PPP adjusted) versus 5-year net survival for CRC. p-value < 0·057 data not shown

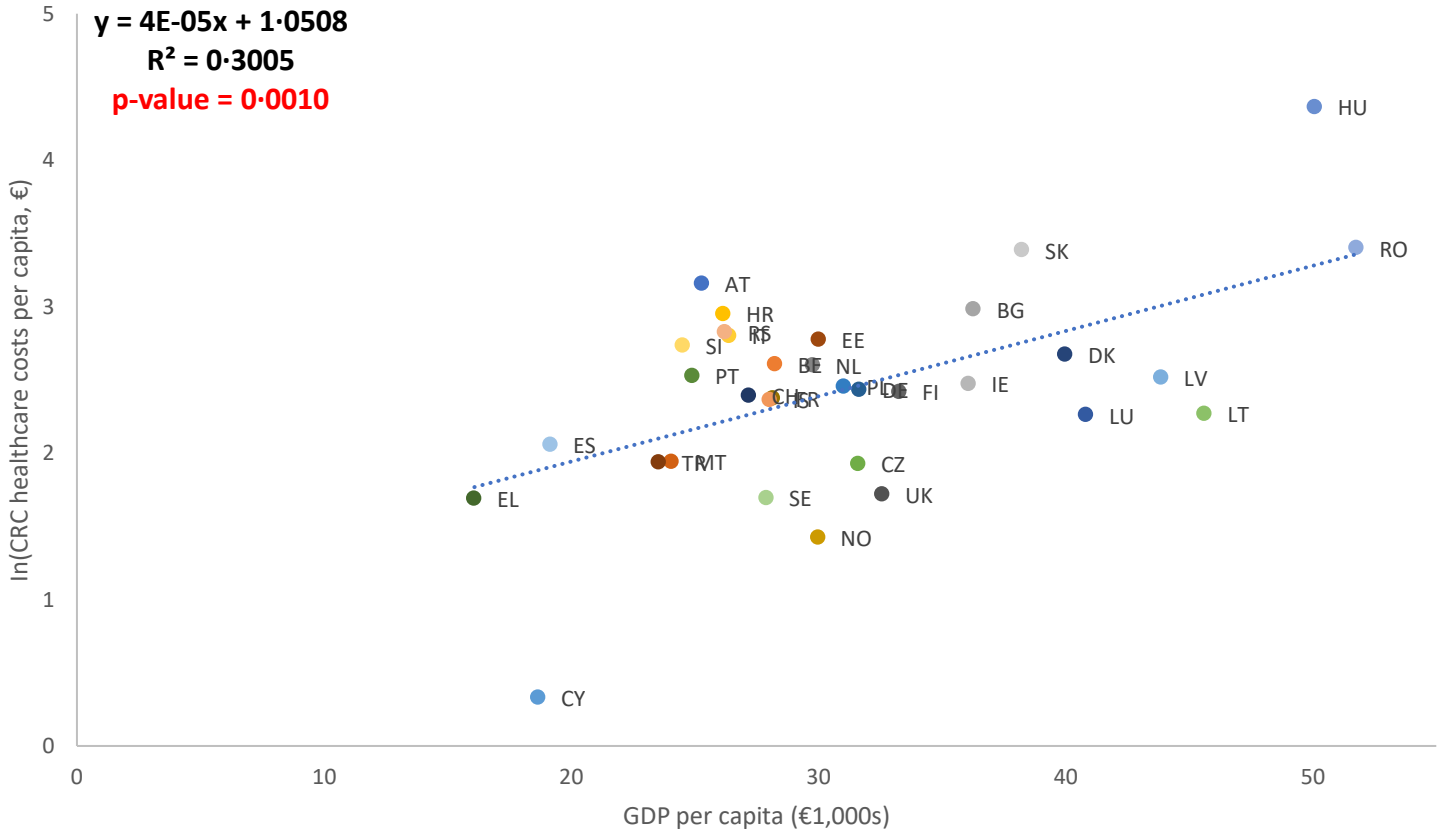

Figure A3 Figure A4. Log of CRC costs per capita (€) versus gross domestic product (GDP) [223] per capita (€), purchasing power parity adjusted for hospital services. [224]

AT Austria; BE Belgium; BG Bulgaria; CH Switzerland; CY Cyprus; CZ Czech Republic; DE Germany; DK Denmark; EE Estonia; EL Greece; ES Spain; FI Finland; FR France; HR Croatia; HU Hungary; IE Ireland; IS Iceland; IT Italy; LU Luxembourg; LT Lithuania; LV Latvia; MT Malta; NL the Netherlands; NO Norway; PL Poland; PT Portugal; RO Romania; RS Serbia; SE Sweden; SI Slovenia; SK Slovakia; TR Turkey; UK United Kingdom.

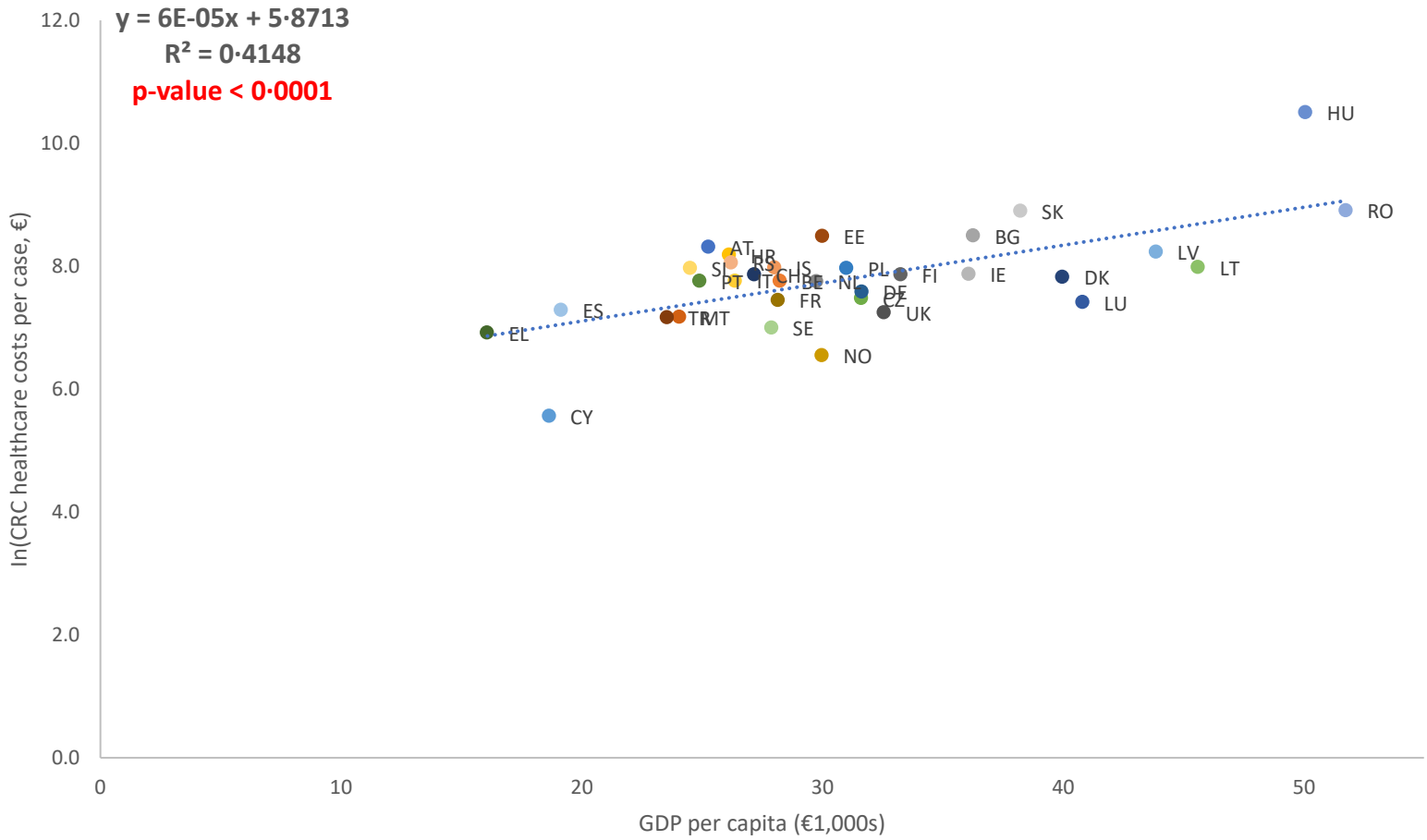

Figure A5 Log of CRC costs per case (€) versus gross domestic product (GDP) per capita (€), purchasing power parity adjusted.

AT Austria; BE Belgium; BG Bulgaria; CH Switzerland; CY Cyprus; CZ Czech Republic; DE Germany; DK Denmark; EE Estonia; EL Greece; ES Spain; FI Finland; FR France; HR Croatia; HU Hungary; IE Ireland; IS Iceland; IT Italy; LU Luxembourg; LT Lithuania; LV Latvia; MT Malta; NL the Netherlands; NO Norway; PL Poland; PT Portugal; RO Romania; RS Serbia; SE Sweden; SI Slovenia; SK Slovakia; TR Turkey; UK United Kingdom.

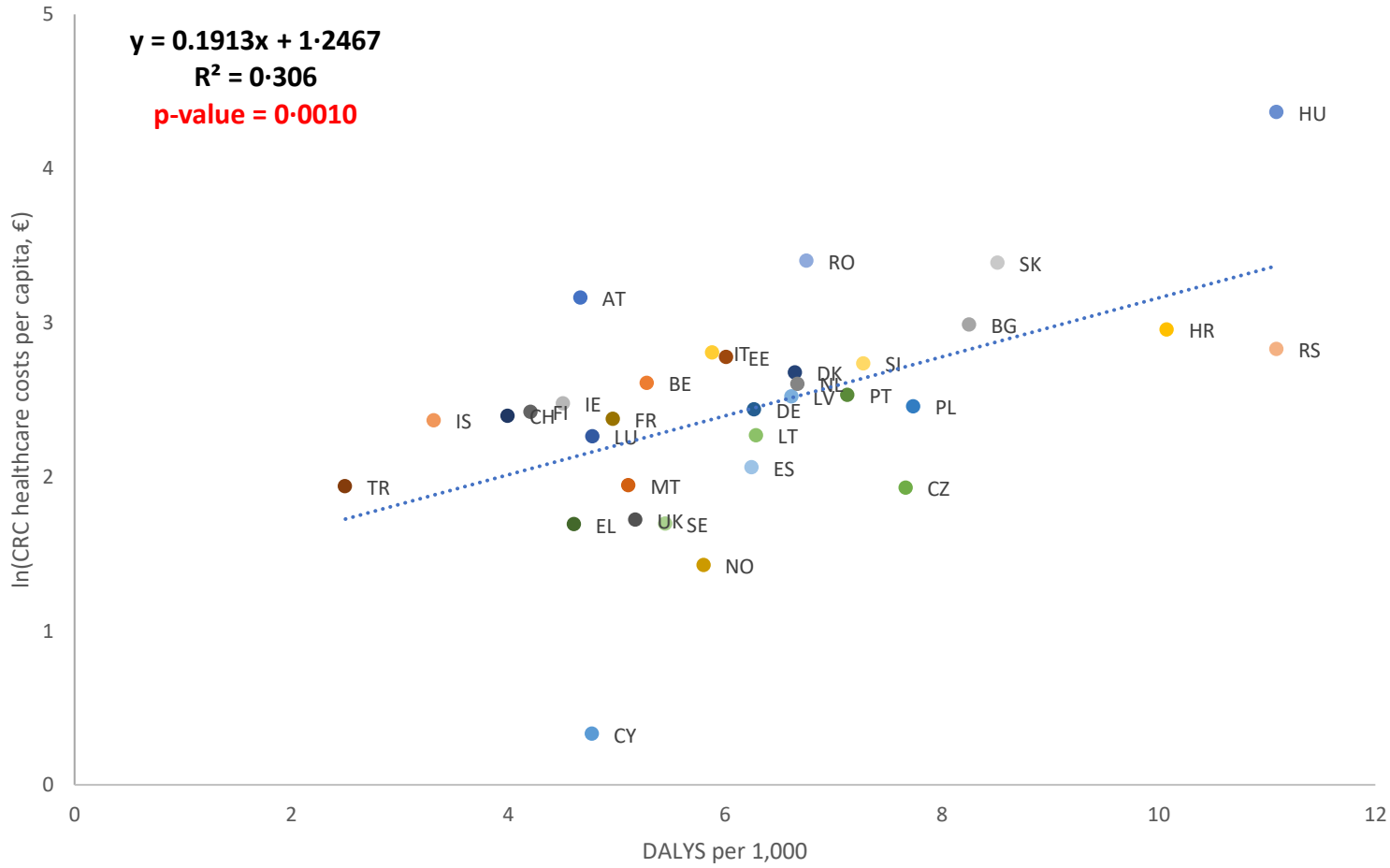

Figure A6 Log of CRC costs per capita (€) (purchasing power parity adjusted) versus DALYs per 1,000.[225]

AT Austria; BE Belgium; BG Bulgaria; CH Switzerland; CY Cyprus; CZ Czech Republic; DE Germany; DK Denmark; EE Estonia; EL Greece; ES Spain; FI Finland; FR France; HR Croatia; HU Hungary; IE Ireland; IS Iceland; IT Italy; LU Luxembourg; LT Lithuania; LV Latvia; MT Malta; NL the Netherlands; NO Norway; PL Poland; PT Portugal; RO Romania; RS Serbia; SE Sweden; SI Slovenia; SK Slovakia; TR Turkey; UK United Kingdom.

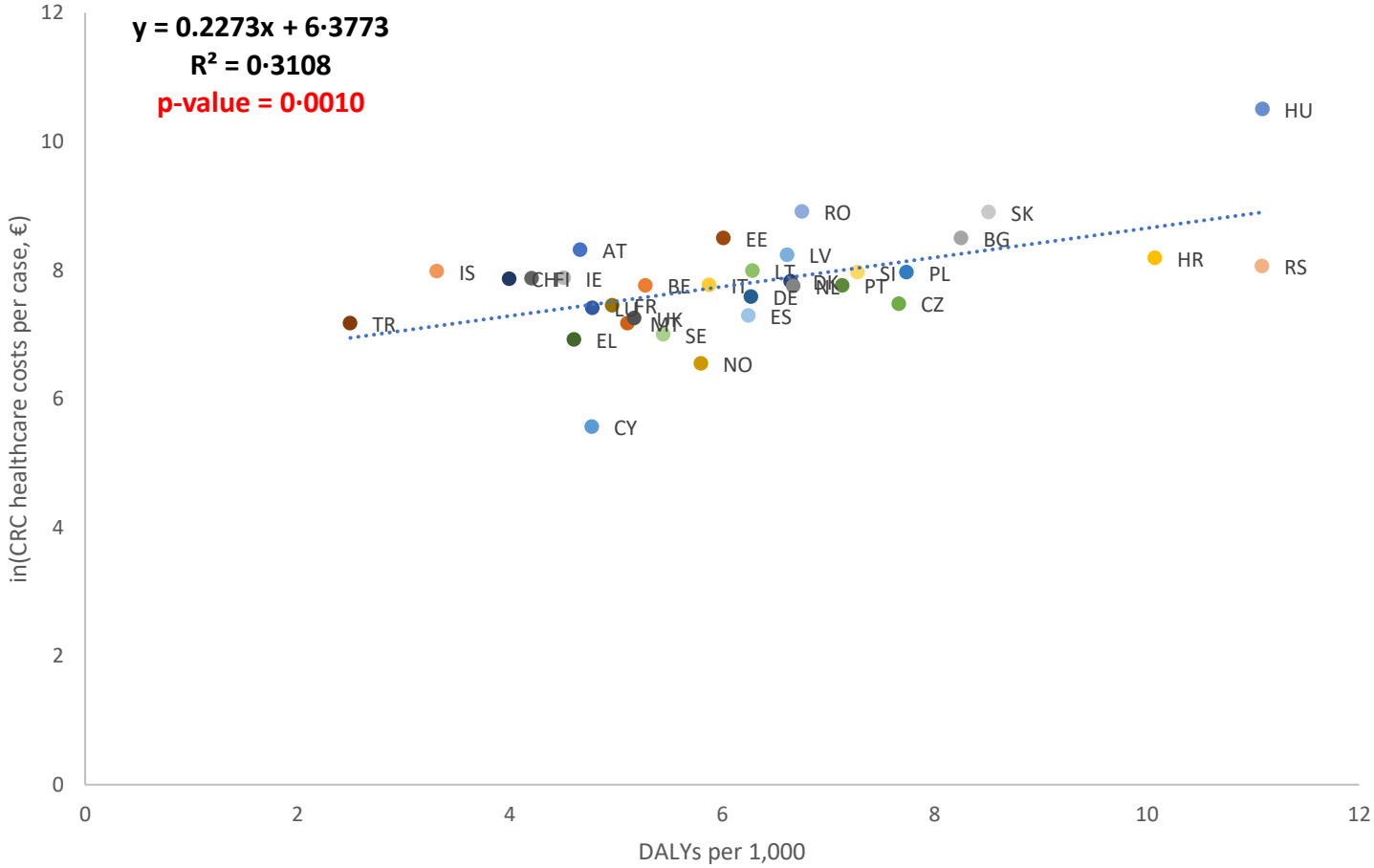

Figure A7 Log of CRC costs per case (€) (purchasing power parity adjusted) versus DALYs per 1,000.[225]

AT Austria; BE Belgium; BG Bulgaria; CH Switzerland; CY Cyprus; CZ Czech Republic; DE Germany; DK Denmark; EE Estonia; EL Greece; ES Spain; FI Finland; FR France; HR Croatia; HU Hungary; IE Ireland; IS Iceland; IT Italy; LU Luxembourg; LT Lithuania; LV Latvia; MT Malta; NL the Netherlands; NO Norway; PL Poland; PT Portugal; RO Romania; RS Serbia; SE Sweden; SI Slovenia; SK Slovakia; TR Turkey; UK United Kingdom.

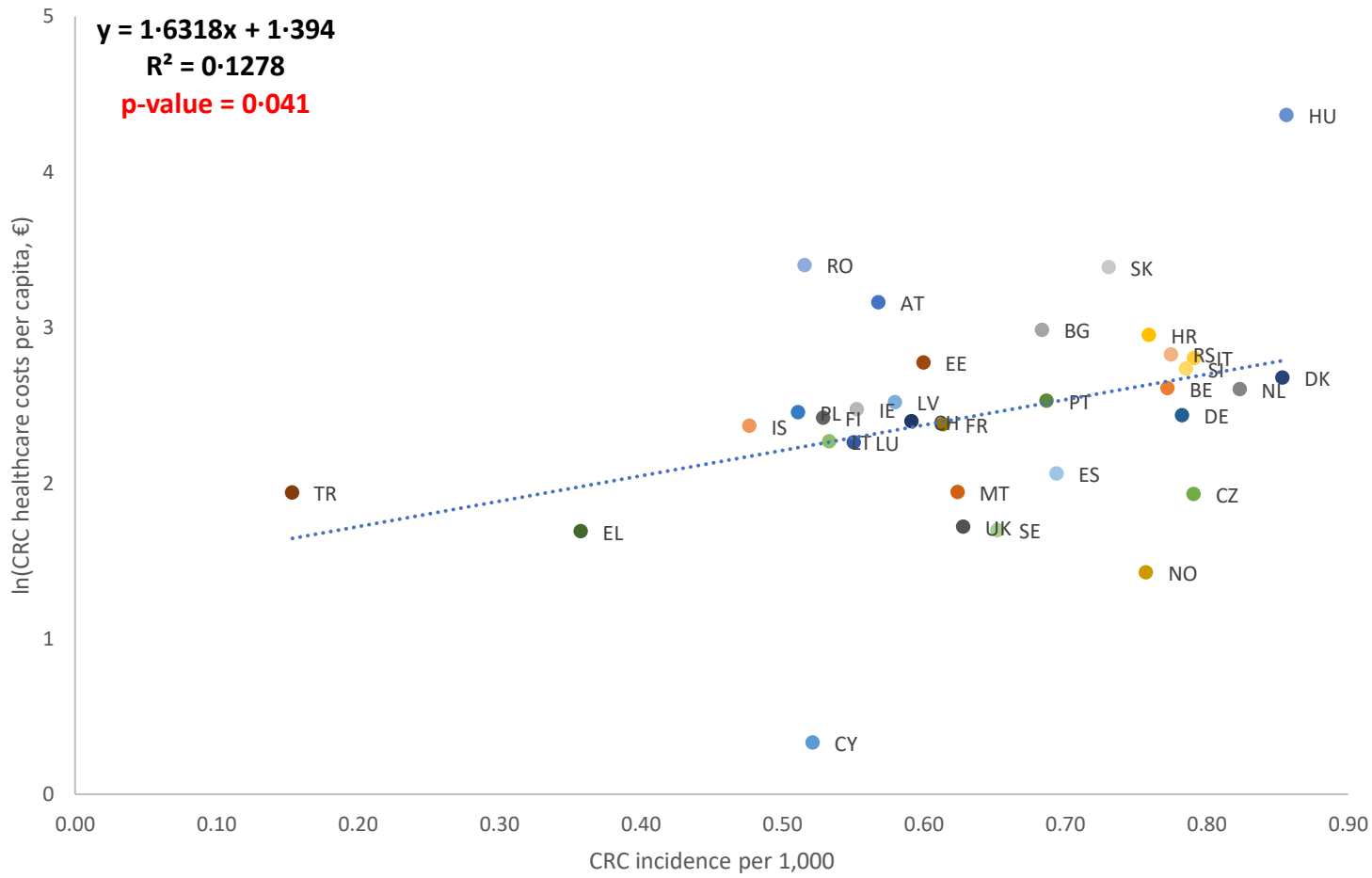

Figure A8 Log of CRC costs per capita (€) (purchasing power parity adjusted) versus CRC incidence (per 1,000). [226]

AT Austria; BE Belgium; BG Bulgaria; CH Switzerland; CY Cyprus; CZ Czech Republic; DE Germany; DK Denmark; EE Estonia; EL Greece; ES Spain; FI Finland; FR France; HR Croatia; HU Hungary; IE Ireland; IS Iceland; IT Italy; LU Luxembourg; LT Lithuania; LV Latvia; MT Malta; NL the Netherlands; NO Norway; PL Poland; PT Portugal; RO Romania; RS Serbia; SE Sweden; SI Slovenia; SK Slovakia; TR Turkey; UK United Kingdom.

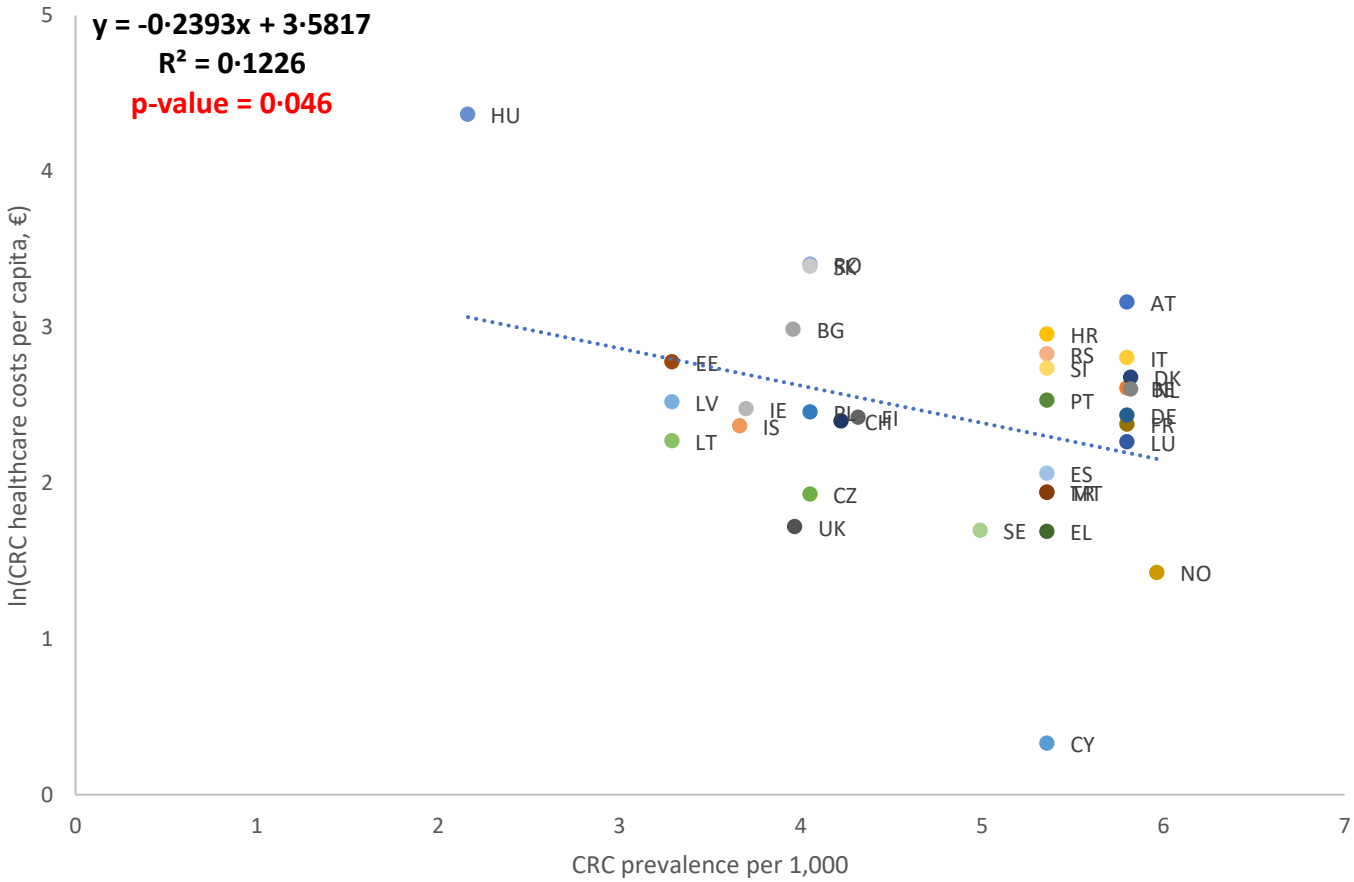

Figure A9 Log of CRC costs per capita (€) (purchasing power parity adjusted) versus CRC prevalence (per 1,000).

AT Austria; BE Belgium; BG Bulgaria; CH Switzerland; CY Cyprus; CZ Czech Republic; DE Germany; DK Denmark; EE Estonia; EL Greece; ES Spain; FI Finland; FR France; HR Croatia; HU Hungary; IE Ireland; IS Iceland; IT Italy; LU Luxembourg; LT Lithuania; LV Latvia; MT Malta; NL the Netherlands; NO Norway; PL Poland; PT Portugal; RO Romania; RS Serbia; SE Sweden; SI Slovenia; SK Slovakia; TR Turkey; UK United Kingdom.

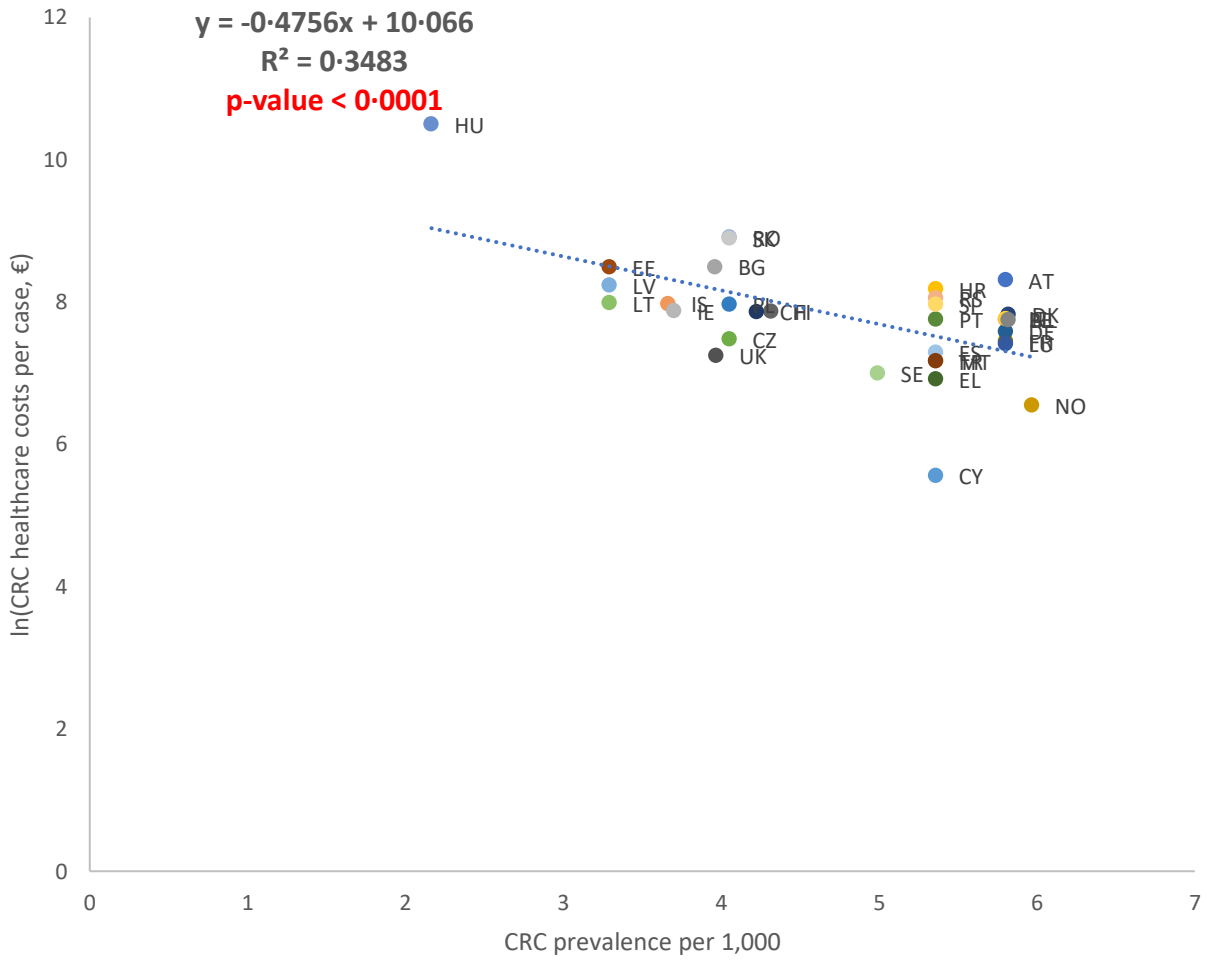

Figure A10 Log of CRC costs per case (€) (purchasing power parity adjusted) versus CRC prevalence (per 1,000).

AT Austria; BE Belgium; BG Bulgaria; CH Switzerland; CY Cyprus; CZ Czech Republic; DE Germany; DK Denmark; EE Estonia; EL Greece; ES Spain; FI Finland; FR France; HR Croatia; HU Hungary; IE Ireland; IS Iceland; IT Italy; LU Luxembourg; LT Lithuania; LV Latvia; MT Malta; NL the Netherlands; NO Norway; PL Poland; PT Portugal; RO Romania; RS Serbia; SE Sweden; SI Slovenia; SK Slovakia; TR Turkey; UK United Kingdom.

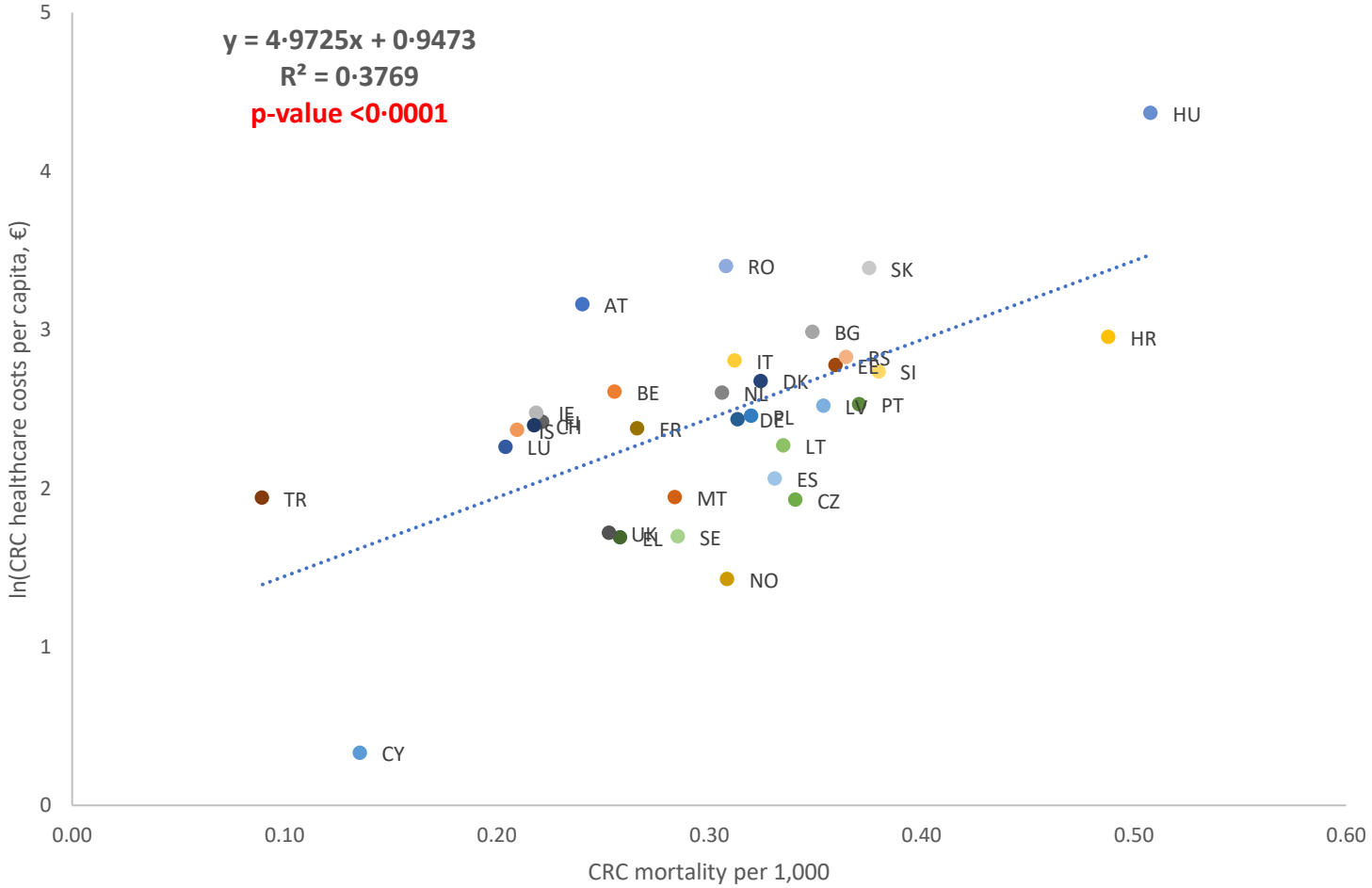

Figure A11 Log of CRC costs per capita (€) (purchasing power parity adjusted) versus CRC mortality (per 1,000).

AT Austria; BE Belgium; BG Bulgaria; CH Switzerland; CY Cyprus; CZ Czech Republic; DE Germany; DK Denmark; EE Estonia; EL Greece; ES Spain; FI Finland; FR France; HR Croatia; HU Hungary; IE Ireland; IS Iceland; IT Italy; LU Luxembourg; LT Lithuania; LV Latvia; MT Malta; NL the Netherlands; NO Norway; PL Poland; PT Portugal; RO Romania; RS Serbia; SE Sweden; SI Slovenia; SK Slovakia; TR Turkey; UK United Kingdom.

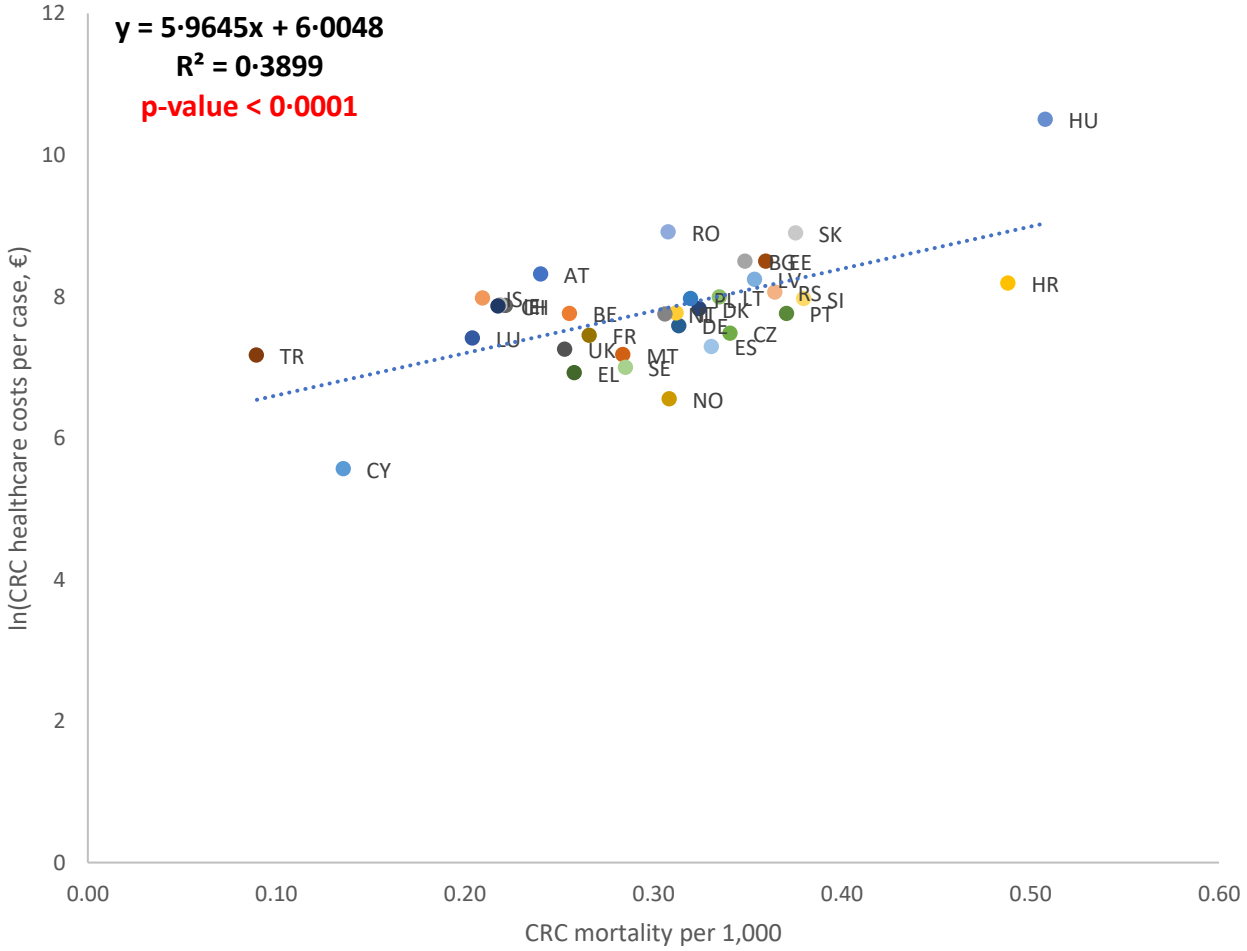

Figure A12. log of colorectal cancer costs per case (€) (PPP adjusted) versus CRC mortality [164] (per 1,000).

AT Austria; BE Belgium; BG Bulgaria; CH Switzerland; CY Cyprus; CZ Czech Republic; DE Germany; DK Denmark; EE Estonia; EL Greece; ES Spain; FI Finland; FR France; HR Croatia; HU Hungary; IE Ireland; IS Iceland; IT Italy; LU Luxembourg; LT Lithuania; LV Latvia; MT Malta; NL the Netherlands; NO Norway; PL Poland; PT Portugal; RO Romania; RS Serbia; SE Sweden; SI Slovenia; SK Slovakia; TR Turkey; UK United Kingdom.

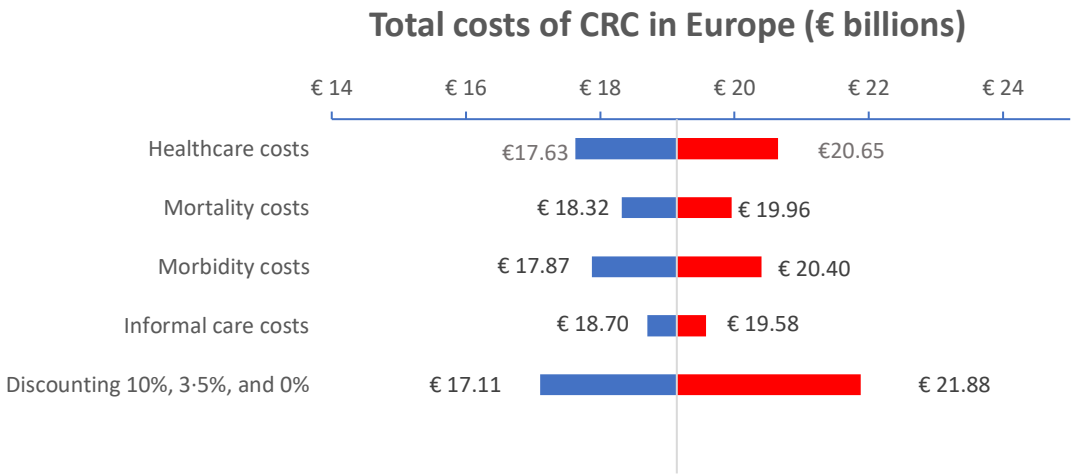

Figure A13 Tornado plot of results of sensitivity analysis on CRC total costs in EUR-33, € billions, 2015.

The total costs of CRC in the EUR-33 are represented on the horizontal axis. Categories (i.e. horizontal bars) are changed by ±20% (or discounting parameter varied by 0%, 3·5%, and 10%) and are indicated on the vertical axis. Blue bars represent reductions (i.e. 20% reduction in costs or 10% discounting from base-case) and red bars represent increases (i.e. 20% increase in costs or 0% discounting from base-case) in total costs of CRC associated with the value of each category or parameter being changed. The labels represent the upper and lower boundaries of total costs of CRC for a given category or parameter. The vertical line cutting through the horizontal bars represents the base-case total costs of CRC (€19.1B).

Supplementary References

1 European Commission. Hospital discharges by diagnosis, in-patients, total number. Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_co_disch1&lang=en (accessed April 18, 2021).

2 European Commission. Population on 1 January by age and sex. Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=demo_pjan&lang=en (accessed April 18, 2021).

3 Hofmarcher MM, Quentin W. Austria: health system review. *Health Syst Transit* 2013; **15**: 1–292.

4 WHO Regional Office for Europe. European Health for All family of databases. 2021. https://www.euro.who.int/en/data-and-evidence/databases/european-health-for-all-family-of-databases-hfa-db (accessed March 26, 2021).

5 Statistik Austria. Frequency of visits of the population in an outpatient clinic or ambulance in 1999. 1999. http://www.statistik.at/web_de/statistiken/gesundheit/gesundheitsversorgung/ambulante_versorgung/index.html (accessed April 12, 2017).

6 European Commission. Hospital discharges by diagnosis, day cases, total number. Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_co_disch3&lang=en (accessed April 18, 2021).

7 European Commission. Hospital days of in-patients. Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_co_hosday&lang=en (accessed Oct 10, 2017).

8 IQVIA. Market Asessment of Selected Oncology Indications in EU Countries. 2017 https://www.iqvia.com.

9 Heyden J Van Der. Contacts avec le médecin généraliste. 2008. https://www.wiv-isp.be/epidemio/EPIFR/crospfr/hisfr/his08fr/r3/3_contactsmedecingeneraliste_gp_report3_fr.pdf .

10 Berchet C. Emergency Care Services: Trends, Drivers and Interventions to Manage the Demand. 2015 DOI:10.1787/5jrts344crns-en.

11 European Commission. Consultation of a medical doctor (in private practice or as outpatient) per inhabitant. Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_hc_phys&lang=en (accessed Feb 21, 2017).

12 Hayes OW, Novkov H. Emergency health services in Bulgaria. *Am J Emerg Med* 2002; **20**: 122–5.

13 Državni zavod za statistiku Republike Hrvatske. Statistical Yearbook of the Republic of Croatia 2016. Zagreb, 2016 DOI:10.1177/1947601911426007.

14 Theodorou M, Charalambous C, Petrou C, Cylus J. Health Systems in Transition. Cyprus Health system review. Copenhagen, 2012.

15 Kyriacou E, Petrou N, Onisiforou K. Health and Hospital Statistics 2014. 2016; : 1–286.

16 Petrou P. Failed Attempts to Reduce Inappropriate Laboratory Utilization in an Emergency Department Setting in Cyprus: Lessons Learned. *J Emerg Med* 2016; **50**: 510–7.

17 European Commission. Health care expenditure by function. Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_sha11_hc&lang=en (accessed April 18, 2021).

18 Institute of Health Information and Statistics of the Czech Republic. Czech Health Statistics Yearbook 2013. Prague, 2014 https://www.uzis.cz/index-en.php?pg=publications--library&id=275.

19 Institute of Health Information and Statistics of the Czech Republic. Activity of health establishments in selected branches of health care. 2013; : 1–156.

20 Statistics Denmark. Statistical Yearbook 2016. Copenhagen, 2016 http://www.dst.dk/Site/Dst/Udgivelser/GetPubFile.aspx?id=22256&sid=sy .

21 Statistics Denmark. AMB01: Out-Patient Treatments by Region, Diagnosis (99 Groups), Age and Sex. Statbank Denmark. 2015. http://www.statbank.dk/10050 (accessed March 11, 2017).

22 Statistics Denmark. SKAD01 Emergency department visits by region, diagnosis (99 groups), age and sex (2006-2015). Statbank Denmark. 2015. http://www.statbank.dk/10050] (accessed March 7, 2017).

23 Organisation for Economic Co-operation and Development. Pharmaceutical spending. 2015. https://data.oecd.org/healthres/pharmaceutical-spending.htm (accessed Sept 16, 2017).

24 Estonian Health Insurance Fund. Estonian Health Insurance Fund Yearbook 2015. Tallinn, 2015 https://www.haigekassa.ee/sites/default/files/uuringud_aruanded/haigekassa_aastaraamat_2015_eng_web_lingitud.pdf .

25 Tervise Arengu Instituut. Health Statistics and Health Research Database. 2020. https://www.tai.ee/en/health-data/health-statistics-and-health-research-database (accessed March 23, 2021).

26 Estonian Health Statistics and Health Research Database. HH05: Existence of emergency medicine department and/or reception department/room and leaving of emergency patients by hospital. Tervise Arengu Inst. 2020. https://www.tai.ee/en/health-data/health-statistics-and-health-research-database (accessed March 23, 2021).

27 Finland National Institute for Health and Welfare. Primary health care 2014. 2014. https://thl.fi/en/web/thlfi-en/statistics/statistics-by-topic/primary-health-care-services (accessed March 23, 2021).

28 Rainio J. Somatic Specialist Medical Care 2013. Helsinki, 2015

http://www.julkari.fi/bitstream/handle/10024/125551/Tr01_15_raportti_fi_sv_en.pdf?sequence=4 .

29 Pines JM, Hilton JA, Weber EJ, *et al.* International Perspectives on Emergency Department Crowding. *Acad Emerg Med* 2011; **18**: 1358–70.

30 Eco-Santé. Consommation en sante et activite medicale. Activite des professions de sante liberales. Professions medicales. Omnipraticiens liberaux: consultations 2013. Inst. Rech. Doc. en Econ. la Santé. 2013. http://www.ecosante.fr/index2.php?base=DEPA&langh=FRA&langs=FRA (accessed March 13, 2017).

31 Dinkel A, Schneider A, Schmutzer G, Brähler E, Häuser W. Family physician–patient relationship and frequent attendance of primary and specialist health care: Results from a German population-based cohort study. *Patient Educ Couns* 2016; **99**: 1213–9.

32 Federal Health Reporting. Total Cost of Illness in millions of Euro for Germany. Classification: years, sex, ICD10, provider of ambulatory health care. 2015. https://www.gbe-bund.de/gbe/pkg_isgbe5.prc_menu_olap?p_uid=gast&p_aid=57964475&p_sprache=D&p_help=2&p_indnr=322&p_indsp=&p_ityp=H&p_fid= (accessed Feb 15, 2017).

33 Tountas Y, Oikonomou N, Pallikarona G, *et al.* Sociodemographic and socioeconomic determinants of health services utilization in Greece: the Hellas Health I study. *Heal Serv Manag Res* 2011; **24**: 8–18.

34 Badó Katalin, Boros Julianna, Feldmann Klára, Ferencz-Kis Ildikó, Györke Judit, Kovács Ferencné, Páll Szilárd, Pásztorné Stokker Erzsébet, Pruzsinszki Judit SZK. Yearbook of Health Statistics 2014. Budapest, 2015 https://www.ksh.hu/docs/hun/xftp/idoszaki/evkonyv/egeszsegugyi_evkonyv_2014.pdf .

35 National Health Insurance Fund Administration. Statistical Yearbook 2012. 2013; : 1–153.

36 Directorate of Health of Iceland. Contacts with health care centres 2005–2015. Consultations, house calls and telephone calls by GPs, nurses and midwives. 2016. https://www.landlaeknir.is/tolfraedi-og-rannsoknir/tolfraedi/allt-talnaefni/ (accessed March 23, 2021).

37 Kalseth J, Halvorsen T, Kalseth B, *et al.* Cross-country comparisons of health-care costs : The case of cancer treatment in the Nordic countries. *Health Policy (New York)* 2014; **115**: 172–9.

38 Sigurgeirsdóttir S, Waagfjörð J, Maresso A. Iceland: Health System Review. 2014 https://www.euro.who.int/__data/assets/pdf_file/0018/271017/Iceland-HiT-web.pdf?ua=1.

39 Layte, Richard, Barry, Michael, Bennett, Kathleen, Brick, Aoife, Morgenroth, Edgar, Normand, Charles, O'Reilly, Jacqueline, Thomas, Stephen, Tilson, Lesley, Wiley, Miriam, and Wren M-A. Projecting the Impact of Demographic Change on the Demand for and Delivery of Health Care in Ireland. Dublin: ESRI, 2009 DOI:10.26504/rs13.

40 Istituto Nazionale di Statistica. HEALTH FOR ALL - ITALY. ISTAT. 2020. https://www.istat.it/it/archivio/14562 (accessed March 26, 2021).

41 Latvian Ministry of Health. State Budget Estimates. 2015. https://www.kase.gov.lv/parskati-un-

tames/valsts-budzeta-tames (accessed April 20, 2021).

42 Central Statistical Bureau of Latvia. Statistical Yearbook of Latvia. Riga, 2016 https://www.csb.gov.lv/en/statistics/statistics-by-theme/economy/gdp/search-in-theme/175-statistical-yearbook-latvia-2015.

43 Health Information Centre of Institute of Hygiene. Health Statistics of Lithuania 2015. Vilnius, 2016 https://hi.lt/uploads/pdf/leidiniai/Statistikos/LT_sveik_stat_health/la2015.pdf.

44 Inspection Générale de la Sécurité Sociale. Rapport Général Sur La Sécurité Sociale Au Grand-Duché De Luxembourg. Luxembourg, 2012 https://sante.public.lu/fr/publications/r/rapport-general-securite-sociale-gdl-2012/index.html.

45 Social Protection: Malta and the EU. Valletta, 2014 https://nso.gov.mt/en/publicatons/Publications_by_Unit/Documents/A2_Public_Finance/Social_Protection_Malta_EU_2014.pdf .

46 Grech K, Podesta M, Calleja A, Calleja N. Report on the Performance of the Maltese Health System, 2015. 2015; : 1–264.

47 Statistics Netherlands. Health, lifestyle, health care use and supply, causes of death; key figures. Statline. 2015. http://statline.cbs.nl/statweb/dome/?TH=5390&LA=en (accessed March 14, 2017).

48 Volksgezondheidenzorg.info. Cost of illness tool. 2015. https://costofillnesstool.volksgezondheidenzorg.info/tool/english/ (accessed Feb 15, 2017).

49 GPs and emergency primary health care. Stat. Norw. 2015. https://www.ssb.no/en/fastlegetj (accessed March 25, 2017).

50 Statistics Norway. Table: 04080: Outpatient consultations at public general hospitals, by diagnosis (ICD-10), sex and age (C) (closed series). Statbank. 2015. https://www.ssb.no/en/sok?sok=outpatient (accessed April 6, 2017).

51 Central Statistical Office. Healthcare, Social Welfare, and Family Benefits. Stat. Pol. 2015. https://bdl.stat.gov.pl/BDL/dane/podgrup/tablica (accessed March 14, 2017).

52 Statistics Portugal. Instituto Nacional de Estatistica. Consultas médicas nos centros de saúde por Localização geográfica e Especialidade da consulta. 2012. https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_indicadores&indOcorrCod=0004703&contexto=pti&selTab=tab10 (accessed March 15, 2017).

53 WHO Regional Office for Europe. Primary care quality management in Romania - Primary care in the WHO European Region. Copenhagen, 2012 http://www.euro.who.int/__data/assets/pdf_file/0005/167576/Evaluation-of-structure-and-provision-of-primary-care-in-Romania.pdf?ua=1 .

54 Simić S, Milićević MŠ, Matejić B, Marinković J, Adams O. Do we have primary health care reform?

The story of the Republic of Serbia. *Health Policy (New York)* 2010; **96**: 160–9.

55 Smatana M, Pažitný P, Kandilaki D, *et al.* Slovakia: Health System Review. Copenhagen, 2016 https://www.euro.who.int/__data/assets/pdf_file/0011/325784/HiT-Slovakia.pdf?ua=1.

56 Statistical Office of the Slovak Republic. Statistical Yearbook of the Slovak Republic 2015. Bratislava, 2015 https://slovak.statistics.sk/wps/wcm/connect/111ae87b-5658-425f-967d-053928d2c94c/Statisticka_rocenka_Slovenskej_republiky_2015.pdf?MOD=AJPERES&CACHEID=111ae87b-5658-425f-967d-053928d2c94c.

57 Poldka Butinar, Blaženka Jeren, Tanja Kustec M, Blaško Markič, Vili Prodan, Irma Renar AZ. Statistical Yearbook of the Republic of Slovenia 2013. 2013; : 184–93.

58 Slovenian National Institute of Public Health. Number and rate of visits to specialist outpatient activities, Slovenia, annually. 2015. https://podatki.nijz.si/Menu.aspx?px_db=NIJZ podatkovni portal&px_language=sl&rxid=a2759f9b-de04-4e19-956b-600722815cba (accessed April 10, 2021).

59 Mckee M, Sagan A, Calltorp J, *et al.* Health Systems in Transition: Slovenia (Vol. 18 No. 3 2016). 2016; **18**: 1–207.

60 Ministerio de Sanidad Servicios Sociales e Igualdad. Database of Primary Care Clinics (BDCAP) Interconsults. 2015. https://www.mscbs.gob.es/estadEstudios/estadisticas/estadisticas/estMinisterio/SIAP/home.htm (accessed March 23, 2021).

61 Ministerio de Sanidad Servicios Sociales e Igualdad. Distribución de Casos por CDM - Actividad Ambulatoria Especializada. A-o 2014. 2014. https://www.mscbs.gob.es/estadEstudios/portada/home.htm# (accessed March 23, 2021).

62 Statistics Sweden. Statistical Yearbook of Sweden 2014. 2014; : 1–616.

63 Statistiksektionen Avdelningen för ekonomi och styrning. Beskrivning av KPP- databasen 2014. Stockholm, 2016 http://webbutik.skl.se/bilder/artiklar/pdf/7585-318-5.pdf .

64 Burström L, Starrin B, Engström M-L, Thulesius H. Waiting management at the emergency department – a grounded theory study. *BMC Health Serv Res* 2013; **13**. DOI:10.1186/1472-6963-13-95.

65 Federal Statistical Office. Swiss Health Survey 2012. 2012. https://www.bfs.admin.ch/bfs/en/home/statistics/health.assetdetail.349060.html (accessed March 19, 2017).

66 Tatar M, Mollahaliloğlu S, Sahin B, Aydin S, Maresso A, Hernández-Quevedo C. Turkey. Health system review. Copenhagen, 2011 http://www.euro.who.int/__data/assets/pdf_file/0006/158883/e96441.pdf?ua=1 .

67 Oktay C, Cete Y, Eray O, Pekdemir M, Gunerli A. Appropriateness of emergency department visits in a Turkish university hospital. *Croat Med J* 2003; **44**: 585–91.

68 Wakeford R. Fire the Medical Schools Council if you want more GPs. *BMJ* 2014; **349**: g6245--g6245.

69 Winter J. Hospital Outpatient Activity 2015-16. 2016 https://files.digital.nhs.uk/publicationimport/pub22xxx/pub22596/hosp-epis-stat-outp-summ-repo-2015-16-rep.pdf.

70 Baker C. Accident and Emergency Statistics: Demand, Performance and Pressure. 2017 researchbriefings.files.parliament.uk/documents/SN06964/SN06964.pdf .

71 Kapalla M, Kapallová D, Turecký L. An overview of the healthcare system in the Slovak Republic. *EPMA J* 2010; **1**: 549–61.

72 Hungarian National Health Fund Manager. Data of public interest. 2015. http://www.neak.gov.hu/felso_menu/rolunk/kozerdeku_adatok (accessed April 20, 2021).

73 Icelandic Health Insurance. Amounts and Tariffs. 2015. https://www.sjukra.is/um-okkur/fjarhaedir-og-gjaldskrar/ (accessed April 21, 2021).

74 European Commission. HICP (2015 = 100) - annual data (average index and rate of change). Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=prc_hicp_aind&lang=en (accessed Oct 11, 2017).

75 Ladurner J, Lawerence K, Rieder A, Rupp B. Incentives and payment systems for physicians in selected countries with a special focus on the Austrian situation. 2006: 1–178.

76 Schiller-Fruehwirth I, Jahn B, Einzinger P, Zauner G, Urach C, Siebert U. The Long-Term Effectiveness and Cost Effectiveness of Organized versus Opportunistic Screening for Breast Cancer in Austria. *Value Heal* 2017; **20**: 1048–57.

77 Linde M, Gustavsson A, Stovner LJ, *et al*. The cost of headache disorders in Europe: The Eurolight project. *Eur J Neurol* 2012; **19**: 703–11.

78 Austrian Federal Ministry for Social Affairs, Health, Care and Consumer Protection. 2015. https://www.sozialministerium.at/public.html (accessed April 21, 2021).

79 Kleintjens J, Li X, Simoens S, *et al.* Cost-Effectiveness of Rivaroxaban Versus Warfarin for Stroke Prevention in Atrial Fibrillation in the Belgian Healthcare Setting. *Pharmacoeconomics* 2013; **31**: 909–18.

80 Institut National d'Assurance Maladie-Invalidite. Tarifs des médecins à partir du 1er janvier 2015. 2015. http://www.riziv.fgov.be/fr/themes/cout-remboursement/par-mutualite/prestations-individuelles/prix/Pages/medecin-partie01.aspx#.WMFGtjvyjIV (accessed March 9, 2017).

81 Simoens S, De Naeyer L, Dedeken P. Cost Effectiveness of Lacosamide in the Adjunctive Treatment of Patients with Refractory Focal Epilepsy in Belgium. *CNS Drugs* 2012; **26**: 337–50.

82 Annemans L, Strens D, Lox E, Petit C, Malonne H. Cost-effectiveness analysis of aprepitant in the prevention of chemotherapy-induced nausea and vomiting in Belgium. *Support Care Cancer* 2008; **16**:

905–15.

83 Kamusheva M, Dimitrova M, van Boven JFM, *et al.* Clinical characteristics, treatment patterns, and socio-economic burden of COPD in Bulgaria. *J Med Econ* 2017; **20**: 503–9.

84 Jukic V, Jakovljevic M, Filipcic I, *et al.* Cost-Utility Analysis of Depot Atypical Antipsychotics for Chronic Schizophrenia in Croatia. *Value Heal Reg Issues* 2013; **2**: 181–8.

85 Vučina VV, Filipović SK, Kožnjak N, *et al.* Cost-effectiveness of pneumococcal conjugate vaccination in Croatia. *Vaccine* 2015; **33**: A209--A218.

86 Ministry of Health. Useful Information. Medical Card. 2013. http://www.moh.gov.cy/moh/moh.nsf/0/FD0134CDED1D026243257A37002C2C47?OpenDocument (accessed March 20, 2017).

87 Petrou P, Talias MA. A pilot study to assess feasibility of value based pricing in Cyprus through pharmacoeconomic modelling and assessment of its operational framework: sorafenib for second line renal cell cancer. *Cost Eff Resour Alloc* 2014; **12**: 12.

88 Zannetos S, Zachariadou T, Zachariades A, Georgiou A, Talias MA. The economic burden of adult asthma in Cyprus; a prevalence-based cost of illness study. *BMC Public Health* 2017; **17**. DOI:10.1186/s12889-017-4184-0.

89 Petrou P, Talias MA. Cost–effectiveness of sorafenib compared to best supportive care in second line renal cell cancer from a payer perspective in Cyprus. *Expert Rev Pharmacoecon Outcomes Res* 2014; **14**: 131–8.

90 Holmerová I, Hort J, Rusina R, Wimo A, Šteffl M. Costs of dementia in the Czech Republic. *Eur J Heal Econ* 2017; **18**: 979–86.

91 Søndergaard J, Christensen HN, Ibsen R, Jarbøl DE, Kjellberg J. Healthcare resource use and costs of opioid-induced constipation among non-cancer and cancer patients on opioid therapy: A nationwide register-based cohort study in Denmark. *Scand J Pain* 2017; **15**: 83–90.

92 Hallinen T, Soini EJ, Asseburg C, Kuosmanen P, Laakkonen A. Warfarin treatment among Finnish patients with atrial fibrillation: retrospective registry study based on primary healthcare data. *BMJ Open* 2014; **4**: e004071.

93 Nielsen R, Kankaanranta H, Bjermer L, *et al.* Cost effectiveness of adding budesonide/formoterol to tiotropium in COPD in four Nordic countries. *Respir Med* 2013; **107**: 1709–21.

94 Moore M, Lopes C, Moore M. Health care in France: facing hard choices. *Can Med Assoc J* 2007; **177**: 1167–9.

95 Benjamin L, Buthion V, Vidal-Trécan G, Briot P. Impact of the healthcare payment system on patient access to oral anticancer drugs: an illustration from the French and United States contexts. *BMC Health Serv Res* 2014; **14**. DOI:10.1186/1472-6963-14-274.

96 de Zélicourt M, de Toffol B, Vespignani H, *et al.* Management of focal epilepsy in adults treated with polytherapy in France: The direct cost of drug resistance (ESPERA study). *Seizure* 2014; **23**: 349–56.

97 Borget I, Bonastre J, Catargi B, *et al.* Quality of life and cost-effectiveness assessment of radioiodine ablation strategies in patients with thyroid cancer: Results from the randomized phase III ESTIMABL trial. *J Clin Oncol* 2015; **33**: 2885–92.

98 Damm O, Eichner M, Rose MA, *et al.* Public health impact and cost-effectiveness of intranasal live attenuated influenza vaccination of children in Germany. *Eur J Heal Econ* 2014; **16**: 471–88.

99 Ihbe-Heffinger A, Paessens BJ, Von Schilling C, *et al.* Management of febrile neutropenia - A German prospective Hospital cost analysis in lymphoproliferative disorders, non-small cell lung cancer, and primary breast cancer. *Onkologie* 2011; **34**: 241–6.

100 Makras P, Athanasakis K, Boubouchairopoulou N, *et al.* Cost-effective osteoporosis treatment thresholds in Greece. *Osteoporos Int* 2015; **26**: 1949–57.

101 Boubouchairopoulou N, Athanasakis K, Chini M, Mangafas N, Lazanas MK, Kyriopoulos JE. Estimation of the Direct Cost of HIV-Infected Patients in Greece on an Annual Basis. *Value Heal Reg Issues* 2014; **4**: 82–6.

102 Syriopoulou V, Kafetzis D, Theodoridou M, *et al.* Evaluation of potential medical and economic benefits of universal rotavirus vaccination in Greece. *Acta Paediatr* 2011; **100**: 732–9.

103 Fragoulakis V, Papagiannopoulou V, Kourlaba G, Maniadakis N, Fountzilas G. Cost-Minimization Analysis of the Treatment of Patients With Metastatic Colorectal Cancer in Greece. *Clin Ther* 2012; **34**: 2132–42.

104 Baji P, Brodszky V, Tamás G, *et al.* Quality of Life and Costs in Parkinson's Disease: A Cross Sectional Study in Hungary. *PLoS One* 2014; **9**: e107704.

105 Boncz I, Brodszky V, Péntek M, *et al.* The disease burden of colorectal cancer in Hungary. *Eur J Heal Econ* 2009; **10**: 35–40.

106 Nielsen R, Johannessen A, Benediktsdottir B, *et al.* Present and future costs of COPD in Iceland and Norway: results from the BOLD study. *Eur Respir J* 2009; **34**: 850–7.

107 Gannon, B., O'Shea, E., & Hudson E. Technical Report 1: The Economic Costs of falls and fractures in people aged 65 and over in Ireland. Galway, 2007.

108 Tilson L, Sharp L, Usher C, *et al.* Cost of care for colorectal cancer in Ireland: A health care payer perspective. *Eur J Heal Econ* 2012; **13**: 511–24.

109 O'Brien C, Fogarty E, Walsh C, *et al.* The cost of the inpatient management of febrile neutropenia in cancer patients - a micro-costing study in the Irish healthcare setting. *Eur J Cancer Care (Engl)* 2015; **24**: 125–32.

110 Capri S, Porta C, Delea TE. Cost-effectiveness of Pazopanib Versus Sunitinib as First-line Treatment

for Locally Advanced or Metastatic Renal Cell Carcinoma from an Italian National Health Service Perspective. *Clin Ther* 2017; **39**: 567--580.e2.

111 Polinder S. APOLLO : The economic consequences of injury Final report. Rotterdam, 2008.

112 Domeikienė A, Vaivadaitė J, Ivanauskienė R, Padaiga Ž. Direct cost of patients with type 2 diabetes mellitus healthcare and its complications in Lithuania. *Medicina (B Aires)* 2014; **50**: 54–60.

113 Ivanauskiene R, Domeikiene A, Kregždyte R, *et al.* The cost of newly diagnosed breast cancer in Lithuania, 2011. *Med* 2015; **51**: 63–8.

114 Caisse Nationale de Sante. Tarifs De La Nomenclature Des Actes Et Services Des Medecins Tenant Compte Du Reglement Grand-Ducal. 2011 http://www.cns.public.lu/content/dam/cns/legislations/texte-coordonne/livre-bleu/livre-bleu-01012017.pdf.

115 World Health Organization. Health service delivery costs. WHO-CHOICE. 2010. http://www.who.int/choice/costs/en (accessed Feb 15, 2017).

116 Bosmans JE, Boeke AJ, van Randwijck-Jacobze ME, *et al.* Addition of a general practitioner to the accident and emergency department: a cost-effective innovation in emergency care. *Emerg Med J* 2012; **29**: 192–6.

117 Van Gils CWM, de Groot S, Tan SS, *et al.* Real-world resource use and costs of adjuvant treatment for stage III colon cancer. *Eur J Cancer Care (Engl)* 2015; **24**: 321–32.

118 Govaert JA, van Dijk WA, Fiocco M, *et al.* Nationwide Outcomes Measurement in Colorectal Cancer Surgery: Improving Quality and Reducing Costs. *J Am Coll Surg* 2016; **222**: 19--29.e2.

119 Shin M, Salamanca BV, Kristiansen IS, Flem E. Healthcare costs of rotavirus and other types of gastroenteritis in children in Norway. *Pediatr Infect Dis J* 2016; **35**: e97--e101.

120 Sørensen M, Arneberg F, Line TM, Berg TJ. Cost of diabetes in Norway 2011. *Diabetes Res Clin Pract* 2016; **122**: 124–32.

121 Norum J, Olsen JAA. A cost-effectiveness approach to the Norwegian follow-up programme in colorectal cancer. *Ann Oncol* 1997; **8**: 1081–7.

122 Angus C, Thomas C, Anderson P, Meier PS, Brennan A. Estimating the cost-effectiveness of brief interventions for heavy drinking in primary health care across Europe. *Eur J Public Health* 2016; : ckw122.

123 Kanarkiewicz M, Szczęsny TJ, Krysiński J, Buciński A, Kowalewski J, Pawłowicz Z. Cost-effectiveness analysis of lung cancer screening with low-dose computerised tomography of the chest in Poland. *Współczesna Onkol* 2015; **6**: 480–6.

124 Czech M, Rosinska M, Rogalska J, Staszewska E, Stefanoff P. Costs of Medically Attended Acute Gastrointestinal Infections: The Polish Prospective Healthcare Utilization Survey. *Value Heal Reg Issues* 2013; **2**: 210–7.

125 Polish National Health Fund. Oncology Package. 2015. http://www.nfz.gov.pl/dla-swiadczeniodawcy/pakiet-onkologiczny/ (accessed April 20, 2021).

126 Reza Maleki-Yazdi M, Molimard M, Keininger DL, *et al.* Cost Effectiveness of the Long-Acting $β$2-Adrenergic Agonist (LABA)/Long-Acting Muscarinic Antagonist Dual Bronchodilator Indacaterol/Glycopyrronium Versus the LABA/Inhaled Corticosteroid Combination Salmeterol/Fluticasone in Patients with Chronic Obstru. *Appl Health Econ Health Policy* 2016; **14**: 579–94.

127 Miguel LS, Lopes FV, Pinheiro B, *et al.* Cost Effectiveness of Pembrolizumab for Advanced Melanoma Treatment in Portugal. *Value Heal* 2017; **20**: 1065–73.

128 Lakić D, Petrova G, Bogavac-Stanojević N, Jelić-Ivanović Z, Kos M. The Cost-Effectiveness of Hypertension Pharmacotherapy in Serbia: A Markov Model. *Biotechnol Biotechnol Equip* 2012; **26**: 3066–72.

129 Janković SM, Kostić M. Cost-Effectiveness of Introducing Point-of-Care Test for Detection of Level of Glycogen Phosphorylase in Early Diagnostic Algorithm of Acute Coronary Syndrome. *Value Heal Reg Issues* 2016; **10**: 79–84.

130 Lane S, Molina J, Plusa T. An international observational prospective study to determine the Cost Of Asthma eXacerbations (COAX). *Respir Med* 2006; **100**: 434–50.

131 Mesti T, Boshkoska BM, Kos M, *et al.* The cost of systemic therapy for metastatic colorectal carcinoma in Slovenia: discrepancy analysis between cost and reimbursement. *Radiol Oncol* 2015; **49**: 200–8.

132 Generalitat de Catalunya. Diari Oficial de la Generalitat de Catalunya. 2013; **6079**: 10715–856.

133 Durán I, Garzón C, Sánchez A, *et al.* Cost analysis of skeletal-related events in Spanish patients with bone metastases from solid tumours. *Clin Transl Oncol* 2014; **16**: 322–9.

134 Sanclemente-Ansó C, Bosch X, Salazar A, *et al.* Cost-minimization analysis favors outpatient quick diagnosis unit over hospitalization for the diagnosis of potentially serious diseases. *Eur J Intern Med* 2016; **30**: 11–7.

135 Edelstein M, Merk H, Deogan C, Carnahan A, Wallensten A. Quantifying the incidence and cost of acute gastrointestinal illness in Sweden, 2013–2014. *Epidemiol Infect* 2016; **144**: 2831–9.

136 Lidgren M, Jonsson B, Rehnberg C, Willking N, Bergh J. Cost-effectiveness of HER2 testing and 1-year adjuvant trastuzumab therapy for early breast cancer. *Ann Oncol* 2007; **19**: 487–95.

137 Gehrman J, Björholt I, Angenete E, Andersson J, Bonjer J, Haglind E. Health economic analysis of costs of laparoscopic and open surgery for rectal cancer within a randomized trial (COLOR II). *Surg Endosc* 2017; **31**: 1225–34.

138 Schmutz C, Mäusezahl D, Bless PJ, Hatz C, Schwenkglenks M, Urbinello D. Estimating healthcare costs of acute gastroenteritis and human campylobacteriosis in Switzerland. *Epidemiol Infect* 2017; **145**:

627–41.

139 Matter-Walstra K, Schwenkglenks M, Betticher D, *et al.* Bevacizumab Continuation Versus Treatment Holidays After First-Line Chemotherapy With Bevacizumab in Patients With Metastatic Colorectal Cancer: A Health Economic Analysis of a Randomized Phase 3 Trial (SAKK 41/06). *Clin Colorectal Cancer* 2016; **15**: 314--320.e2.

140 Eichler K, Hess S, Chmiel C, *et al.* Sustained health-economic effects after reorganisation of a Swiss hospital emergency centre: a cost comparison study. *Emerg Med J* 2013; **31**: 818–23.

141 Bakir M, Standaert B, Turel O, Bilge ZE, Postma M. Estimating and comparing the clinical and economic impact of paediatric rotavirus vaccination in Turkey using a simple versus an advanced model. *Vaccine* 2013; **31**: 979–86.

142 Akın L, Macabéo B, Caliskan Z, Altinel S, Satman I. Cost-Effectiveness of Increasing Influenza Vaccination Coverage in Adults with Type 2 Diabetes in Turkey. *PLoS One* 2016; **11**: e0157657.

143 Bullement A, Underhill S, Fougeray R, Hatswell AJ. Cost-effectiveness of Trifluridine/tipiracil for Previously Treated Metastatic Colorectal Cancer in England and Wales. *Clin Colorectal Cancer* 2018; **17**: e143--e151.

144 Gordon H, Brindley JH, Zheng C, *et al.* PWE-033 The Incidence and Cost of Unexpected Hospital Attendance Following Elective Outpatient Flexible Sigmoidoscopy: Abstract PWE-033 Table. *Gut* 2013; **62**: A143.3--A144.

145 Franks PJ, Bosanquet N, Thorpe H, *et al.* Short-term costs of conventional vs laparoscopic assisted surgery in patients with colorectal cancer (MRC CLASICC trial). *Br J Cancer* 2006; **95**: 6–12.

146 Dimitrova N, Petkova Y, Uzunova L, *et al.* Cancer Incidence in Bulgaria 2011. Bulg. Natl. Cancer Regist. 2013; **XXII**. http://www.sbaloncology.bg/index.php/bg/ (accessed March 23, 2021).

147 NORDCAN. Cancer statistics for the Nordic countries. 2015. http://www-dep.iarc.fr/NORDCAN/english/frame.asp (accessed Jan 14, 2018).

148 National Cancer Registry Ireland. Cancer Factsheet - Colorectal Cancer. 2018 https://www.ncri.ie/sites/ncri/files/factsheets/Factsheet colorectal.pdf.

149 Centre for Disease Prevention and Control of Latvia. Statistical data on oncological patients. 2015. https://www.spkc.gov.lv/lv/statistikas-dati (accessed March 23, 2021).

150 Zadnik V, Primic Žakelj M. Cancer in Slovenia 2014. Ljubljana, 2017 https://www.onko-i.si/fileadmin/onko/datoteke/dokumenti/RRS/LP_2014.pdf .

151 Lorez M, Heusser R, Arndt V. Prevalence of Cancer Survivors in Switzerland. *Schweizer Krebsbulletin* 2014; : 285–8.

152 di Oncologia Medica AI. I NUMERI DEL CANCRO IN ITALIA 2015. 2016 https://www.registri-tumori.it/cms/sites/default/files/pubblicazioni/2015_numeri_del_cancro.pdf.

153 Colonna M, Mitton N, Grosclaude P. Estimation de la prévalence (partielle et totale) du cancer en France métropolitaine chez les 15 ans et plus en 2008 Étude à partir des registres. Boulogne-Billancourt, 2014 https://www.santepubliquefrance.fr/maladies-et-traumatismes/cancers.

154 Pavlík T, Mu J, Koptíková J, Slaví L, Feltl D. Estimating the number of colorectal cancer patients treated with anti-tumour therapy in 2015 : the analysis of the Czech National Cancer Registry. *BMC Public Health* 2012; **12**: 1–10.

155 Robert Koch Institute. Cancer in Germany in 2013/2014. Berlin, 2018 DOI:10.17886/rkipubl-2017-008.

156 Public Health England. NCRAS-TCST Partnership. Natl. Cancer Regist. Anal. Serv. 2015. http://www.ncin.org.uk/local_cancer_intelligence/tcst (accessed Jan 15, 2018).

157 Ferlay, J, Ervik, M, Lam, F, Colombet, M, Mery, L, Piñeros, M, Znaor, A, Soerjomataram, I, Bray F. Global Cancer Observatory: Cancer Today. Int. Agency Res. Cancer. 2020. https://gco.iarc.fr/today.

158 Allemani C, Matsuda T, Carlo V Di, *et al.* Global surveillance of trends in cancer survival 2000 – 14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet* 2018; **14**. DOI:10.1016/S0140-6736(17)33326-3.

159 European Commission. Physicians by medical speciality. Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_rs_spec&lang=en (accessed April 1, 2018).

160 European Commission. Medical technologies - examinations by medical imaging techniques (CT, MRI and PET). Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_co_exam&lang=en (accessed April 1, 2018).

161 European Commission. Medical Technology. Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_rs_equip&lang=en (accessed April 1, 2018).

162 European Commission. Surgical operations and procedures performed in hospitals by ICD-9-CM. Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_co_proc2&lang=en (accessed April 1, 2018).

163 Borsch-Supan A. Survey of Health, Ageing and Retirement in Europe (SHARE) Wave 6. 2017 DOI:10.6103/SHARE.w6.600.

164 European Commission. Causes of death - deaths by country of residence and occurrence. Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_cd_aro&lang=en (accessed April 18, 2021).

165 European Commission. Minimum wages. Eurostat. 2015. https://ec.europa.eu/eurostat/databrowser/view/tps00155/default/table?lang=en (accessed Aug 4, 2017).

166 Statistics Austria. Structure of Earnings Survey. 2014. http://www.statistik.at/web_en/statistics/PeopleSociety/social_statistics/personal_income/structure_of_earnings/index.html (accessed Aug 4, 2017).

167 Ministry of Finance. Structure of Earnings Survey - Hourly Earnings of Employees. Stat. Serv. 2014. http://www.mof.gov.cy/mof/cystat/statistics.nsf/labour_34main_en/labour_34main_en?OpenForm&sub=4&sel=2 (accessed Aug 4, 2017).

168 Statistics Denmark. Labour, Income and Wealth. Statbank Denmark. 2015. https://www.dst.dk/en/Statistik/emner/arbejde-indkomst-og-formue (accessed April 11, 2021).

169 Hanushek EA. Structure of Earnings. 2015 http://www.stat.fi/til/pra/2015/pra_2015_2017-04-06_en.pdf.

170 Statistics Iceland. Landshagir, Statistical Yearbook of Iceland. 2015. https://hagstofan.s3.amazonaws.com/media/public/2019/b852a2d6-8eca-41f2-9e4d-89cf0e324829.pdf (accessed Nov 16, 2020).

171 Istituto Nazionale di Statistica. Gross earnings in enterprises with more than 500 employees -monthly data. Labour and Wages. 2015. https://www.istat.it/en/labour (accessed March 23, 2021).

172 Lien HH, Beyrer S, Lunde H. Quality Report on the Norwegian Structure of Earnings Survey 2006. Oslo, 2009 https://www.ssb.no/a/english/publikasjoner/pdf/rapp_200920_en/rapp_200920_en.pdf.

173 Statistics Sweden. Salary structures, whole economy. 2015. https://www.scb.se/en/finding-statistics/statistics-by-subject-area/labour-market/wages-salaries-and-labour-costs/salary-structures-whole-economy/ (accessed Nov 16, 2020).

174 Lohncomputer. Switzerland Wages Computer. 2015. https://www.lohncomputer.ch/en/wages/ (accessed Aug 4, 2017).

175 OECD. Ageing and Employment Policies - Statistics on average effective age of retirement. Employ. policies data. 2018. https://www.oecd.org/els/emp/average-effective-age-of-retirement.htm (accessed April 18, 2021).

176 Stokic LP. Debate on the early retirement scheme in Serbia. 2017; : 1–2.

177 European Commission. Structure of earnings survey: annual earnings. Eurostat. 2014. https://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=earn_ses_annual&lang=en (accessed April 18, 2021).

178 European Commission. Employment rate by sex. Eurostat. 2015. https://ec.europa.eu/eurostat/databrowser/view/sdg_08_30/default/table?lang=en (accessed April 18, 2021).

179 European Commission. Activity rates by sex, age and citizenship (%). Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/submitViewTableAction.do (accessed March 23, 2021).

180 Macioch T, Hermanowski T. The Indirect Costs of Cancer-Related Absenteeism in the Workplace in

Poland. *J Occup Enviromental Med* 2011; **53**: 1472–7.

181 Oliva J. Pérdidas laborales ocasionadas por las enfermedades y problemas de salud en España en el año 2005. Madrid Papeles Trab. del Inst. Estud. …. 2010; : 1–71.

182 Vahtera J, Westerlund H, Ferrie JE, *et al.* All-cause and diagnosis-specific sickness absence as a predictor of sustained suboptimal health: a 14-year follow-up in the GAZEL cohort. *J Epidemiol Community Heal* 2009; **64**: 311–7.

183 Barbini N, Beretta GG, Minnucci MP, Andreani M. Le principali patologie causa di assenza dal lavoro . Analisi della banca dati INPS. 2006; : 14–9.

184 Ritachelová I, Bechtold R, Elischer D, *et al.* Statistical Yearbook of the Czech Republic. 2016; : 1–823.

185 Federal Health Reporting. Inability to work of compulsory members of the Local Statutory Health Insurance (AOK) without pensionsers (cases and days of inability to work, days per case). 2015. http://www.gbe-bund.de/ (accessed Sept 4, 2017).

186 European Commission. Pensions beneficiaries at 31st December. Eurostat. 2015. https://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=spr_pns_ben&lang=en (accessed April 18, 2021).

187 Lidwall U. Long-term sickness absence: Aspects of Society, Work, and Family. 2010. https://openarchive.ki.se/xmlui/handle/10616/38927.

188 Statistik Austria. Statistisches Jahrbuch Österreichs. 2015. http://www.marktmeinungmensch.at/studien/statistisches-jahrbuch-oesterreichs-2015/ (accessed Nov 16, 2020).

189 Mazoyer T. L'Absentéisme Pour Cause de Maladie en 2012. 2013 http://www.observatoire-absenteisme.public.lu/chiffres_cles/Absenteisme_maladie_2012.pdf.

190 Roelen CAM, Koopmans PC, Anema JR, van der Beek AJ. Recurrence of Medically Certified Sickness Absence According to Diagnosis: A Sickness Absence Register Study. *J Occup Rehabil* 2010; **20**: 113–21.

191 Gjesdal S, Bratberg E. Diagnosis and duration of sickness absence as predictors for disability pension: Results from a three-year, multi-register based* and prospective study. *Scand J Public Health* 2003; **31**: 246–54.

192 Luengo-Fernandez R, Leal J, Gray A, Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol* 2013; **14**: 1165–74.

193 Institut National d'Assurance Maladie-Invalidite. Disability statistics for employed and unemployed. 2014. http://www.inami.fgov.be/fr/statistiques/indemnites/2014/Pages/statistiques-invalidite.aspx#.Waf1BciGPIV (accessed Aug 31, 2017).

194 Eurofound. Absence from Work - Bulgaria. 2010.

https://www.eurofound.europa.eu/observatories/eurwork/comparative-information/national-contributions/bulgaria/absence-from-work-bulgaria (accessed Aug 31, 2017).

195 Hellenic Statistical Authority. Statistical Yearbook of Greece 2009 & 2010. 2012. http://dlib.statistics.gr/portal/page/portal/ESYE/showdetails?p_id=14052938&p_derive=book&p_topic=10007369 (accessed Sept 4, 2017).

196 Statistics Denmark. Absence by sector, sex, cause of absence, occupation and indicator of absence. Statbank Denmark. 2014. http://www.statistikbanken.dk/statbank5a/SelectVarVal/Define.asp?Maintable=FRA020&PLanguage=1 (accessed Sept 2, 2017).

197 Statistics Estonia. Statistical Yearbook of Estonia. 2016; : 1–439.

198 Social Insurance Institution of Finland. Sickness allowance: Number of recipients and allowances paid out. Kela. 2015. http://raportit.kela.fi/ibi_apps/WFServlet?IBIF_ex=NIT098AL&YKIELI=E (accessed Sept 4, 2017).

199 Social Insurance Institution of Finland. Sickness allowance: Duration of new payments. Kela. 2015. http://raportit.kela.fi/ibi_apps/WFServlet?IBIF_ex=NIT123AL&YKIELI=E (accessed Sept 4, 2017).

200 Social Insurance Institution of Finland. Recipients of disability benefit by diagnosis. Kela. 2015. http://raportit.kela.fi/ibi_apps/WFServlet?IBIF_ex=NIT147BL&YKIELI=E (accessed Sept 4, 2017).

201 Organisation for Economic Co-operation and Development. Health Status. OECD.Stat. 2015. http://stats.oecd.org/index.aspx?DataSetCode=HEALTH_STAT# (accessed Sept 4, 2017).

202 Cuerq A, Païta M, Ricordeau P. Les causes medicales de l'invalidite. *Vacarme* 2014; **4**–**5**: 1–8.

203 Federal Health Reporting. Absenteeism Due to Ill Health, Number of staff away sick. 2015. http://www.gbe-bund.de/ (accessed Sept 4, 2017).

204 Federal Health Reporting. Lost workforce years in 1,000 years for Germany. Classification: years, sex, causes, ICD10. 2015. http://www.gbe-bund.de/ (accessed Sept 4, 2017).

205 Statistics Iceland. Pension Beneficaries. 2015. https://www.statice.is/statistics/society/social-affairs/pension-beneficiaries/ (accessed March 23, 2021).

206 Health and Safety Authority. Summary of workplace injury, illness and fatality statistics 2014-2015. 2016 DOI:10.12688/f1000research.11057.1.

207 Giaccon M. Absence from work - Italy. Eurofound. 2010. https://www.eurofound.europa.eu/observatories/eurwork/comparative-information/national-contributions/italy/absence-from-work-italy (accessed Sept 6, 2017).

208 Fit for Work Italia. Malattie reumatiche croniche invalidanti, tra salute e lavoro. Natl. Heal. Plan. 2011; : 1–28.

209 Curkina I, Berdnikovs A. Absence from work - Latvia. Eurofound. 2010. https://www.eurofound.europa.eu/observatories/eurwork/comparative-information/national-contributions/latvia/absence-from-work-latvia (accessed Sept 6, 2017).

210 Blaziene I. Absence from work - Lithuania. Eurofound. 2010. https://www.eurofound.europa.eu/observatories/eurwork/comparative-information/national-contributions/lithuania/absence-from-work-lithuania (accessed Sept 6, 2017).

211 Hooff M Van, Bossche S Van Den, Smulders P. The Netherlands Working Conditions Survey. 2008.

212 Statistics Norway. Sickness Absence. 2014. https://www.ssb.no/en/arbeid-og-lonn/statistikker/sykefratot/kvartal/2015-03-12 (accessed Sept 6, 2017).

213 Patek A. Social Security in Poland. Warsaw, 2017 https://www.zus.pl/documents/10182/167615/Social+Security+in+Poland/71ffe1b1-c142-48fa-a67b-0c7e1cec6eb6 (accessed March 23, 2021).

214 Ministerio do Trabalho e da Solidariedade Social. Balanco Social. 2015 https://www.dgert.gov.pt/wp-content/uploads/2017/02/DGERT_BS_2015_Relatorio.pdf.

215 Ciutacu C. Absence from work – Romania. Eurofound. 2010. https://www.eurofound.europa.eu/observatories/eurwork/comparative-information/national-contributions/romania/absence-from-work-romania (accessed Sept 7, 2017).

216 Statistical Office of the Republic of Serbia. Statistical Yearbook of The Republic of Serbia 2015. 2016; : 1–439.

217 Matulová S. Absence from work – Slovakia. Eurofound. 2010. https://www.eurofound.europa.eu/observatories/eurwork/comparative-information/national-contributions/slovakia/absence-from-work-slovakia (accessed Sept 7, 2017).

218 Mrcela M. Absence from Work – Slovenia. Eurofound2. 2010. https://www.eurofound.europa.eu/observatories/eurwork/comparative-information/national-contributions/slovenia/absence-from-work-slovenia (accessed Sept 7, 2017).

219 Federal Statistics Bureau. Annual volume of absences of employees according to different reasons of absence, sex, nationality and occupation rate. 2017. https://www.bfs.admin.ch/bfs/fr/home/statistiques/travail-remuneration/activite-professionnelle-temps-travail/temps-travail/absences.assetdetail.2967236.html (accessed Sept 7, 2017).

220 Jakovljevic M, Malmose-Stapelfeldt C, Milovanovic O, Rancic N, Bokonjic D. Disability, Work Absenteeism, Sickness Benefits, and Cancer in Selected European OECD Countries—Forecasts to 2020. *Front Public Heal* 2017; **5**. DOI:10.3389/fpubh.2017.00023.

221 Department for Work and Pensions. Incapacity Benefits detailed medical conditions and duration. 2011. https://www.gov.uk/government/statistics/incapacity-benefits--2 (accessed Sept 7, 2017).

222 Chartered Institute of Personnel and Development. Absence management. 2014. https://www.cipd.co.uk/knowledge/fundamentals/relations/absence/absence-management-surveys (accessed Sept 7, 2017).

223 European Commission. GDP and main components (output, expenditure and income). Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=nama_10_gdp&lang=en (accessed Sept 17, 2017).

224 European Commission. Purchasing power parities (PPPs), price level indices and real expenditures for ESA 2010 aggregates. Eurostat. 2015. http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=prc_ppp_ind&lang=en (accessed April 18, 2021).

225 Institute for Health Metrics and Evaluation. Global Health Data Exchange - GBD Results Tool. 2015. http://ghdx.healthdata.org/gbd-results-tool (accessed Nov 11, 2020).

226 International Agency for Research on Cancer. Estimated number of incident cases, both sexes, colorectal cancer, worldwide in 2012. Cancer Today. 2012.