European Journal of Cancer 100 (2018) 75–84

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Mapping the European cancer research landscape: An evidence base for national and Pan-European research and funding

Mursheda Begum [a,*], Grant Lewison [a], Mark Lawler [b], Richard Sullivan [a]

[a] *King's College London, School of Cancer and Pharmaceutical Sciences, Guy's Hospital Campus, Great Maze Pond, London SE1 9RT, UK*
[b] *Centre for Cancer Research and Cell Biology, Queen's University Belfast, 97 Lisburn Rd, Belfast, BT9 7AE, UK*

Received 9 April 2018; accepted 11 April 2018
Available online 4 July 2018

KEYWORDS
Cancer research in Europe;
Cancer burden;
Cancer research papers;
Cancer research funding

Abstract ***Background:*** Cancer research is among the most active biomedical research domains for the European Union (EU). However, little quantitative empirical evidence is available to guide the decisions on the choice of disease site to study, specific research domain focus or allocation of research resources. To inform national/supranational cancer research policy, high-resolution intelligence is needed.
Methods: We performed a bibliometric analysis of European cancer research papers in the Web of Science from 2002 to 2013 to quantify research activity in each of the 28 EU Member States, along with Iceland, Norway and Switzerland (EUR31), which cancer sites/research domains they addressed, and their sources of financial support (2009–2013).
Findings: Cancer research papers from EUR31 correlated well with national Gross Domestic Products ($r^2 = 0.94$). However, certain cancer sites (lung, oesophagus and pancreas) were under-researched relative to their disease burden, whereas central nervous system and blood cancers were more generously supported than their burden would warrant. An analysis of research domains indicated a paucity of research on radiotherapy (5%), palliative care (1.2%) and quality of life (0.5%). European cancer research funding in 2012–2013 amounted to ~€7.6 billion and came from diverse sources, especially in western Europe/Scandinavia, where in nine countries the charitable sector outspent the government but not in Eastern Europe where charitable research funding barely exists.
Interpretation: Several countries need to increase their cancer research outputs substantially, and/or alter their research portfolios to better match their growing (and changing) cancer burden. More co-ordination among funding agencies is required, so that resources can be

* *Corresponding author.*
E-mail addresses: mursheda.begum@kcl.ac.uk (M. Begum), grant.lewison@kcl.ac.uk (G. Lewison), mark.lawler@qub.ac.uk (M. Lawler), richard.sullivan@kcl.ac.uk (R. Sullivan).

https://doi.org/10.1016/j.ejca.2018.04.017

attuned to align activities to research gaps and perceived clinical needs. In Eastern Europe, the charitable funding sector needs to be developed, so that both public and patient advocacy can have an active role in research.

Research in Context

Evidence before this study

Previous papers on cancer research outputs have only given details on the total numbers of papers published, without division by cancer site or research domain. Moreover, most of these studies only examined papers in specialist cancer journals, which account for fewer than half of total papers. A study on funding did estimate total global research expenditure, but without a detailed analysis of funding sources.

Added value of this study

This study examined effectively all cancer research papers published in Europe for a 12-year period and their division by cancer site and research domain. Comparisons were made with national wealth and with disease burden. Funding data, both explicit and implicit, were obtained for a 5-year period and analysed by country and by sector, and the leading funders were identified.

Implications of all the available evidence

Research publications on cancer in Europe are somewhat low compared with its large and growing disease burden, especially in some countries relative to their Gross Domestic Product. From 2002 to 2013, cancer's fraction of biomedical research increased from 11.6% to 11.9%, but the burden of cancer across Europe was much higher, accounting for 16% of all disability-adjusted life years in 2002 and 20% in 2012. The data indicate that cancer sites such as central nervous system and blood cancers appear to be over-researched, whereas lung, pancreatic and oesophageal cancers are under-researched. Certain research domains, such as radiotherapy, palliative care and quality of life, are also under-researched, particularly in Southern and Eastern Europe. Funding is very diffuse, which makes potential co-ordination and any change in research direction or prioritisation difficult, especially in Scandinavia which has many private non-profit sources. New funding modalities are also needed to help certain European countries to improve their performance in neglected research areas.

1. Introduction

Cancer research is one of the largest components of biomedical research in European countries, but a quantitative analysis has been lacking. Many studies only covered specialist cancer literature [1,2], whereas we have previously found that more than half of all cancer papers were published in general medical journals [3]. Some papers have looked at individual cancer sites, for example, lung cancer [4] and colorectal cancer [5] or research domains, for example, palliative care [6] and surgery [7], and are limited in scope. There is less information on the funding of cancer research in Europe, and existing data are now out of date [8].

Cancer research paper outputs can be compared with the burden of the disease, as measured by disability-adjusted life years (DALYs), where one DALY corresponds to 1 year of 'healthy' life lost [9]. Globally, cancer accounts for a growing burden (5.1% of DALYs in 2002; 8.1% in 2012) but it is over-researched relative to this burden (11.9% of biomedical research in 2002 and 13.2% in 2012). However, in Europe, although the burden of cancer has increased (16.0% of total causes of DALYs in 2002, rising to 19.5% in 2012), the level of cancer-specific biomedical research has remained almost static (12.1% of biomedical research in 2012 compared to 11.6% in 2002) (all $p < 0.001\%$), thus rendering cancer an under-researched disease in Europe. This is also true in other high-income countries [10].

Data on disease burden were obtained from the World Health Organization (WHO) websites for each of the 28 European Union Member States (EU MS) and for Iceland, Norway and Switzerland (EUR31), for the years 2002 and 2012 [9]. Increases in disease burden have occurred across the EUR31, with the Netherlands having the highest (2002: 18% and 2012: 23%), Cyprus (8%) the lowest in 2002, and Bulgaria (15%) the lowest in 2012.

We examined cancer research papers published by the EUR31 from 2002 to 2013, and their funding from 2009 to 2013. Papers were accessed both from specialist and from general medical journals and analysed by cancer anatomical site and research domain. Country Gross Domestic Product (GDP) data were used to contextualise the findings.

2. Methodology

2.1. Outputs of research papers and classification by subject area

Articles and reviews in the Web of Science (WoS©; Clarivate Analytics) for the years 2002–2013 and for the

Table 1
List of 31 European countries used to identify cancer research papers.

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

EUR31 countries (see International Standards Organization (ISO) digraph codes, Table 1) were identified using a complex filter. This included both specialist journals and title words [3], including the various types of cancer, genes that increase (or decrease) individuals' chance of having particular cancers and drug therapies and other approaches used exclusively for the treatment of cancer. The filter was originally developed in consultation with Cancer Research UK and updated by the Escuela Andaluza de Salud Pública. The filter had a precision (p, specificity) of 0.95 and recall (r, sensitivity) of 0.98, so the true number of cancer papers was 0.95/0.98 = 0.97 times the apparent number.

Details of the selected papers were downloaded and combined into a single Excel spreadsheet by means of a visual basic program (written by Philip Roe, Evaluametrics Ltd). Papers were categorised by the fractional presence of addresses from each of the EUR31 countries. Because biomedical research outputs strongly correlate with a country's wealth [11], fractional cancer research counts for each EUR31 country were plotted against its GDP to identify countries that were overperforming or underperforming relative to their wealth.

Papers were also analysed by cancer site (e.g. breast, bladder, and so forth) and research domain (e.g. chemotherapy, surgery, and so forth) using a set of subfilters (see Tables 2 and 5). Each subfilter consisted of a set of title words and journal name strings. The performance of individual countries in each subject area, relative to the EUR31 as a whole, was calculated.

2.2. Research funding

The WoS includes funding information in the acknowledgement sections of papers as searchable fields in the Science Citation Index (SCI) since late 2008, so we confined our analysis to SCI papers from 2009 to 2013 (N = 135,798). The amount of funding in earlier years was less than in 2012–2013, so if we assume that the latter level was more correct, there was an apparent overall shortfall of 14%. Funding data were corrected to allow for this and for the calibration factor for the filter (0.97). The research funding organisations included those explicitly listed and ones implicit from the paper's addresses, but excluded any mentioned in conflict of interest statements as having paid the authors for unrelated work [12]. We used a double fractionation method to assign credit. It was assumed that governmental and private non-profit (PNP) funders would only support researchers in their respective countries but that international and industrial funders could support research in any country [13].

A survey of leading researchers in different countries had previously indicated that the mean cost of a biomedical research paper in 2013 was approximately €260,000 [14]. This figure was multiplied by the average annual contributions for each funding source and corrected for the two shortfalls outlined above to give its estimated annual contribution.

3. Results

3.1. Output of cancer papers

The 282,545 cancer research papers from the EUR31 comprised individual country fractional contributions of 252,718 papers; the difference representing non-European contributions. EUR31 cancer research papers increased by 4.3% per annum on a fractional count basis from 2002 to 2013, but world output increased by 6.5% per annum, mainly because of rapid expansion of cancer research in East Asia.

Table 2
List of 23 cancer sites as defined by subfilters with their associated codes, numbers of papers from 2002 to 2013, percent of all papers (% total) and annual average percentage growth (AAPG).

Site	Code	Papers	% Total	AAPG	Site	Code	Papers	% Total	AAPG
Blood	HAE	33,389	11.8	2.4	Pancreas	PAN	5154	1·8	6·6
Breast	MAM	29,111	10.3	5.8	Sarcoma	SAR	5149	1·8	1·9
Central nervous system	CNS	19,438	6.9	4.5	Cervix	CER	4549	1·6	4·4
Colon/rectum	COL	18,955	6.7	6.8	Bladder	BLA	3949	1·4	2·5
Lung, trachea, bronchus	LUN	13,483	4.8	5.3	Uterus	UTE	3440	1·2	4·0
Prostate	PRO	13,057	4.6	7.4	Oesophagus	OES	2038	0·7	6·9
Head and neck	HEN	11,313	4.0	5.0	Testes	TES	1593	0·6	−0·8
Stomach	STO	10,517	3.7	2.7	Eye	EYE	685	0·2	−0·5
Skin	SKI	10,309	3.6	3.9	Penis	PEN	582	0·2	7·7
Liver	LIV	9886	3.5	5.0	Vulva	VUL	228	0·1	2·8
Kidney	KID	6713	2.4	5.6	Gall bladder	GAL	214	0·1	−3·2
Ovaries	OVA	6230	2.2	5.4					

Table 3
Ratio of observed to expected numbers of papers on the leading 10 cancer sites for the 18 leading European countries, 2002–2013.

	Papers	HAE	MAM	CNS	COL	LUN	PRO	HEN	STO	SKI	LIV
Papers	252718	29885	25836	17570	17524	12066	11454	10349	9601	9303	8946
DE	45436	1.06	0.75	1.24	0.85	0.79	1.06	0.98	1.19	1.12	1.20
IT	37876	1.13	0.92	1.09	0.93	1.25	0.89	1.21	1.03	1.04	1.38
UK	37541	0.90	1.19	0.76	1.15	0.82	1.10	0.95	0.77	0.85	0.66
FR	30127	1.06	0.92	1.07	0.89	1.13	1.00	0.76	0.92	0.89	1.28
NL	16068	0.84	1.09	0.77	1.32	1.13	1.10	1.18	1.03	0.99	0.79
ES	15654	1.05	0.99	1.06	1.10	1.17	0.78	1.09	0.97	0.95	1.12
SE	9205	0.94	1.17	0.96	1.14	0.68	1.61	0.62	0.83	0.85	0.53
PL	7543	1.04	1.01	1.06	0.92	1.08	0.47	1.01	1.16	1.06	0.56
GR	7243	1.03	1.23	0.74	1.06	1.49	0.82	1.23	1.40	0.67	0.87
CH	6837	1.00	0.84	1.19	0.73	1.09	0.90	1.08	0.65	1.38	0.98
BE	6253	0.85	1.11	1.02	0.74	1.24	0.98	1.01	0.97	0.94	1.08
AT	5563	1.18	1.00	0.98	0.75	0.69	1.27	0.99	0.66	1.39	1.06
DK	4713	0.92	1.41	0.67	1.48	1.04	0.69	0.78	0.75	1.16	0.39
NO	4054	0.81	1.31	0.93	1.41	0.89	1.07	0.67	0.87	0.93	0.45
FI	3721	0.66	1.48	0.80	0.94	0.73	1.96	1.39	1.09	0.91	0.35
CZ	3005	1.52	0.66	1.21	1.00	0.62	0.61	0.70	0.80	0.84	0.93
IE	2247	0.56	1.59	0.61	1.35	0.98	1.36	0.83	1.08	0.75	0.45
PT	2079	0.57	1.38	0.72	0.85	0.87	0.92	1.59	2.22	0.75	0.53

Countries (based on fractional counts) and sites (based on integer counts) are ranked by total research papers. Contributions by non-European countries are not included. Values > 2 shaded blue; values > 1.41 shaded green; values < 0.71 shaded yellow; values < 0.5 shaded pink. See Table 1 for country ISO codes and Table 2 for cancer site codes. See Tables 9 and 10 in Appendix for data on all 31 European countries.

Table 4
Percentage of cancer papers that received funding by cancer site, 2009–2013.

Site	N	Mean	% Funded	Site	N	Mean	% Funded
HAE	15,035	2.79	69.1	TES	631	1.63	54.7
MAM	14,260	2.68	68.2	SAR	2287	1.99	51.6
SKI	4887	2.22	62.4	STO	4679	1.77	51.1
EYE	271	2.28	61.6	BLA	1760	1.56	47.8
COL	9572	2.07	60.7	KID	3304	1.48	47.6
LUN	6614	2.05	59.2	UTE	1661	1.69	47.4
PRO	6673	2.12	59.1	OES	1001	1.47	45.3
CNS	9439	2.08	58.7	HEN	5475	1.33	44.4
OVA	3056	2.68	58.6	GAL	84	1·04	31.0
PAN	2637	2.42	56.8	PEN	295	0·81	30.2
CER	2124	1.74	56.3	VUL	106	0·73	26.4
LIV	4816	1.86	55.4				

N, number of papers; mean, mean number of funders per paper and % Funded, percentage of papers with explicit or implicit funding acknowledgements. Sites ordered by % Funded. See Table 2 for cancer site codes.

The amount of cancer research from each of the EUR31 countries correlated strongly with GDP ($r^2 = 0.94$), see Fig. 1. Almost all noticeable departures from the correlation line were statistically significant with $p < 0.001\%$. Luxembourg, Latvia and Cyprus showed the lowest outputs of cancer research papers relative to their GDP (red-coloured ISO codes). However, they were also among the countries with the fastest annual average percentage growth (AAPG): Cyprus 18%, Lithuania 16% and Luxembourg 15%. Romania contributed to very few papers relative to its GDP but showed the fastest expansion of its output (36% per annum). The countries with the highest outputs, with twice the expected number of papers, were Slovenia, Croatia, Iceland and Greece (green-coloured ISO codes), all of which increased their annual outputs (AAPG: 11%, 10%, 4% and 4% respectively). Scandinavian countries, except Denmark, showed some of the

Table 5
List of 12 research domains as defined by subfilters with their associated codes, numbers of papers from 2002 to 2013, percent of all papers (% total) and annual average percentage growth (AAPG).

Research domain	Code	Papers	% Total	AAPG
Genetics	GENE	55,873	19.8	2.3
Prognosis	PROG	30,479	10.8	8.8
Surgery	SURG	28,336	10.0	6.0
Standard chemotherapy	CHEM	23,601	8.4	2.1
Pathology	PATH	23,174	8.2	3.4
Radiotherapy	RADI	15,103	5.3	6.2
Epidemiology	EPID	14,766	5.2	8.1
Diagnosis	DIAG	12,213	4.3	6.8
Targeted chemotherapy	TARG	7156	2.5	18.7
Screening	SCRE	5392	1.9	7.0
Palliative care	PALL	3413	1.2	9.6
Quality of life	QUAL	1540	0.5	12.6

lowest levels of growth in their cancer research, with Finland having no growth over the 12-year period.

The amount of international collaboration in cancer research for the European countries tended to vary inversely with their output (Fig. 2). International collaboration is much higher in 'western' European countries, especially Nordic countries and Switzerland, than in 'eastern' countries, with Croatia, the most recent EU member, showing the least international collaboration. This difference may reflect the shorter time that 'accession' Member States in the east have been the EU MS.

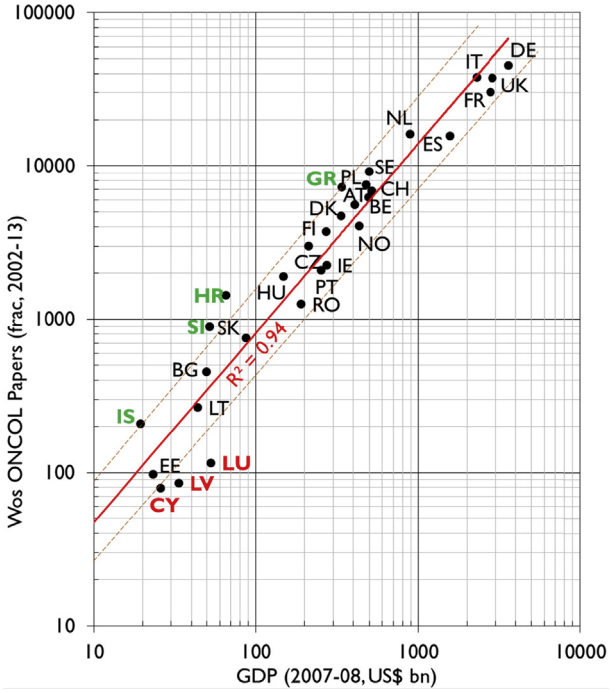

Fig. 1. Plot of cancer (ONCOL) paper output on a fractional count basis, 2002–2013, against GDP (2007–2008) in billion US dollars for European countries. MT was omitted as output and GDP is too small, and graph is on a log–log scale. Dashed lines show values ×2 or ×0.5 relative to least-squares correlation line. See Table 1 for country ISO codes.

3.2. Research output by cancer sites

A majority (68%) of cancer papers from 2002 to 2013 could be classified into one or more of the 23 cancer sites (Table 2). Cancers of the blood and breast received the most attention, but pancreatic and oesophageal cancers had much smaller outputs, as did several female cancers (ovaries, cervix, uterus and vulva). Fig. 3 indicates a rather weak correlation between the disease burden from the different cancers and the amount of research performed, with the central nervous system appearing over-researched in 2011–2013 (expected output 3129, observed output 5887; $p < 0.001$ on Poisson distribution with one degree of freedom) and lung cancer significantly under-researched (expected output 18,262, observed output 4271, $p < 0.001\%$). The arrows from the red spots to the green spots quantify changes from the beginning to the end of the study period. These data also reveal the relative paucity of research in 2011–2013 on oesophageal (expected output 2247, observed output 640, $p < 0.001\%$) and pancreatic (expected output 4809, observed output 1634, $p < 0.001\%$) cancers. The burden of pancreatic cancer has increased by more than a third between 2000 and 2010 (from 1406 to 1723 k DALYs, $p < 0.001\%$).

Table 3 shows the research performance of the leading 18 European countries on the top 10 cancer sites (see Appendix for data on all countries and sites). If the shortfalls in papers for particular cancers, such as those of the lung, pancreas and oesophagus, are to be rectified, then greater collaboration will be needed with countries with a strong commitment to relevant research on these cancer sites. For example, Germany is very active in both pancreatic (1425 papers, ×1.73-fold higher) and oesophageal (465 papers, ×1.44-fold higher) cancers, so more collaboration with other EUR31 countries could be beneficial.

Analysis of funding for the EUR31 countries in 2009–2013 showed that 59% of the 119,753 papers had one or more explicit or implicit funding acknowledgements that vary by cancer site (see Table 4). The three sites identified previously as requiring greater research attention (lung, oesophagus and pancreas) all received the same or lower levels of funding than this average (for pancreatic cancer, $p \sim 0.02$; for oesophageal cancer, $p < 0.001$).

3.3. Cancer research output by research domain

Research domain was identified for 59% of papers evaluated (see Table 5). Genetics was the dominant research domain, followed by prognosis and surgery. There was very little research on quality of life, palliative care or screening, although these domains have been expanding their outputs rapidly. Standard chemotherapy showed the slowest growth rate, whereas targeted chemotherapy showed the fastest annual growth in output.

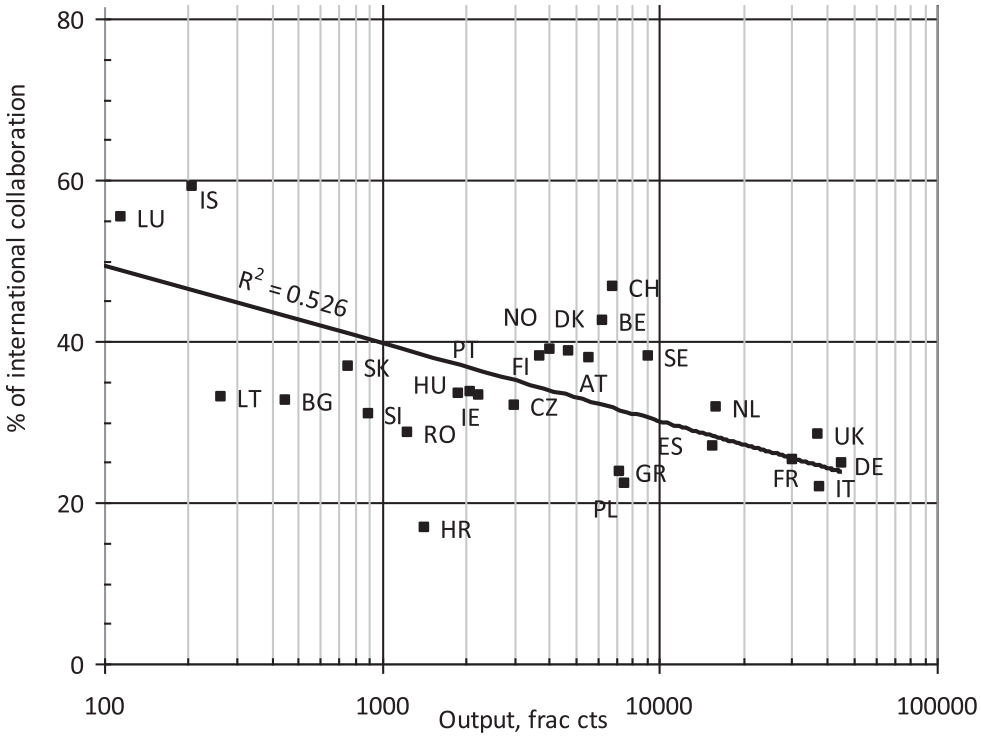

Fig. 2. Percentages of international collaboration in cancer research (ONCOL), 2002–2013, by European countries plotted against their output (fractional counts of papers). Abscissa is on a log scale. See Table 1 for country ISO codes.

Commitment of the 18 leading European countries to different research domains is shown in Table 6. In the three neglected research domains (quality of life, palliative care and screening), the Scandinavian countries performed well, as did the UK and the Netherlands. However, most of the large countries (France, Germany, Italy, Poland and Spain) relatively underperformed in these domains.

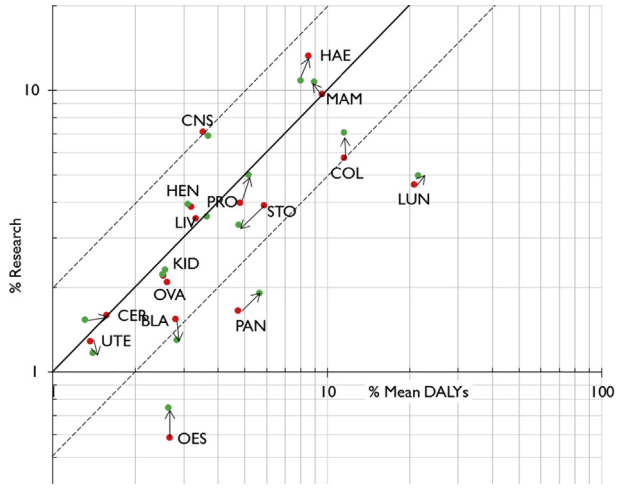

Fig. 3. Scatterplot of European cancer research paper outputs on different cancer sites, 2002–2004 and 2011–2013, as a percentage of the total European burden of cancer as measured by disability-adjusted life years (DALYs) from the different cancer sites, log–log plot. Red and green dots indicate the beginning and end of the study period, respectively. See Table 2 for cancer site codes.

Table 7 shows the amount of funding for papers in each research domain. Radiotherapy (49%) and surgery (30%) received much less funding than chemotherapy (67%) and targeted chemotherapy (73%). For all four treatment modalities, the differences from the mean funding level of 59% were significant with $p < 0.001\%$.

3.4. Sources of research funding

In 2013, the fractional European output was 29,254 research papers, and at an average cost of €260,000, the estimated public domain cancer research expenditure resulting in a published paper in Europe was €7.6 billion.

Fig. 4 shows the amount of funding from each sector for 18 leading countries. Government supported the largest share of European cancer research (30%), followed by the PNP (19%), industrial (7%) and international sectors (3%). The European Commission was the largest single funder of European cancer research, with 2836 papers (2.4% of the total), amounting to approximately €147 million spent, with the number of research papers receiving its support increasing by 16% per annum.

Funding from government, including departments, agencies and local authorities, ranged from 63% in Estonia to 7% in Greece. In nine countries in Western Europe, PNP funders outspent the public sector, notably in Scandinavia (data for Iceland not shown) and the UK. Collecting charities formed the largest PNP group, supporting 10% of all cancer research, but more

Table 6
Ratio of observed to expected numbers of papers in 12 research domains for the leading 18 European countries, 2002–2013, with >2000 papers.

	Papers	GENE	PROG	SURG	CHEM	PATH	RADI	EPID	DIAG	TARG	SCRE	PALL	QUAL
Papers	252718	48258	27188	26584	21480	20715	13939	12296	11333	6200	4840	3151	1409
DE	45436	1.03	0.94	1.09	0.88	1.06	1.10	0.69	1.12	1.02	0.75	0.70	0.83
IT	37876	0.86	0.94	1.17	1.27	0.97	0.75	0.88	0.93	1.36	0.81	0.84	0.49
UK	37541	0.96	1.02	1.03	0.85	0.92	0.95	1.11	0.92	0.80	1.26	1.62	1.49
FR	30127	0.85	0.92	1.06	1.15	0.85	1.17	0.94	0.92	1.14	0.82	0.65	0.59
NL	16068	0.97	1.13	1.07	1.03	0.97	1.70	1.25	1.03	0.78	1.80	1.32	2.28
ES	15654	1.12	1.05	0.75	1.00	1.14	0.62	0.91	1.11	1.15	0.92	0.89	0.75
SE	9205	1.31	1.31	0.67	0.78	0.80	1.00	2.29	0.90	0.61	1.26	1.78	1.88
PL	7543	1.28	0.73	0.74	0.97	0.95	0.81	0.95	1.00	0.70	0.42	0.74	0.62
GR	7243	0.99	1.01	1.08	1.51	1.07	0.68	0.77	0.97	0.99	1.12	0.94	0.87
CH	6837	0.86	0.91	0.92	0.95	1.07	1.21	0.64	1.27	1.23	0.65	0.74	0.60
BE	6253	0.76	0.81	0.95	1.06	0.86	1.43	0.54	0.79	1.22	1.16	0.74	0.53
AT	5563	1.01	1.06	0.99	1.05	1.14	1.04	0.62	1.20	1.37	0.83	0.48	0.40
DK	4713	1.07	1.39	0.69	0.80	0.94	1.40	2.59	1.08	0.70	1.48	1.78	2.02
NO	4054	1.21	1.53	0.74	0.63	1.19	1.14	1.68	0.89	0.44	1.69	2.80	3.05
FI	3721	1.51	1.51	0.61	0.65	1.19	0.63	1.81	0.83	0.67	1.98	0.75	1.04
CZ	3005	1.34	0.83	0.83	1.24	1.07	0.71	0.86	0.82	1.01	0.49	0.27	0.33
IE	2247	0.96	1.10	1.37	0.67	1.06	0.69	0.58	1.03	0.81	1.30	1.01	1.04
PT	2079	1.43	0.81	0.41	0.74	1.48	0.35	1.24	1.13	0.65	0.85	0.63	0.97

Countries (based on fractional counts) and research domains (based on integer counts) ranked by number of papers. Values > 2 shaded blue; values > 1.41 shaded green; values < 0.71 shaded yellow; values < 0.5 shaded pink. See Table 1 for country ISO codes and Table 5 for research domain codes.

in Sweden (23%), the UK, Iceland (both 22%) and Denmark (20%). Endowed foundations supported 3787 papers (3.2%), with some countries receiving significantly more than the EUR31 average, namely Denmark (17%), Finland (12%) and Sweden (9%) (all $p < 0.001\%$). Their individual contributions were mostly small, but their huge number meant that their collective support was important, particularly in Germany (892 papers) and Italy (639), the latter mostly from banking foundations. In Eastern Europe, the PNP sector was almost non-existent.

Industrial companies supported 6.6% of all European cancer research, with significantly more funding in Switzerland (13%) and Germany (10%) (for both, $p < 0.001\%$). Industry-funded support went largely to Germany (2042 research papers) and the UK (1187 research papers). Very little support went to the 13 accession countries of Eastern Europe (348 research papers in total).

The French National Health and Medical Research Institute (INSERM) and the Italian Ministry of Health were the leading government bodies to support research, contributing to the equivalent of 2800 (estimated at

Table 7
Percentage of cancer papers that received funding by research domain, 2009–2013.

Research domain	N	Mean	% Funded	Research domain	N	Mean	% Funded
GENE	24,815	3.41	79.2	QUAL	851	1.59	64.3
EPID	7661	4.38	76.2	PALL	1803	1.40	59.4
TARG	4636	2.56	72.7	PATH	10,756	1.82	56.1
CHEM	10,518	2.14	67.2	RADI	7658	1.25	49.2
SCRE	2680	2.11	65.0	DIAG	6207	1.48	48.0
PROG	16,512	2.51	64.6	SURG	14,163	0.73	30.5

Mean, mean number of funders per paper; N, number of papers and % Funded, percentage of papers with explicit/implicit funding acknowledgements. See Table 5 for domain codes.

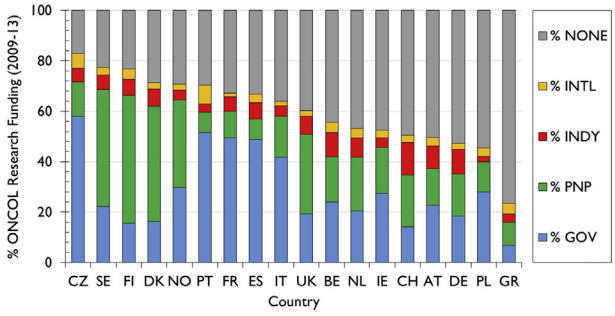

Fig. 4. Percentages of cancer research funding by sector, 2009–2013, for the leading 18 countries (fractional counts >1000 papers and integer counts >1500 papers). NONE, no acknowledged funding; INTL, international; INDY, industry; PNP, private non-profit; GOV, government. See Table 1 for country ISO codes.

€161m/year) and 2468 (€142m/year) papers, respectively, over the 5-year period, see Table 8 in the Appendix. Cancer Research UK was by far the largest of the collecting charities (2004 research papers, €115m/year). The two leading industrial funders were Novartis AG (546 papers) and Hoffmann-La Roche SA (529 papers). Based on their support for published papers, we estimate that they each spent in excess of €30 million per annum in Europe.

Of the four treatment approaches evaluated, targeted chemotherapy papers received 23% of their support from industry, compared with standard chemotherapy (14%) (both above the European average), radiotherapy (6.1%) and surgery (3.0%) ($p < 0.001$). Some 37% of the papers did not acknowledge any funding sources and probably were supported by the university and/or hospital in which the research was conducted.

4. Discussion and conclusions

Cancer research is a critical component of a country's performance in providing optimal cancer care for its citizens [15,16]. Our research reveals that certain European countries are underperforming in cancer research relative to their GDP and need to do more to address the rising burden of cancer. They may also need to change their research emphasis/prioritisation to respond to the challenges posed by neglected cancer sites or research domains. This will be challenging given the multiplicity of funding sources. Umbrella organisations such as the (British) Association of Medical Research Charities, which do not appear to exist elsewhere in the EU, offer a possible solution. [In Ireland, there is the Medical Research Charities Group, but many of its members do not actually support research.] They can provide comprehensive information on their members' research expenditure, ensure that peer review is used in grant allocation, and lobby for better conditions for research, such as fiscal benefits for collecting charities. Research or disease-specific organisations can also help to co-ordinate research funding and identify and fund research gaps (as Breast Cancer Campaign has done for breast cancer [17], and Bowel Cancer UK has just published for colorectal cancer research prioritisation [18]). Investigating the potential for short international exchange visits to spread good practice may also help individual MS to benefit from expertise elsewhere in Europe.

There is a particular need to encourage charitable and philanthropic funding in Eastern Europe, where cancer research support comes almost entirely from central government. Recent data from the Charities Aid Foundation [19] ranked the Eastern European MS very low for charitable giving, whereas the older MS (and particularly the Scandinavian ones) fared much better. However, there is no lack of cancer research in all the accession MS: Croatia and Slovenia are clearly performing at a strong level (Fig. 1). Greater international collaboration may help (see Fig. 2), e.g. through targeted collaborative funding mechanisms.

Despite large financial support from the PNP sector, the UK's research outputs are low relative to its GDP (Fig. 1), and cancer survival rates in the UK are among the lowest in Western Europe [20]. Because treatment in institutions heavily involved in research is strongly associated with better outcomes for cancer patients, including postoperative mortality and 5-year survival [21], more cancer research in the UK is likely to lead to improved survival rates. Moreover, greater government and PNP support may stimulate additional industrial support [22].

An important finding of our study is the lack of research on three particular cancer sites—lung, oesophageal and pancreatic—whose burden is increasing and whose prognosis is usually poor [23]. Given the challenges related to early diagnosis in these cancers, there is a need to identify biomarkers and better screening tools, with more research funding directed to these cancer sites. For example, only 1.7% of lung cancer research papers focussed on screening, and fewer for oesophageal (0.59%) and pancreatic (0.33%) cancers, whereas screening accounts for 8% of breast cancer papers ($p < 0.001\%$).

The European research portfolio also needs to include more activity in surgery [24] and radiotherapy [25], given their significant role in cancer cure and control. Research in these domains is poorly funded, which may reflect the erroneous public perception, reinforced by media stories [26,27] that chemotherapy, which is well funded, is the main way through which cancers are cured. We also found a movement from funding of standard chemotherapy towards more targeted chemotherapy/biological therapy approaches.

Critically, there is a lack of research on quality of life and palliative care, especially in Eastern and Southern Europe (except for Cyprus). This may both reflect and contribute to barriers to effective palliative care across Eastern Europe [28]. A greater focus on and investment in these areas is needed [29]. On the other hand, there appears to be a substantial support for two basic research domains, namely genetics and epidemiology. While these areas are undoubtedly important, this focus may also reflect the amount of publicity given to these domains in media stories [26,27].

This study has certain limitations. The filter only covers papers that are overtly concerned with cancer, so basic biology may be under-represented. However, many cancer charities devote substantial resources to this type of research. For example, Cancer Research UK devoted 37% of their annual research activity to the biology of cancer in 2010 [30]. Second, the quality and impact of the research were not addressed here but will be examined in a subsequent paper. Third, the coding of research funding organisations is a complex activity that is constantly evolving [13]. Fourth, we had to assume that financial contributions to a country on each paper

were equal, but this will often not be the case. Larger funders will probably give bigger grants, or multiple ones, and so our estimates of their support may be too low. Thus, our estimate of the funding from Cancer Research UK is much less than the expenditure in their annual reports [13]. In contrast, we will have overestimated contributions by the smaller funders. This is a problem inherent with funding analysis. Finally, many papers have no explicit or implicit funding but are likely to have received support from their university or health service. This has not been addressed.

Notwithstanding these caveats, we have reached evidence-informed conclusions that we consider to be robust. The analysis of research papers from both specialist cancer journals and general medical journals provides a more comprehensive picture of European cancer research activity than has previously been attempted. Results have been contextualised with data on cancer burden and with the GDP for different European countries. These data can help support more policy-focussed cancer research agenda for individual European governments. Such agenda would be particularly relevant to those EU MS that perform low levels of cancer research or require a better alignment between country-specific cancer challenges and research priorities. We have identified certain research gaps in individual countries, both for cancer sites and specific research domains. Addressing these research and funding gaps through a more EUR31-wide focussed collaborative approach can help to ensure better cancer control and care for European citizens.

Conflict of interest statement

M.B. reports grants from the European Commission and from Pfizer, during the conduct of the study. G.L. also reports grants from the European Commission and from Pfizer, during the conduct of the study. He holds shareholdings in three pharma companies: AstraZeneca plc, GlaxoSmithKline plc and Shire Pharmaceuticals plc. M.L. reports funding from Pfizer, unrelated to this study. R.S. has nothing to disclose.

Author contributions

M.B. and G.L. contributed equally to the design of the study, literature search, data analysis and production of figures; M.B. collected the data with guidance from G.L; M.B., G.L., M.L. and R.S. wrote and edited the final version of the manuscript and R.S. had overall responsibility for the direction of the project.

Funding

This project was funded by the European Commission's Seventh Framework Program (grant no. EC/FP7/602536) and an unrestricted grant from Pfizer (grant no. 1125586). The funders had no role in the study design, data collection, analysis or interpretation of the data and preparation of, or decision to publish, the manuscript.

Acknowledgements

The authors are grateful to Philip Roe of Evaluametrics Ltd for the provision of VBA programs, and Elena Pallari of KCL who helped with the provision of some important references.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ejca.2018.04.017.

References

[1] Ugolini D, Mela GS. Oncological research overview in the European Union. A 5-year survey. Eur J Cancer 2003;39:1888–94. Available from: https://doi.org/10.1016/S0959-8049(03)00431-3 [Accessed 6 February 2017].

[2] Micheli A, Salvo FD, Lombardo C, Ugolini D, Baili P, Pierotti MA. Cancer research performance in the European Union: a study of published output from 2000 to 2008. Tumori 2011;97:683–9. Available from: https://doi.org/10.1700/1018.11081 [Accessed 26 January 2017].

[3] Lewison G. Definition of cancer research: journals, titles, abstracts or keywords? DESIDOC J Lib Inform Technol 2011;31(5):333–9.

[4] Aggarwal A, Lewison G, Idir S, et al. The state of lung cancer research: a global analysis. J Thorac Oncol 2016;11(7):1040–50. Available from: https://doi.org/10.1016/j.jtho.2016.03.010 [Accessed 24 October 2016].

[5] Wrafter PF, Connelly TM, Khan J, Devane L, Kelly J, Joyce WP. The 100 most influential manuscripts in colorectal cancer: a bibliometric analysis. Surgeon 2016;14(6):327–36. Available from: https://doi.org/10.1016/j.surge.2016.03.001 [Accessed 6 February 2017].

[6] Cummings G, Biondo PD, Campbell D, Stiles C, Fainsinger R, Muise M, et al. Can the global uptake of palliative care innovations be improved? Insights from a bibliometric analysis of the Edmonton Symptom Assessment System. Palliat Med 2011;25(1):71–82. Available from: https://doi.org/10.1177/0269216310381449 [Accessed 6 February 2017].

[7] Purushotham AD, Lewison G, Sullivan R. The state of research and development in global cancer surgery. Ann Surg 2012;255(3):427–32. Available from: https://doi.org/10.1097/SLA.0b013e318246591f [Accessed 6 February 2017].

[8] Eckhouse S, Lewison G, Sullivan R. Trends in the global funding and activity of cancer research. Mol Oncol 2008;2(1):20–32. Available from: https://doi.org/10.1016/j.molonc.2008.03.007 [Accessed 6 February 2017].

[9] World Health Organization. Health statistics and information systems- Estimates for 2000–2012. 2012. Available from: http://www.who.int/healthinfo/global_burden_disease/estimates/en/index2.html [Accessed 4 January 2017].

[10] Lewison G. Biomedical research and the regional burden of disease. In: Ingwersen P, Larsen B, editors. Proceedings of the 10th international conference of the International Society for Scientometrics and Informetrics. Stockholm, Sweden:

Karolinska University Press; 2005. p. 585–94. ISBN: 91-7140-339-6.

[11] Frame JD, Narin F. The international distribution of biomedical publications. Fed Proc 1977;36(6):1790–5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/856633 [Accessed 24 October 2016].

[12] Lewison G, Sullivan R. Conflicts of interest statements on biomedical papers. Scientometrics 2015;102(3):2151–9. Available from: https://doi.org/10.1007/s11192-014-1507-0 [Accessed 24 October 2016].

[13] Begum M, Lewison G. Web of science research funding information: methodology for its use in analysis and evaluation. J Scientometric Res 2017;6(2):179–89. Available from: https://www.jscires.org/article/189 [Accessed 13 July 2017].

[14] Begum M, Lewison G, Wright JSF, Pallari E, Sullivan R. European non-communicable respiratory disease research, 2002-13: bibliometric study of outputs and funding. PLoS One 2016;1(4): e0154197. Available from: https://doi.org/10.1371/journal.pone.0154197 [Accessed 24 October 2016].

[15] Duffy S, Richards M, Selby P, Lawler M. Addressing cancer disparities in Europe: a multifaceted problem that requires interdisciplinary solutions. Oncologist 2013;18:e29–30.

[16] European Commission's Scientific Panel for Health. Better research for better health: a vision for health and biomedical research from the Scientific Panel for Health. European Commission; 2016. Available from: https://ec.europa.eu/programmes/horizon2020/sites/horizon2020/files/SPH_VisionPaper_02062016.pdf.

[17] Eccles SA, Aboagye EO, Ali S, Anderson AS, Armes J, Berditchevski F, et al. Critical research gaps and translational priorities for the successful prevention and treatment of breast cancer. Breast Cancer Res 2013;15(5):R92. Available from: https://doi.org/10.1186/bcr3493 [Accessed 30 March 2017].

[18] Lawler M, Alsina D, Adams RA, et al. Critical research gaps and recommendations to inform research prioritisation for more effective prevention and improved outcomes in colorectal cancer. Gut 2018;67(1):179–93.

[19] Charities Aid Foundation. CAF world giving index 2016: The world's leading study of generosity. Available from: https://www.cafonline.org/about-us/publications/2016-publications/download-the-caf-world-giving-index-2016. [Accessed 15 February 2017].

[20] Baili P, Di Salvo F, Marcos-Gragera R, Siesling S, Mallone S, Santaquilani M, et al. Age and case mix-standardised survival for all cancer patients in Europe 1999–2007: results of EUROCARE-5, a population-based study. Eur J Cancer 2015;51:2120–9. Available from: https://doi.org/10.1016/j.ejca.2015.07.025 [Accessed 7 August 2017].

[21] Downing A, Morris EJA, Corrigan N, Sebag-Montefiore D, Finan PJ, Thomas JD, et al. High hospital research participation and improved colorectal cancer survival outcomes: a population-based study. Gut 2017;66(1):89–96. Available from: https://doi.org/10.1136/gutjnl-2015-311308 [Accessed 24 July 2017].

[22] Sussex J, Feng Y, Mestre-Ferrandiz J, Pistollato M, Hafner M, Burridge P, et al. Quantifying the economic impact of government and charity funding of medical research on private research and development funding in the United Kingdom. BMC Med 2016; 14(1):1–23. Available from: https://doi.org/10.1186/s12916-016-0564-z [Accessed 7 August 2017].

[23] De Angelis RM, Sant MP, Coleman S, Francisci P, Baili D, Pierannunzio A, et al. Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-5-a population-based study. Lancet Oncol 2014;15(1):23–34. Available from: https://doi.org/10.1016/S1470-2045(13)70546-1 [Accessed 14 August 2017].

[24] Sullivan R, Alatise OI, Anderson BO, Audisio R, Autier P, Aggarwal A, et al. Global cancer surgery: delivering safe, affordable, and timely cancer surgery. Lancet Oncol 2015;16(11): 1193–224. Available from: https://doi.org/10.1016/S1470-2045(15)00223-5 [Accessed 11 April 2017].

[25] Delaney G, Jacob S, Featherstone C, Barton M. The role of radiotherapy in cancer treatment. Cancer 2005;104(6):1129–37. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16080176 [Accessed 7 August 2017].

[26] Lewison G, Tootell S, Roe P, Sullivan R. How do the media report cancer research? A study of the UK's BBC website. Brit J Cancer 2008;99(4):569–76. Available from: https://doi.org/10.1038/sj.bjc.6604531 [Accessed 7 August 2017].

[27] Pallari E, Lewison G. European newspaper reports of non-communicable disease research, 2002-13. In: ISSI-International Conference on Scientometrics & Informetrics; 2017. p. 602–13.

[28] Lynch T, Clark D, Centeno C, Rocafort J, Flores LA, Greenwood A, et al. Barriers to the development of palliative care in the countries of central and eastern Europe and the commonwealth of independent states. J Pain Symptom Manage 2009; 37(3):305–15. Available from: https://doi.org/10.1016/j.jpainsymman.2008.03.011 [Accessed 8 August 2017].

[29] Daveson BA, Harding R, Derycke M, Berghe PV, Edwards S, Higginson IJ. The PRISMA symposium 4: how should Europe progress end-of-life and palliative clinical care research? recommendations from the proceedings. J Pain Symptom Manage 2011;42(4):511–6. Available from: https://doi.org/10.1016/j.jpainsymman.2011.06.006 [Accessed 8 August 2017].

[30] Cancer Research UK. Annual report and accounts 2010/11. Available from: http://www.cancerresearchuk.org/prod_consump/groups/cr_common/@abt/@gen/documents/generalcontent/cr_075236.pdf. [Accessed 27 July 2017].