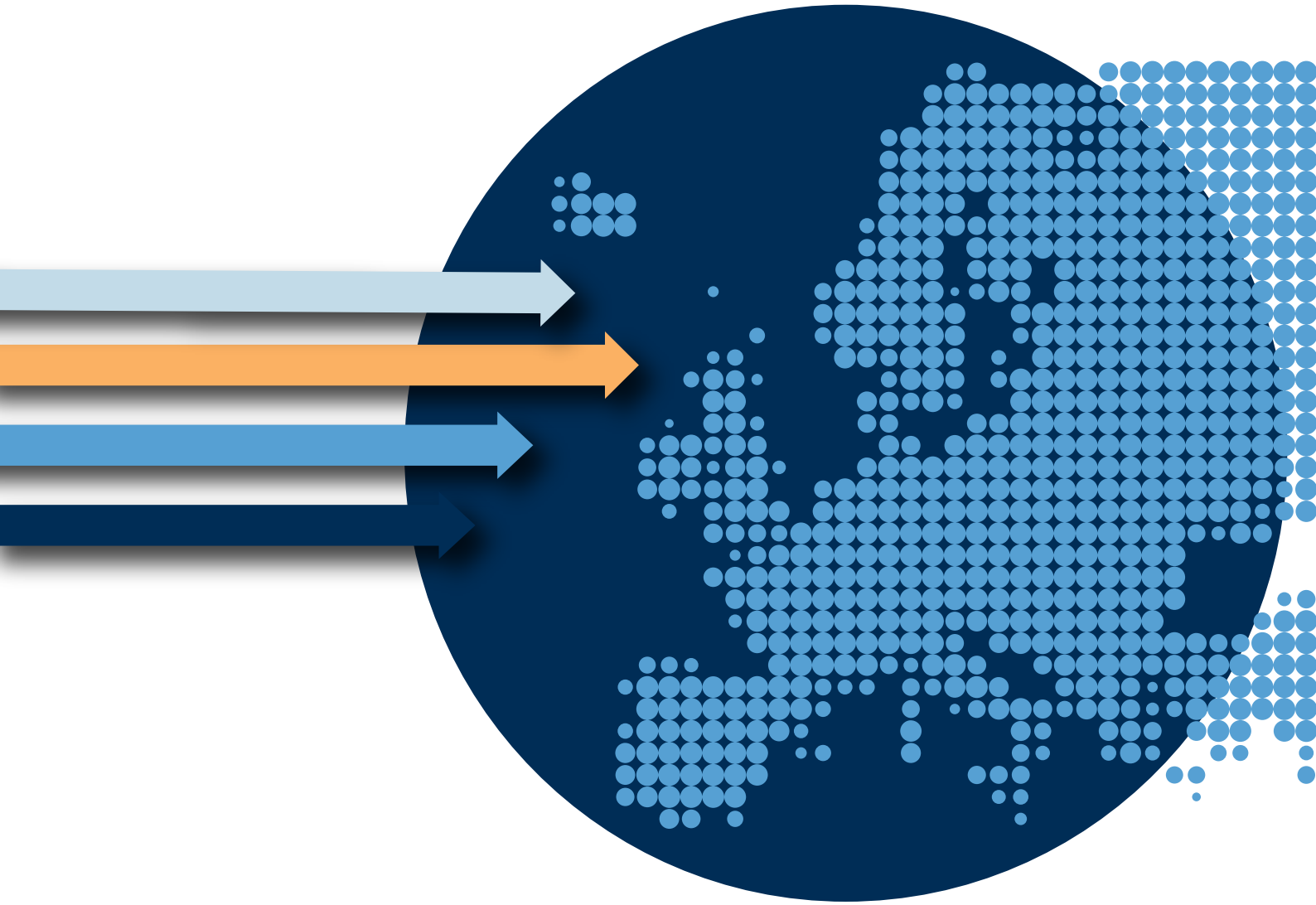
COMPARATOR REPORT ON PATIENT ACCESS TO CANCER MEDICINES IN EUROPE REVISITED – A UK PERSPECTIVE



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COMPARATOR REPORT ON PATIENT ACCESS TO CANCER MEDICINES IN EUROPE REVISITED – A UK PERSPECTIVE

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Content

Foreword

Oncology represents one of the disease areas that receives considerable attention in both the public and scientific debate around health care and its associated costs. There are several likely reasons for this: About 1 in 3 persons will receive a cancer diagnosis during their life and for some – but thanks to many treatment advances far from all – the prognosis is grim. Due to demographic changes but also due to advances in other areas such as cardiovascular disease the incidence of cancer is increasing. This puts the area top of mind. The rate of development of new therapies in the area, and during the last ten years more than 100 new drugs have been approved by the European Medicines Agency. The price tag for this drugs is higher than previous which has spurred the debate about drug costs.

The present report focuses on the developments in cancer epidemiology, economic burden and uptake of new drugs during the last 10 years with a focus on the UK and how the UK performs compared to other European countries. This report is an extension of a report previously published by the Swedish Institute for Health Economics (IHE), IHE Report 2016:4. This previous report presented a European comparison of costs, developments in treatment options and patient access to new drugs across the continent and revealed large differences in spending on cancer and uptake of new medicines. Some of these difference can be explained by economic factors, but large variations between countries of similar economic status was also observed. When conducting an analysis covering the 28 EU countries plus Norway and Switzerland which was the case in the previous report, it is of course necessary to paint a rather broad picture. This may mask important observations at the country level. This report is an attempt to alleviate this problem somewhat by providing an in-depth analysis of a single country – in this case the UK, a country presently undergoing changes in how cancer care is financed and followed.

The work on this report was funded by the Association of the British Pharmaceutical Industry (ABPI).

Lund, February 2017

Ulf Persson
Managing Director at IHE

Executive Summary

- Since the millennium, the burden of cancer disease has overtaken CVD in the UK.
- Like the rest of Europe, incidence continues to increase in the UK. Survival and mortality in the UK lag behind economically comparative countries.
- During the last two decades mortality increased in absolute numbers but decreased across Europe once demographic factors were accounted for. This decrease was largely driven by advances in medical treatment, screening and diagnostics.
    - UK mortality is lower than the EU average rate among men but 4th highest among women
    - UK relative survival lower than both EU and the G5 mean
- Cancer care is a highly complex eco-system and there are without a doubt many reasons behind the UK's relatively low performance. One factor may be the overall investment level. The UK invests less than the EU average in health care (9.1% compared to 10.1%) with many economically comparative countries investing significantly more: Netherlands 12.9% France at 11.7% Germany at 11.3%.
- The UK also spends less of its health care resources on cancer than leading Western European countries. Though the proportion of direct costs spent on cancer medicines in the UK has increased from 8% in 2005 to 25% in 2014, the total share spent on cancer care has remained stable. The introduction of over 100 new medicines between 1996 and 2015 has to a large extent been funded by a shift from inpatient to outpatient care.
- Uptake of cancer medicines varies between countries but is generally slower for the UK compared to other G5 countries. Of the eight individual drugs included here, the UK had the lowest or 2nd lowest use for six of them.
- The newest drugs (launched within the last three years) make up only 8% of total average sales across Europe, varying between 4% and 11% per year in different countries, with higher percentages in richer countries. In the UK that figure has historically been lower than 5%. In 2013 it started to increase, likely related to the introduction of the Cancer Drugs Fund. Though the investment in new medicines has increased, little effort has been made to monitor how CDF expenditure has translated into patient outcomes.
- Collection of real world data as a core part of new routes to market, such as EAMS, the CDF and the accelerated access review (AAR), will test the readiness of the infrastructure with respect to governance, transparency, safety reporting and analytics.
- The revamped Cancer Drugs Fund should help carve a path for data driven managed access agreements. It could also prove useful as a test bed for new pricing arrangements for combination therapies and indication based pricing. The use of its funds need to be properly monitored to ensure that they are used effectively to

generate the knowledge needed for future cost-effectiveness assessment, to improve access and patient outcomes.

- The CDF has recently undergone substantial change. Whether it will be enough to close the access gap compared to other countries remain to be seen. If the CDF fail to attract the desired type and number of cancer medicines and NICE rate of positive recommendation doesn't improve the UK will be back at the access level which led to the launch of the CDF in the first place.
- Act now to ensure the future of cancer care tomorrow. As the number of new cancer treatments continue to increase and become ever more targeted, the overall access environment need to be closely monitored and regularly revisited to ensure it is fit for the future.

List of Abbreviations

ALL	Acute Lymphatic Leukaemia
AML	Acute Myeloid Leukaemia
ASCO	American Society of Clinical Oncology
ATC	Anatomical Therapeutic Chemical classification
CML	Chronic Myeloid Leukaemia
CRC	Colorectal Cancer
CT	Computerized Tomographic Scanning
DDD	Defined Daily Dose, used to standardize the comparison of drug usage between different drugs or between different health care environments
EGFR	Epidermal Growth Factor Receptor
EMA	European Medicines Agency
ESMO	European Society for Medical Oncology
GIST	Gastrointestinal Stromal Tumours
HER2	Human Epidermal Growth-factor Receptor 2
IGF1	Insulin-like Growth Factor 1
MRI	Magnetic Resonance Imaging
NCE	New Chemical Entity
NCCN	National Comprehensive Cancer Network
NSCLC	Non-Small Cell Lung Cancer
PET	Positron Emission Tomography
PDGF	Platelet-Derived Growth Factor
RCC	Renal Cell Carcinoma
VEGF	Vascular Endothelial Growth Factor

Country abbreviations

AT	Austria
BE	Belgium
BG	Bulgaria
HR	Croatia
CH	Switzerland
CY	Cyprus
CZ	Czech Republic
DK	Denmark
EE	Estonia
FI	Finland
FR	France
DE	Germany
EL	Greece
HU	Hungary
IE	Ireland
IS	Iceland
IT	Italy
LV	Latvia
LT	Lithuania
LU	Luxembourg
MT	Malta
NL	Netherlands
NO	Norway
PL	Poland
PT	Portugal
RO	Romania
SK	Slovakia
SI	Slovenia
ES	Spain
SE	Sweden
UK	United Kingdom
EU-27	27 member states of the European Union before the accession of Croatia
EU-28	28 member states of the European Union
EU+2	28 member states of the European Union plus Norway and Switzerland
G5	5 largest EU economies (France, Germany, Italy, Spain, UK)

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1 Introduction

In June 2016, we published a report on cancer in Europe investigating the developments in the cancer field over the last decade from an economic, clinical and also a patient access perspective. [1] This report built on previous work, namely two reports following similar methodology allowing us to compare cancer care over the last twenty years. [2, 3]

A number of observations can be made: Cancer incidence continues to increase across Europe, driven by several factors but with demographic factors potentially being the most important. Advances in medical treatment, screening and diagnostics have helped bring mortality rates down in relative terms. Cancer care is changing fast, with treatment characterised by a multimodal therapy approach including surgery, radiotherapy and an increasing number of anti-tumour drugs.

Our report revealed stunning differences in terms of spending on cancer across Europe and large variations in the usage of newer drugs. Low national income and health care spending per capita are major obstacles for access to new cancer drugs. New cancer drugs are traded in an international market, and while the absolute price per unit is similar, the relative price is higher for countries with lower income. Parallel trade and international reference pricing limit the opportunities for price differentiation. But, importantly, there are also large variations between countries with similar economics status, as well as very large differences between countries in the usage of drugs that have now lost patent protection which cannot be explained by the ability to pay for the drugs. Economics are important, but are clearly not the only factor in play.

When conducting a comparison at a European level, it is necessary to use a broad brush. This may mask important observations when considering individual countries. This report is an attempt to alleviate this by providing a more concise version of the full comparator report focusing on the UK. The work on this summary was funded through a grant from the Association of the British Pharmaceutical Industry (ABPI).

2 Disease burden

The disease burden of cancer can be described in several different ways: in terms of the number of new cases (incidence), in terms of the number of deaths caused (mortality), in terms of survival and in terms of the number of healthy years of life lost. In this section we cover these aspects in turn.

2.1 Incidence

The incidence of cancer is increasing across Europe, with 31% more cases between 1995 and 2012. The growth in the UK is more modest, with a 12% increase over the same period. There are several factors contributing to this increase including population aging and reduced incidence and mortality in other diseases, primarily decreased cardiovascular mortality. Factors such as life-style changes and increased use of screening programs may also have contributed. The incidence of cancer in the UK is very close to the European average (**Figure 1**), however this masks differences between women and men where UK has the 7th lowest incidence among men but the 7th highest incidence among women (**Figure 2** and **Figure 3**). The incidence among women is driven by a high incidence of breast cancer (**Figure 4**). This could partly be explained by a comparatively high degree of screening, but incidence rates in Northern and Western Europe have also been higher historically. Women in the UK also have a higher incidence of lung cancer, which is the second most common cancer form. In men, incidence of the more common cancer forms is generally close to or below the European mean.

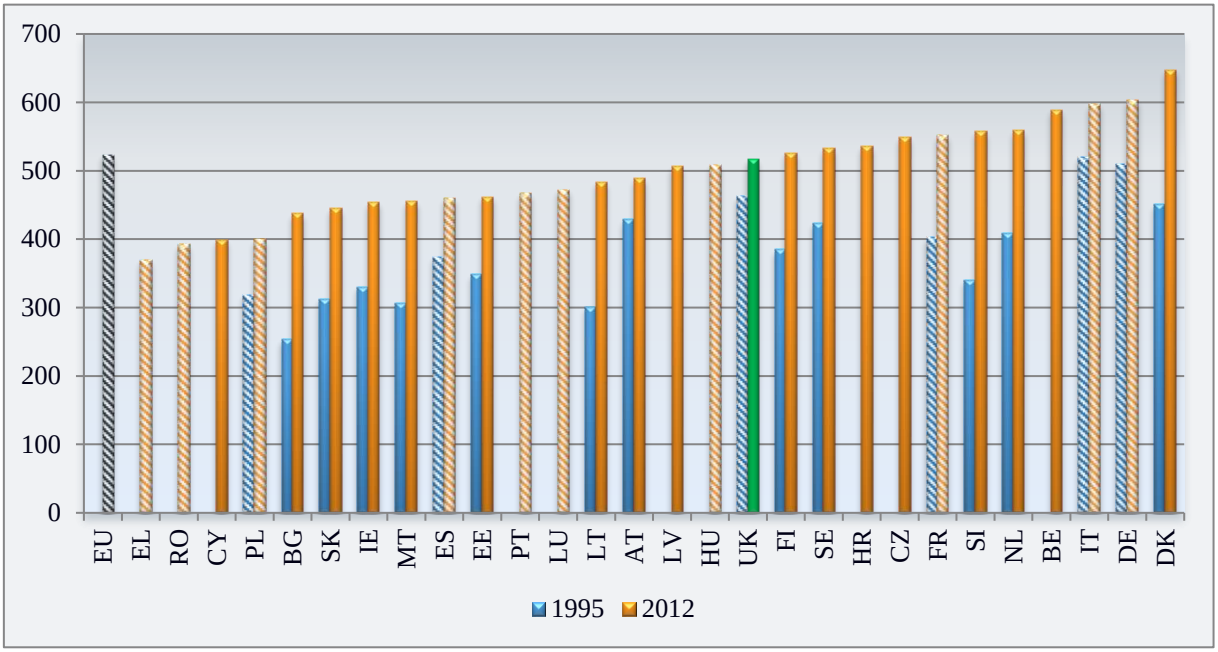


Figure 1: Estimated cancer incidence, cases per 100,000 inhabitants (crude rates for both sexes), 1995–2012

Source: European Cancer Observatory [4, 5]

Notes: Hatched bars indicate that national estimates are based on regional data or based on neighboring countries.
Estimates include all cancers combined, excluding non-melanoma skin cancer (ICD-10 C00-C97/C44).
BE, HR, CY, CZ, EL, HU, LV, LU, PT, RO, CH in 1995 are missing due to lack of data on incidence cases.
Incidence cases in 1995 were based on regional data in Germany (Hamburg, Saarland), France (Doubs, Haut-Rhin, Hérault, Isère, Manche, Somme, Tarn), Italy (Umbria, Veneto), Poland (Lower Silesia), Spain (Balearic Islands, Basque country, La Rioja, Navarre, Region of Murcia), and the UK (East of England, Northern Ireland, Scotland, Wales) and scaled-up to the national level based on population data from Eurostat.
The incidence estimates for France refer to metropolitan France.

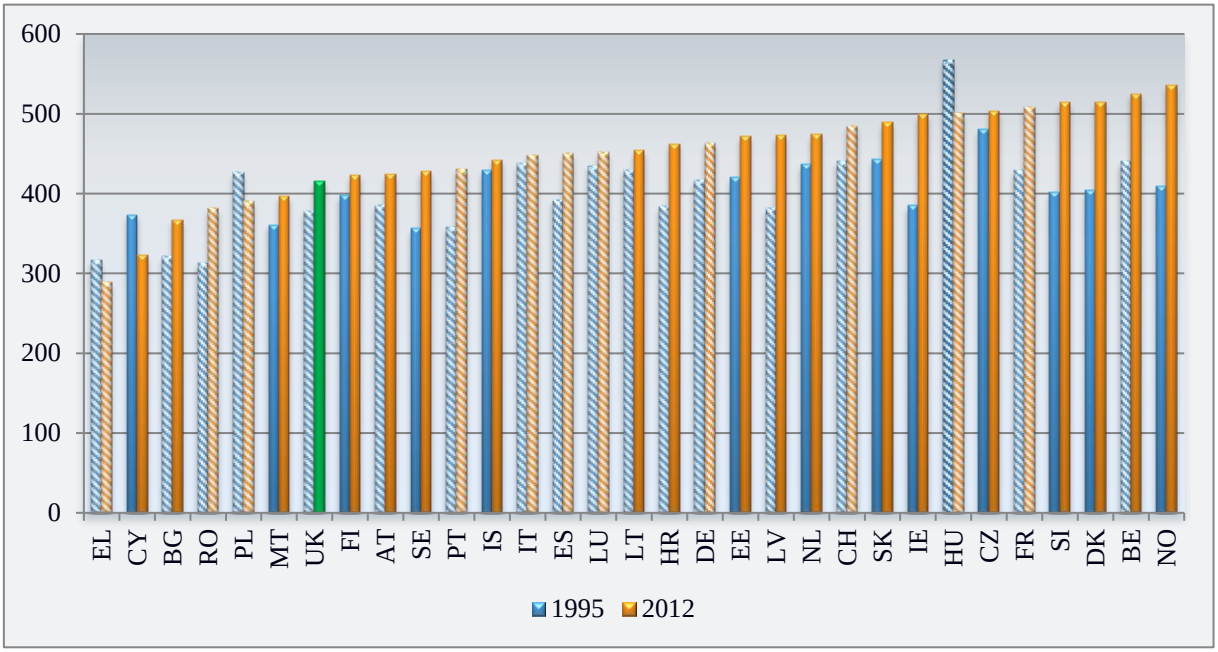


Figure 2: Estimated cancer incidence, cases per 100,000 inhabitants (age standardized rates, men), 1995–2012

Source: European Cancer Observatory [4, 5]
Notes: See Figure 1.

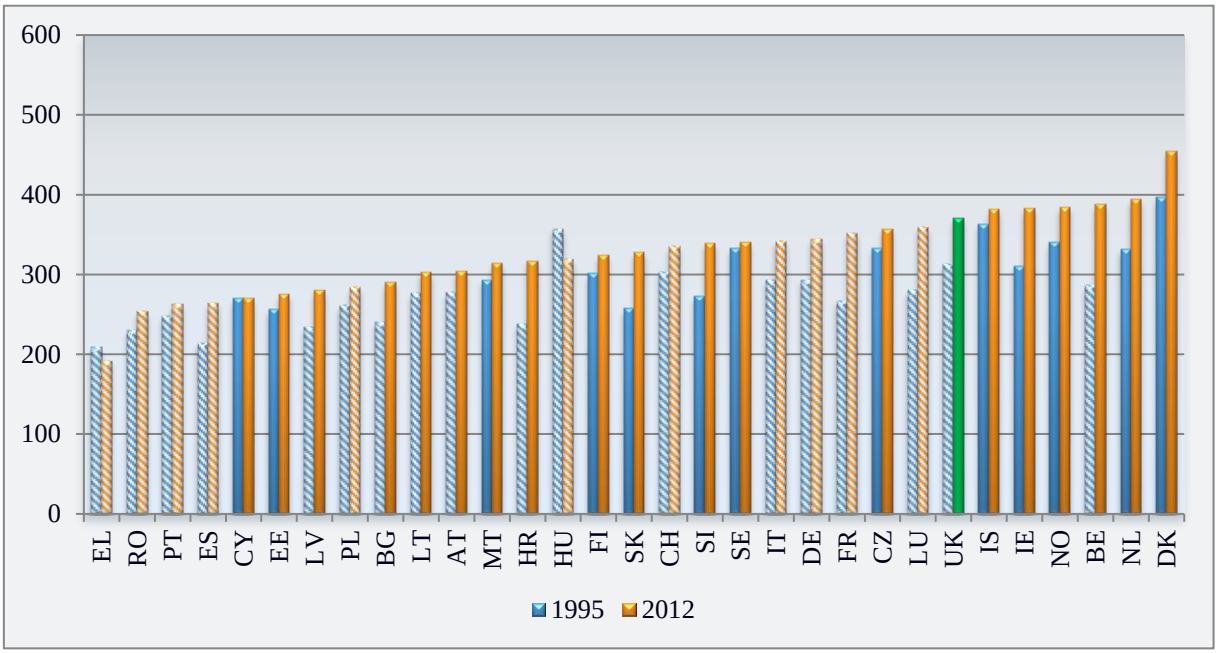


Figure 3: Estimated cancer incidence, cases per 100,000 inhabitants (age standardized rates, women), 1995–2012

Source: European Cancer Observatory [4, 5]

Notes: See Figure 1.

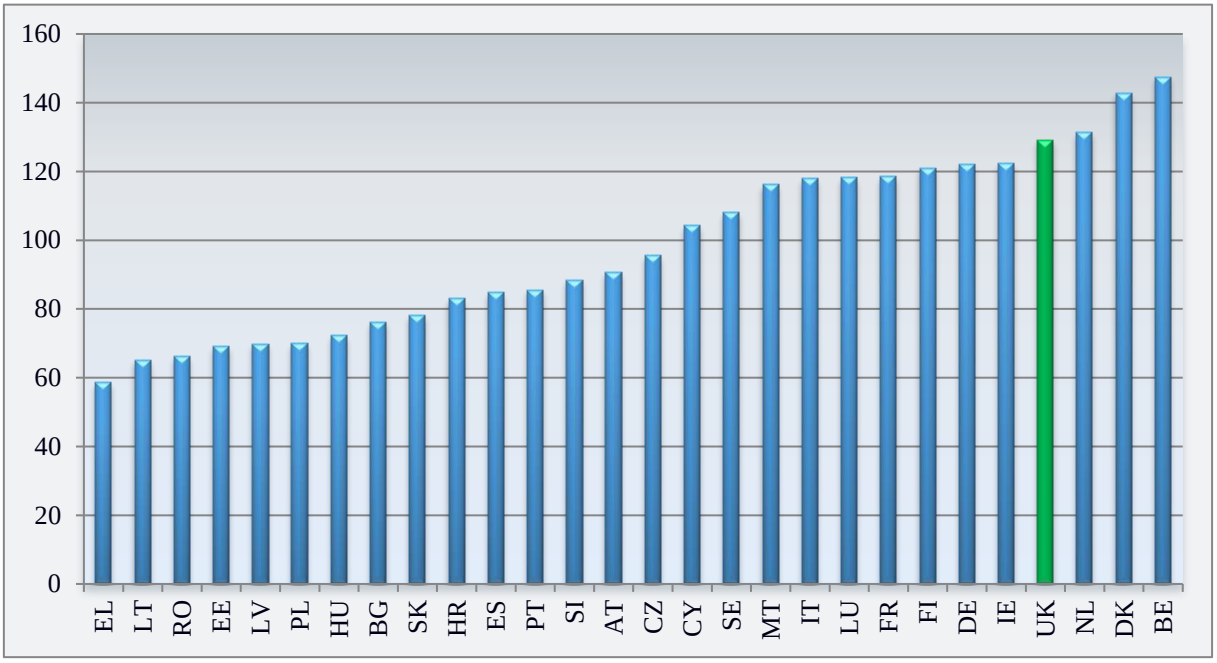


Figure 4: Estimated breast cancer incidence, cases per 100,000 inhabitants (age standardized rates, women), 2012

Source: European Cancer Observatory [5, 6]

Notes: See Figure 1.

There is country-specific data from the UK spanning a longer period to indicate that cancer incidence has increased over time, even when adjusting for the changing age patterns (**Figure 5**). The incidence of cancer is higher among males, although the gap between men and women has become somewhat smaller over time.

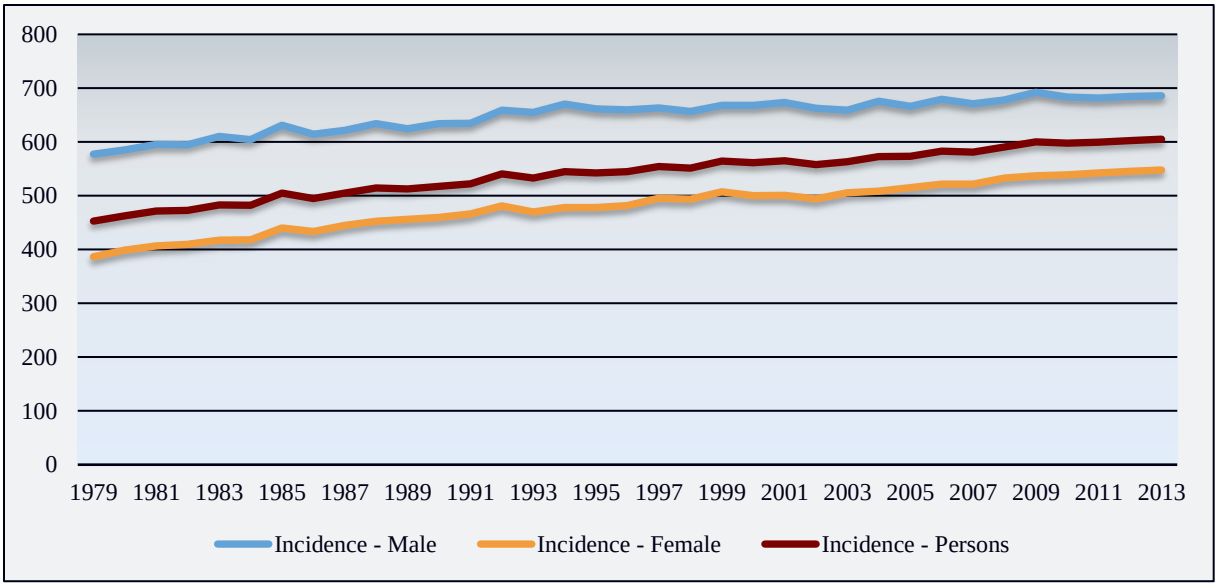


Figure 5: Age standardized incidence cases of cancer per 100,000 inhabitants in the UK, 1979–2013

Source: Cancer Research UK [7]

2.2 Mortality

The number of cancer deaths in Europe increased by 11% between 1995 and 2012. This differs between countries, and the number of cancer deaths per 100,000 inhabitants has decreased by 6% in the UK during this time (**Figure 6**). Age-standardized mortality rates (**Figure 7** and **Figure 8**) decreased markedly in all countries but Romania and Bulgaria, whereas crude mortality rates increased in a majority of countries. Since the key difference between age-standardised rates and crude rates is that the effect of population aging is not considered in the crude rate, it is apparent that population aging is of importance in the UK. The UK has the fourth highest age-standardized mortality among women, in line with the high incidence described above, while the age-standardised mortality for men is the 10th lowest.

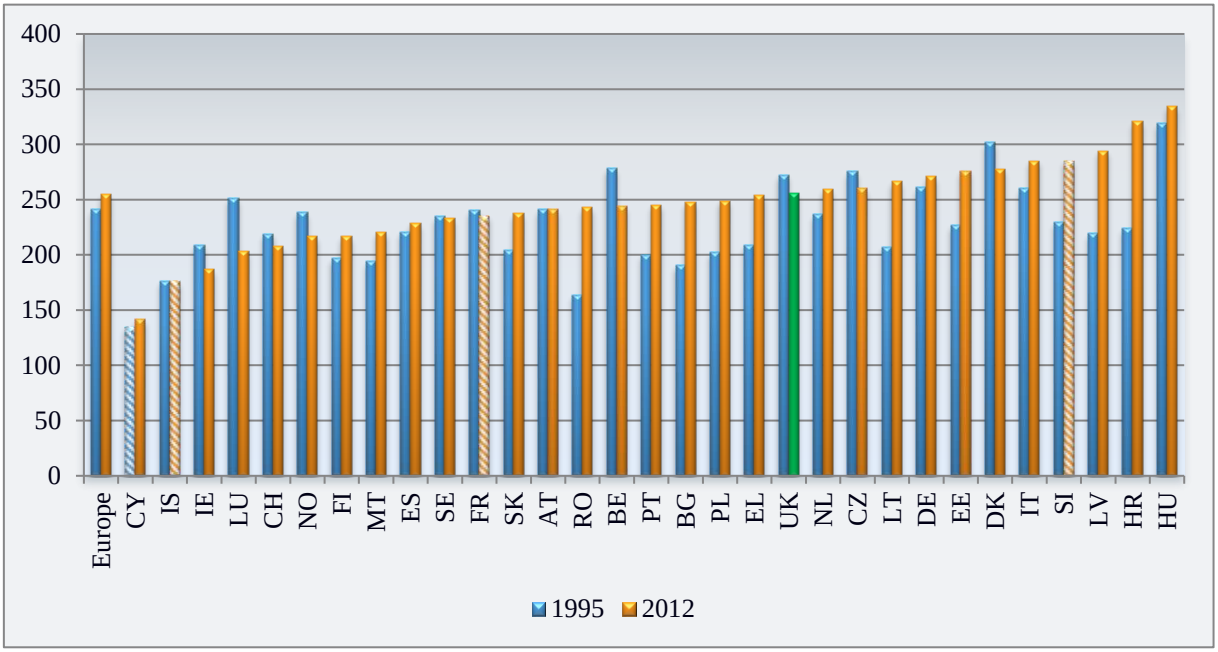


Figure 6: Mortality per 100,000 inhabitants (crude rates)

Source: European Cancer Observatory [4, 5]
Notes: Cancer is defined as ICD-10 C00-C97,B21.
Hatched bars indicate that data for 1995 for Cyprus refer to 2004; data for 2012 for France refer to 2011, for Slovenia to 2010, and for Iceland to 2009.

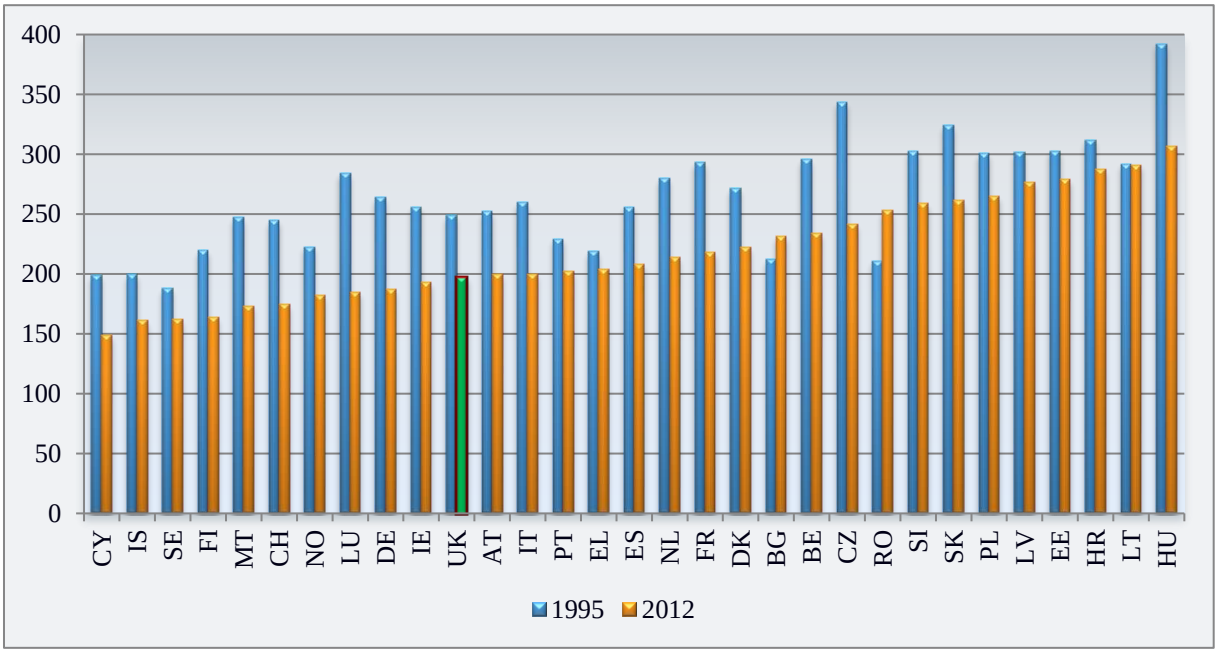


Figure 7: Age standardized mortality per 100,000 inhabitants (men)

Source: European Cancer Observatory [4, 5]

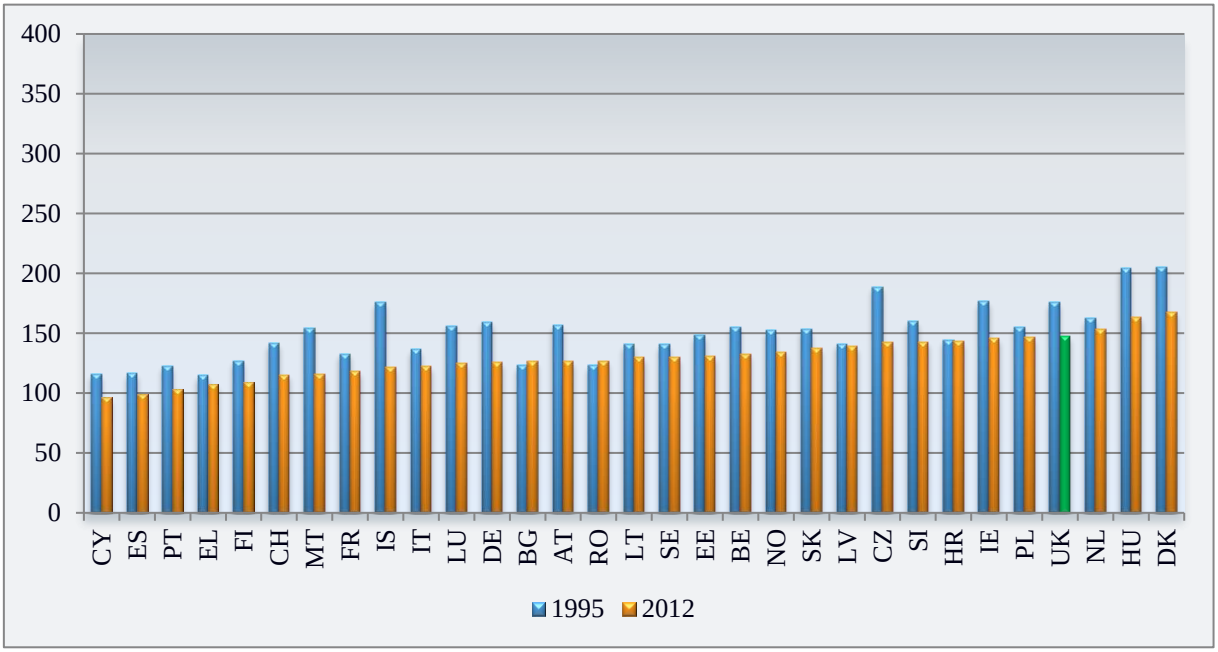


Figure 8: Age standardized mortality per 100,000 inhabitants (women)

Source: European Cancer Observatory [4, 5]

Looking over a longer time horizon (**Figure 9**) it can be noted that age-standardized mortality was fairly stable or increasing somewhat until the early 1990s, when figures started to improve. This downward trend appears to have been stable the last 20 years, but the absolute improvement has been greater among men. An increased incidence of lung cancer, an area with modest improvements in survival, in women due to smoking habits is one explanatory factor.

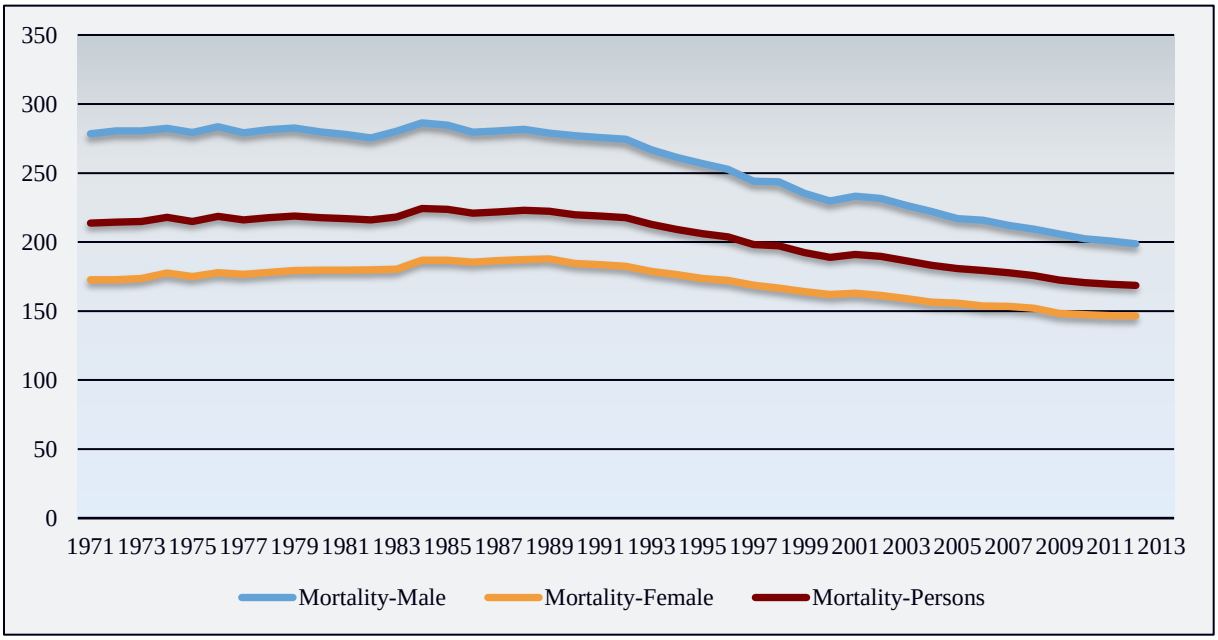


Figure 9: Age standardized mortality per 100,000 inhabitants in the UK, 1971–2012

Source: Cancer Research UK [7]

2.3 Survival

Survival is the central concept that connects the two epidemiological measures of incidence and mortality. It measures the share of people that have been diagnosed with cancer in a certain year and that are still alive after a specified period of time. Survival rates reflect both how early cancers are being detected and the effectiveness of cancer treatment.

Comparable data on cancer survival for European countries are collected and provided by EUROCARE, the EUROpean CAncer REgistry-based study on survival and care of cancer patients. The projects EUROCARE-3, EUROCARE-4, and EUROCARE-5 cover cancer patients diagnosed between 1990 and 2007. The data availability has been improving over the years. The latest project, EUROCARE-5, provided survival rates for Iceland, Norway, Switzerland, and 23 of the EU-28 member states, only Cyprus, Greece, Hungary, Luxembourg, and Romania are missing. The coverage of the population has been improving over time in countries with cancer registries that originally only covered certain regions. Overall, survival is improving across Europe (**Figure 10**). Wealthier countries tend to have better survival, but UK ranks the 8th lowest.

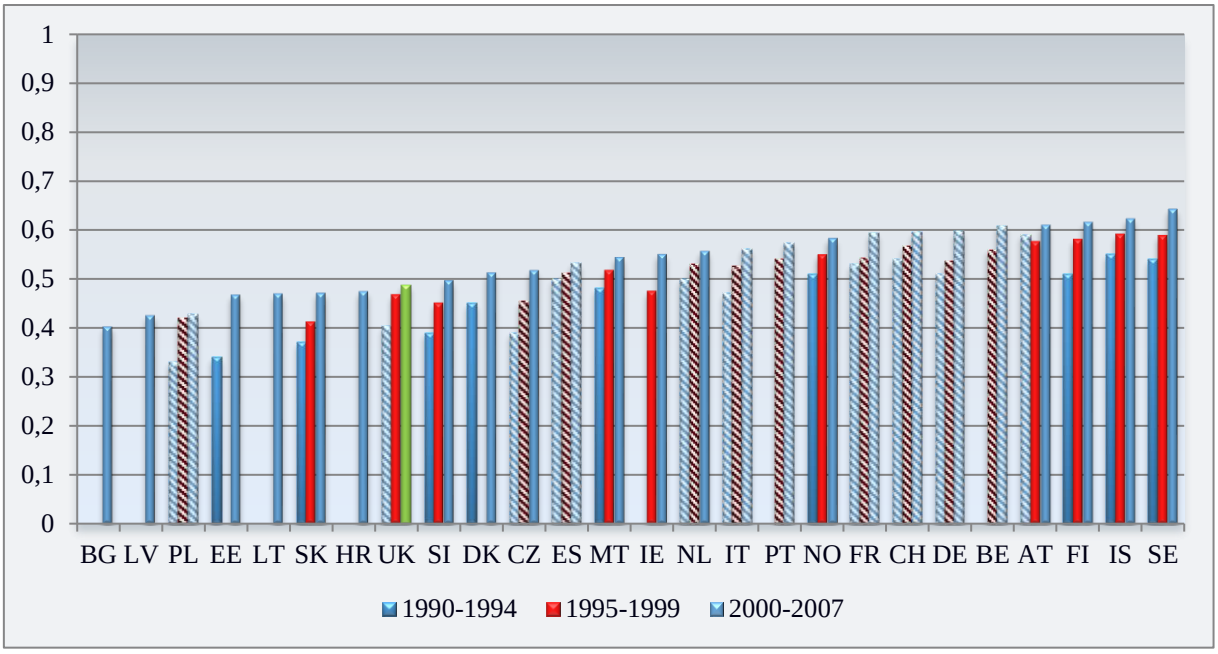


Figure 10: Age-adjusted 5-year relative survival rates in patients ≥ 15 years

Source: EUROCARE 3 – 5 [8, 9]

Notes: Hatched bars indicate that national estimates are based on regional data.
The survival rates for the UK are calculated as the arithmetic average of the rates from England, Northern Ireland, Scotland, and Wales (in 1990-1994 only from England, Scotland, and Wales).
CY, EL, HU, LU, and RO are missing due to lack of data.

Even though comprehensive country-specific data for different cancer types have been published [8, 9], the accompanying online databases[1] provide greater detail and are used for the analysis below. Survival rates for common cancers forms are presented below. The outcome measure is the 5-year age-adjusted relative survival rate in adult patients (age ≥15 years).

[1] Available from: http://www.eurocare.it/ (accessed January 19, 2016)

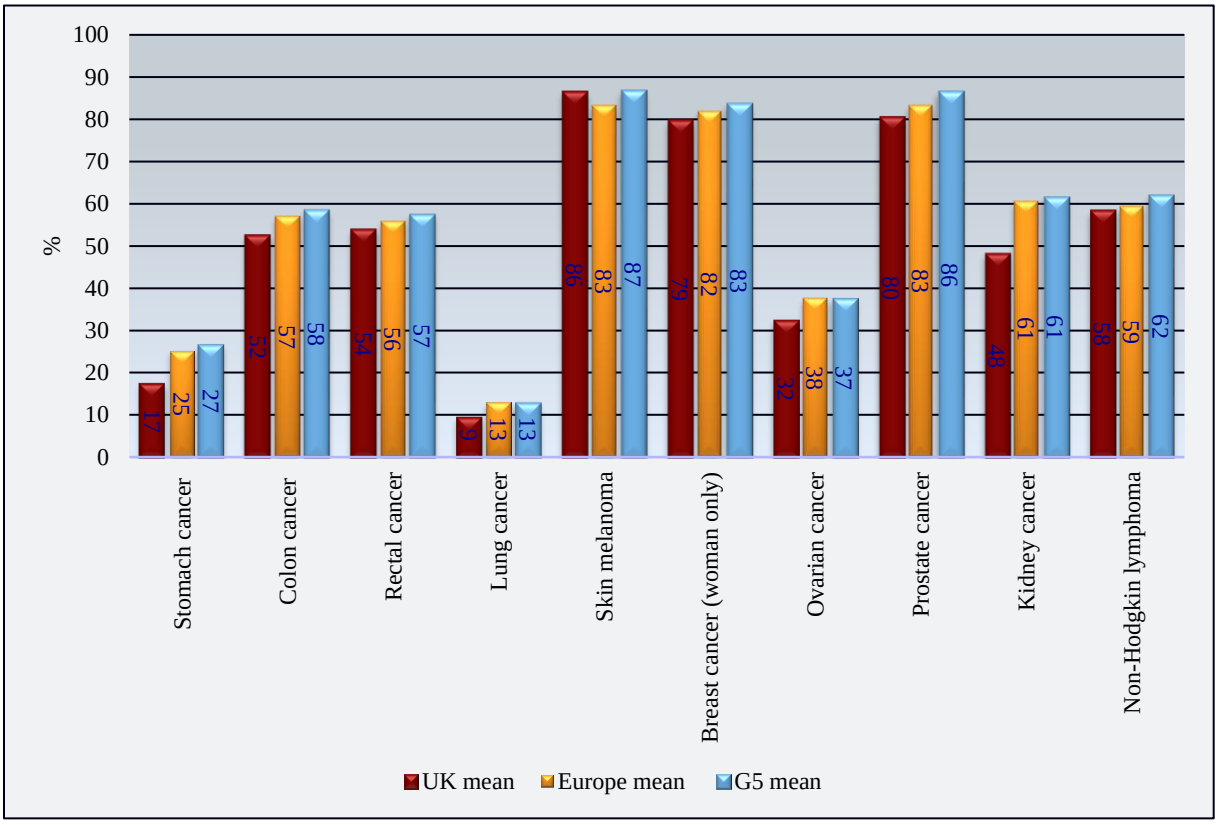


Figure 11: 5-year survival rates for different forms of adult cancers (2000-2007)

Source: EUROCARE-5 [9]

Notes: G5 is the five large economies in Europe.

As can be seen in **Figure 11** cancer survival rates are lower in the UK than in the other large economies for all cancer forms except for skin melanomas. In many cases, survival rates are also lower than the EU average. There is no large variation between the UK nations (**Figure 12**).

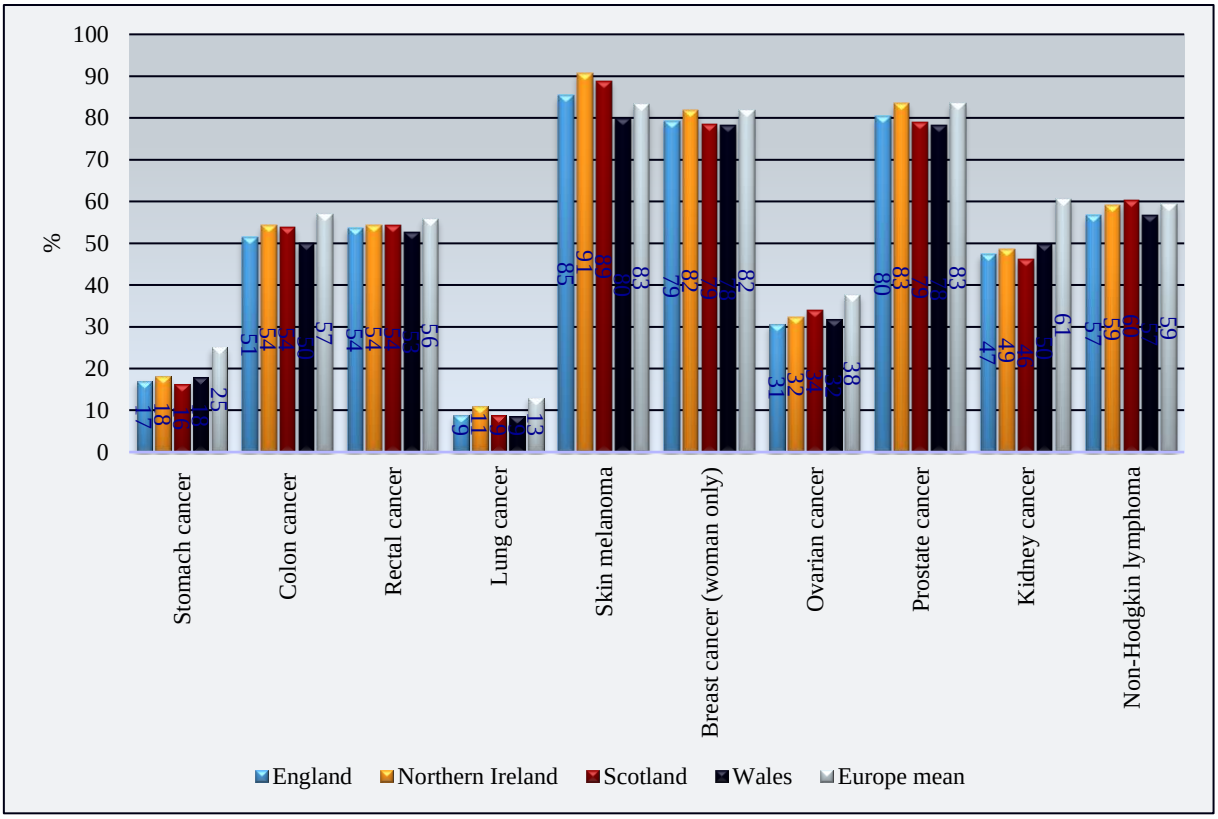


Figure 12: 5-year survival rates across the UK nations

Source: EUROCARE-5 [9]

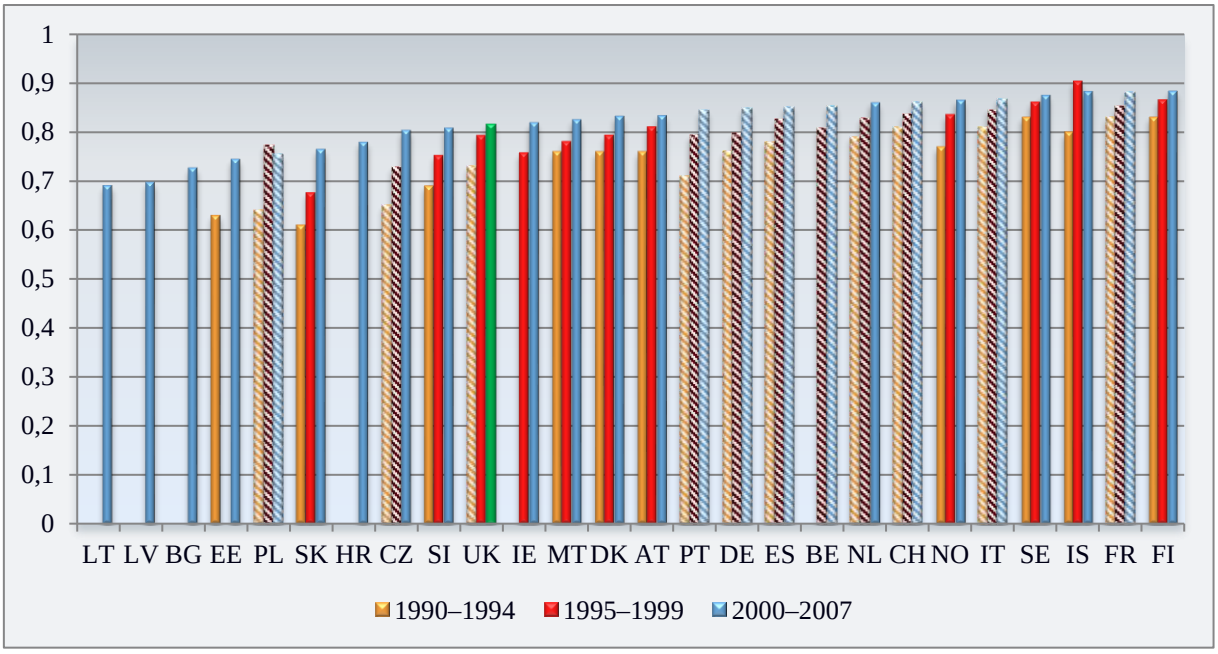


Figure 13: 5-year age-adjusted relative survival rates for breast cancer in patients aged ≥15 years, 1990–2007

Source: EUROCARE-5 [9]

Breast cancer survival rates have improved in all countries (**Figure 13**), and the UK follow the overall trend. The same is true for prostate cancer (**Figure 14**), although there are more marked differences between countries with the UK in the bottom third. The same is also true for colorectal cancer, although the gain has been smaller than for prostate cancer (**Figure 16**). It can be noted that opportunistic PSA screening (and thus differences in detected cases) makes data on prostate cancer more difficult to interpret.

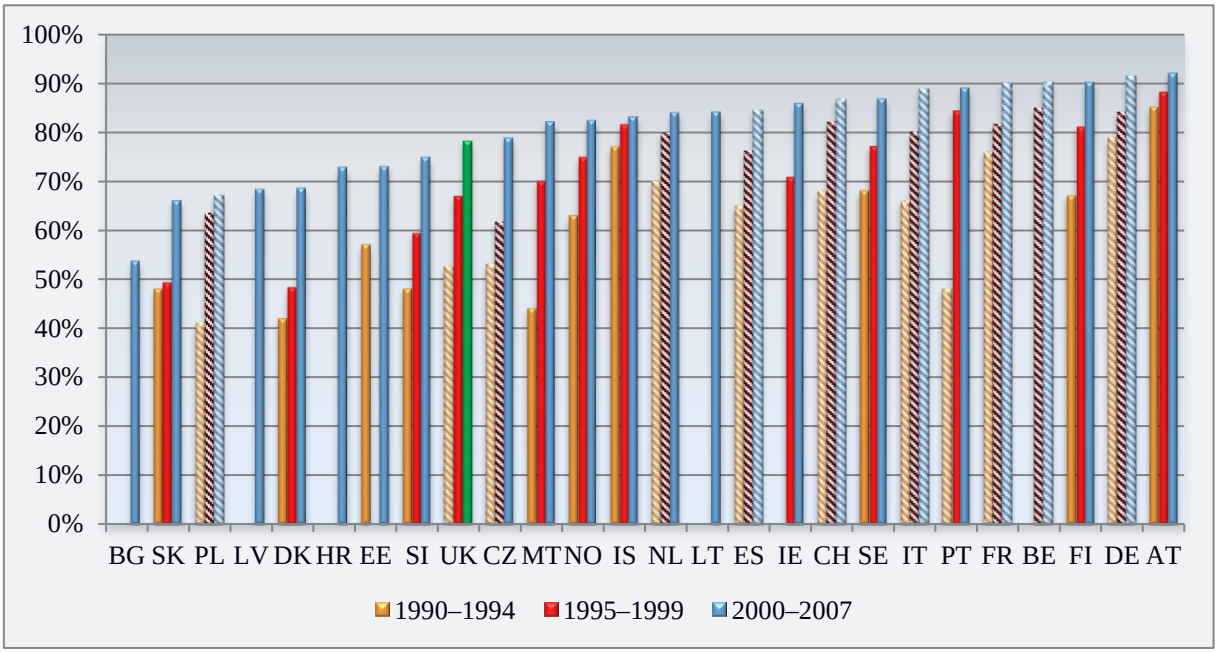


Figure 14: 5-year age-adjusted relative survival rates for prostate cancer in patients aged ≥15 years, 1990–2007

Source: EUROCARE-5 [9]

EUROCARE paints a more varied picture for lung cancer, with both improvements and declines over the period depending on the country (**Figure 15**). UK had the second worst performance, with a slight decline in survival rates between 1995-1999 and 2000-2007. More recent data from England and Wales indicates an estimated 5-year survival rate of 8.6% in 2010-11. [10] It has previously been noted that the proportion of patients with stage 1 – 2 disease eligible for surgery is similar in the UK as in Scandinavia. [11]

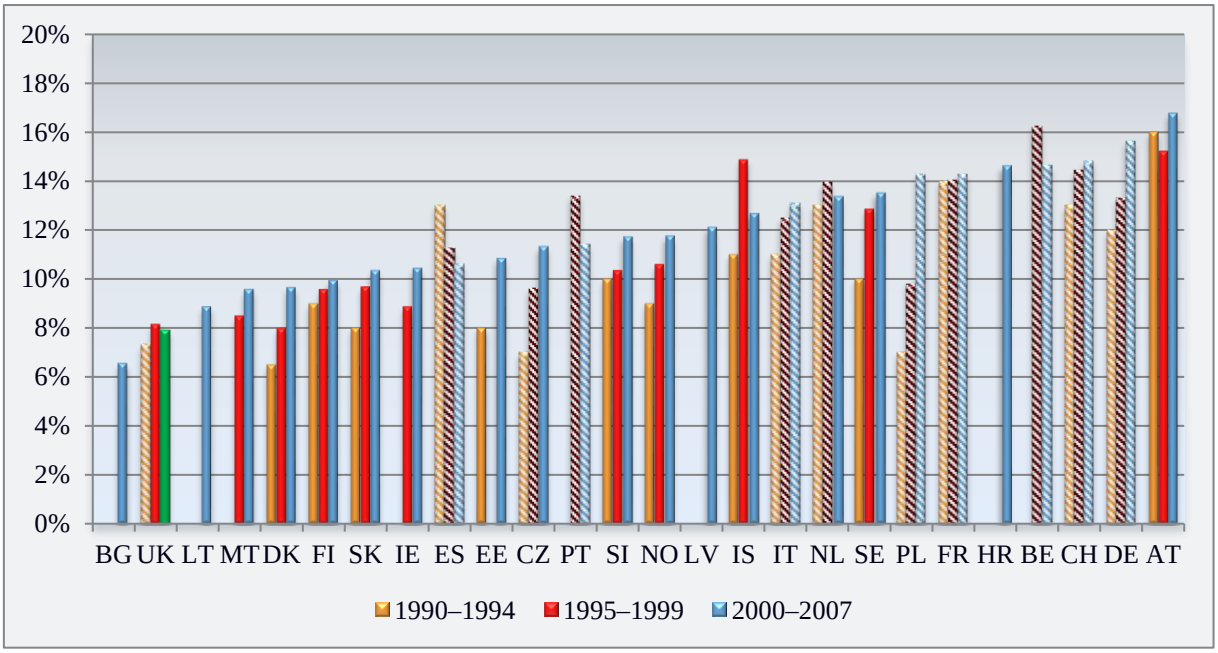


Figure 15: 5-year age-adjusted relative survival rates for lung cancer in patients aged ≥15 years, 1990–2007

Source: EUROCARE-5 [9]

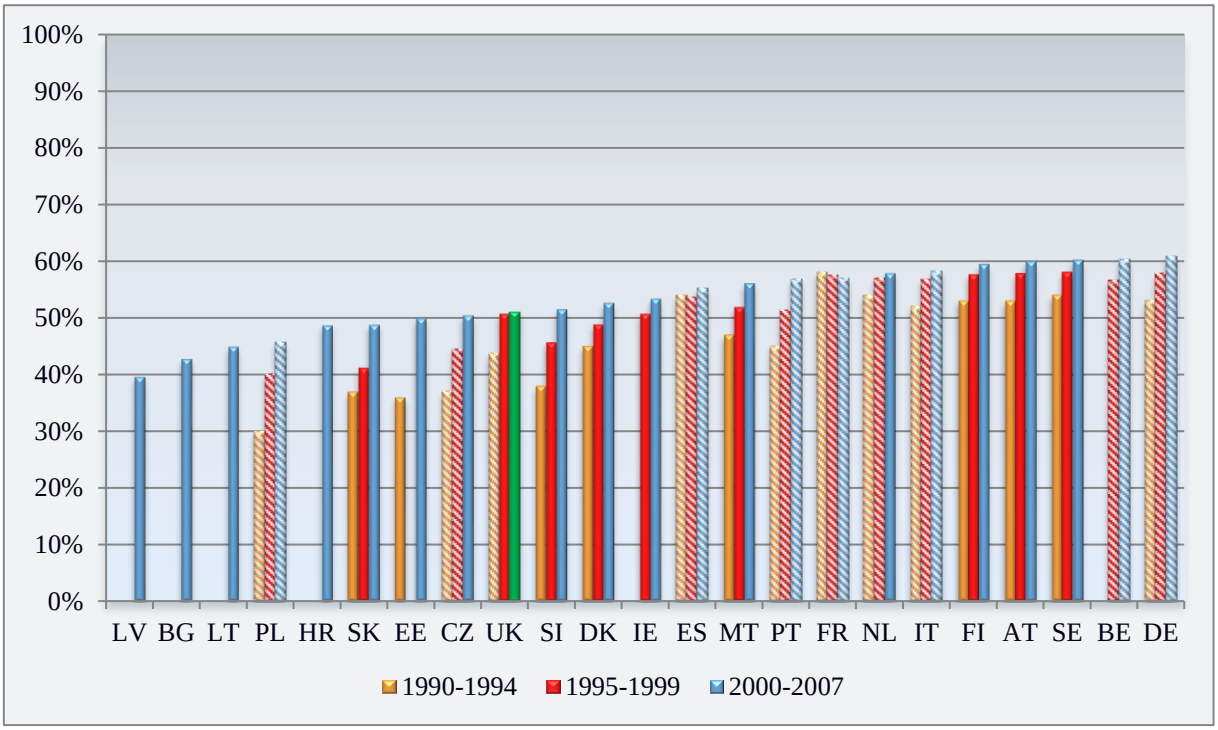


Figure 16: 5-year age-adjusted relative survival rates for colorectal cancer in patients aged ≥15 years, 1990–2007

Source: EUROCARE-5 [9]

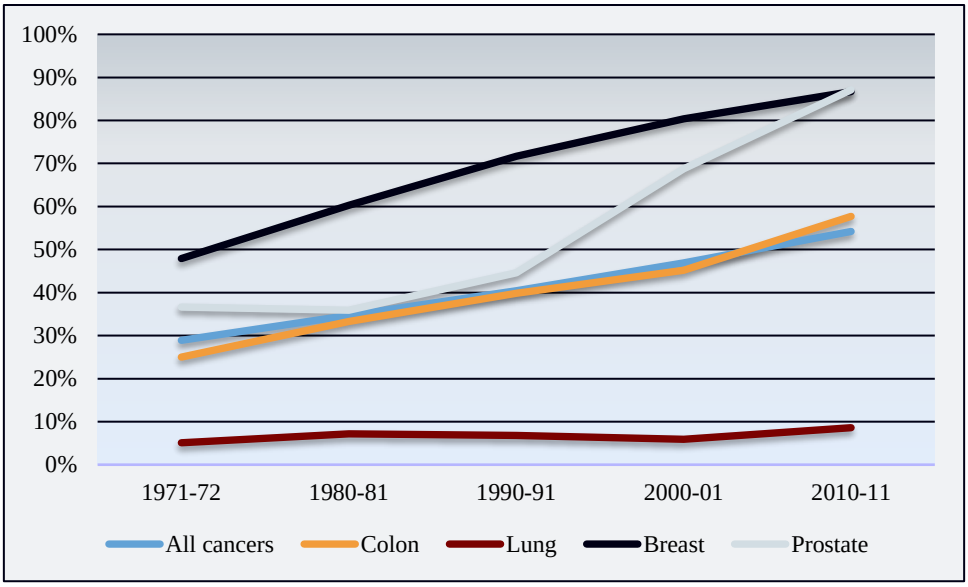


Figure 17: 5-year survival in England and Wales 1971 - 2011

Source: [10]

In a recently published study, Quaresma and colleagues studied the long-term development of cancer survival based on data from England and Wales. [10] As can be seen in **Figure 17**, this highlights the lack of progress in lung cancer compared to many other cancer forms. The developments in prostate cancer are in part artificial due to cases now being detected earlier through opportunistic screening.

2.4 Disability adjusted life years (DALY)

When studying the burden of a disease it is important to not only consider deaths caused by it, but to also consider morbidity aspects. One such measure is the disability adjusted life year developed for the WHO. One DALY represents one lost year of "healthy" life and consists of two components: Years of Life Lost (YLL) due to premature death caused by the disease or health condition, and Years Lost due to Disability (YLD) for people living with the disease or health condition. Comparable country-level data are available for 2000 and 2012. [12]

As can be seen in **Figure 18** cancer has now overtaken cardiovascular disease as the leading contributor to disease burden in the UK driven by a reduction in cardiovascular disease mortality. A similar trend can be seen across Europe, but the change in the UK has been more pronounced.

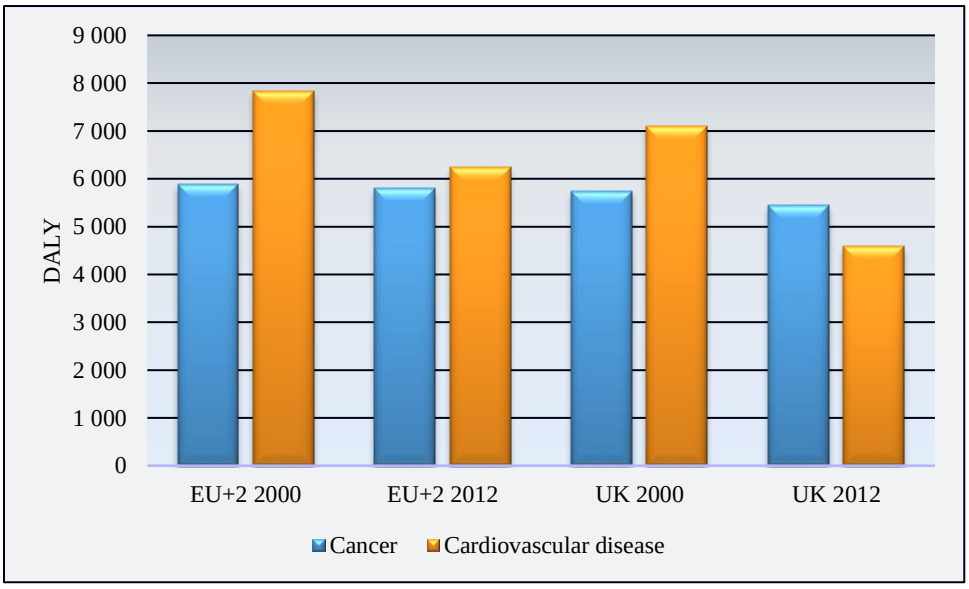


Figure 18: Disease burden (DALY per 100 000 inhabitants) from cancer and cardiovascular disease 2000 – 2012

EU+2 is the 28 members of the European Union plus Norway and Switzerland
Source. WHO. [12]

Table 1 shows the top ten cancers contributing to disease burden in 2012 in the UK and EU. The contributions of the different cancer forms is fairly similar, with the smoking-related cancers of the trachea, bronchus and lung being the by far largest contributor, followed by colon and breast cancer. The only substantial difference observed is for oesophageal cancer which is a much larger contributor to disease burden in the UK than it is in the EU overall. Over the period 2000 to 2012 cancers of the trachea, bronchus and lung remained the largest contributors to disease burden and increased somewhat during the period 2000 and 2012, while colon, rectum and breast cancer decreased. These three groups contribute to more than 40% of the disease burden.

TABLE 1: DISEASE BURDEN OF THE TOP 10 CANCERS (MALIGNANT NEOPLASMS) IN THE UK AND EU +2 IN 2012

	UK				EU+2		
		Total DALYs ('000)	DALY per 1000	Share		Total DALYs ('000)	DALY per 1000	Share
1	Trachea. bronchus. lung cancers	761.3	12.1	22%	Trachea. bronchus. lung cancers	6,611	12.7	22%
2	Colon and rectum cancers	363.6	5.8	11%	Colon and rectum cancers	3,492	6.7	12%
3	Breast cancer	313.6	5.0	9%	Breast cancer	2,598	5.0	9%
4	Prostate cancer	200.0	3.2	6%	Pancreatic cancer	1,780	3.4	6%
5	Oesophagus cancer	183.7	2.9	5%	Prostate cancer	1,420	2.7	5%
6	Pancreas cancer	175.8	2.8	5%	Stomach cancer	1,394	2.7	5%
7	Lymphomas. multiple myeloma	172.1	2.7	5%	Lymphomas. multiple myeloma	1,355	2.6	4%
8	Leukaemia	110.2	1.8	3%	Liver cancer	1,137	2.2	4%
9	Stomach cancer	101.9	1.6	3%	Leaukemia	1,027	2.0	3%
10	Bladder cancer	97.0	1.5	3%	Mouth & oropharynx	940	1.8	3%
	Cancer	3417.5	54.4	100%	Cancer	3417.5	57.9	100%

Source. WHO. [12]

EU+2 is the 28 member states of the EU + Switzerland and Norway.

3 Cancer expenditure

NHS England provides expenditure data broken down by 23 so-called "programme budgeting categories" based on the WHO International Classification of Disease (ICD-10). The most recent data are from 2012/13. The NHS' expenditure on "cancers & tumours" amounted to GBP £5.68 billion, while total health expenditure amounted to GBP £94.78 billion. [13] This equals a share of 6.0% for England within the remit of the NHS. However, governmental expenditures only comprised 84% of the total health expenditure in the UK in 2012. [14] Assuming that this share of governmental expenditure is the same in England and assuming that that all cancer expenditures were exclusively paid for by the NHS, then the share of cancer expenditure within total health expenditure would be about 5.0% (6.0%*84%). Since co-payments for cancer drugs do occur [15], this estimate represents probably an underestimation of the true total expenditure. Following the principle of providing conservative estimates, 5.0% represents nonetheless the best available estimate for England. In absence of any data covering all of the UK, the estimate for England of 5.0% is used as the best available estimate for the UK as a whole. The share remained stable at around 5% between 2003/2004 and 2012/2013. As can be seen in Table 2, this share is lower than the European average (6.0%) which in combination with a comparatively low spending on health care overall leads to a lower spending on cancer per capita compared to other countries in Western and Northern Europe.

TABLE 2: TOTAL HEALTH EXPENDITURE AND ESTIMATED DIRECT HEALTH COST OF CANCER IN EUROPE (ADJUSTED FOR PPP), 2014

	Total health expenditure			Direct health cost of cancer		
	% of GDP	total (million €, PPP)	per capita (€, PPP)	% of THE	total (million €, PPP)	per capita (€, PPP)
Luxembourg	7.1%	2,785	4,990	6.2%*	174	311
Switzerland	11.5%	38,239	4,708	6.2%	2,371	292
Germany	11.3%	309,380	3,757	6.8%	21,038	255
Netherlands	12.9%	71,863	4,260	5.7%	4,096	243
Austria	11.0%	31,678	3,716	6.5%*	2,059	242
Sweden	9.7%	31,168	3,213	6.8%	2,119	219
Belgium	11.2%	38,750	3,465	6.2%*	2,415	216
France	11.7%	216,787	3,275	6.2%	13,441	203
Norway	9.6%	23,991	4,672	3.4%	816	159
Denmark	10.6%	19,542	3,461	4.5%	879	156
Italy	9.1%	141,385	2,308	6.7%	9,473	155
Ireland	8.9%	14,002	3,040	5.0%*	700	152
Slovenia	9.2%	4,230	2,051	6.7%	283	137
Malta	8.7%	870	2,033	6.5%*	57	132
Spain	8.9%	102,776	2,238	5.8%	5,961	130
United Kingdom	9.1%	165,950	2,566	5.0%	8,298	128
Greece	9.8%	20,939	1,945	6.5%	1,361	126
Finland	9.4%	14,775	2,706	4.4%	650	119
Iceland	9.1%	923	2,821	3.8%	35	107
Slovakia	8.2%	9,095	1,682	6.2%*	564	104
Cyprus	7.4%	1,405	1,636	6.3%	88	103
Hungary	8.0%	14,345	1,455	7.0%	1,004	102
Czech Republic	7.2%	16,398	1,559	5.4%	885	84
Croatia	7.3%	4,919	1,161	6.9%*	337	80
Poland	6.7%	46,628	1,212	6.5%	3,031	79
Lithuania	6.2%	3,677	1,252	6.2%*	226	77
Portugal	9.7%	20,395	1,957	3.9%	795	76
Bulgaria	7.6%	6,904	960	6.8%*	466	65
Estonia	5.7%	1,500	1,124	5.8%	87	65
Latvia	5.7%	2,077	1,043	6.2%*	128	64
Romania	5.3%	15,533	783	6.8%*	1,048	53
Europe	10.1%†	1,453,522‡	2,793	6.0%§	87,895‡	169

Notes: GDP = gross domestic product, PPP = purchasing power parity, THE = total health expenditure.
THE in 2014 was calculated with GDP data from 2014 and the share of THE on GDP from 2013 [33].
The underlying GDP data are based on ESA 95. The 2014 values are calculated by applying the nominal growth rate between 2013 and 2014 based on ESA 2010 to the 2013 values [16-18].
Source for THE on cancer: own estimate based on national sources; see the full comparator report [1]
* Estimated share based on data from similar countries; see full report for methodology.
† The estimate is calculated as THE of all countries (not adjusted for PPP) divided by total GDP.
‡ The sum of all PPP-adjusted national estimates does not equal the estimate for Europe, because the different shares of GDP

spent on THE, and the different shares of THE spent on cancer, respectively, change the weighting of the national estimates.
§ The estimate is calculated as THE on cancer of all countries (not adjusted for PPP) divided by THE.

Whilst expenditure on cancer has remained stable as a share of GDP, the total amount spent on cancer has increased as GDP has increased. There has been a 113% increase in the cost of cancer between 1995 and 2014, while the incidence of cancer has increased by 11% during the same period (**Figure 19**). The corresponding increase in spending was 67% in Europe as a whole and 44% in the other G5 countries during this period.

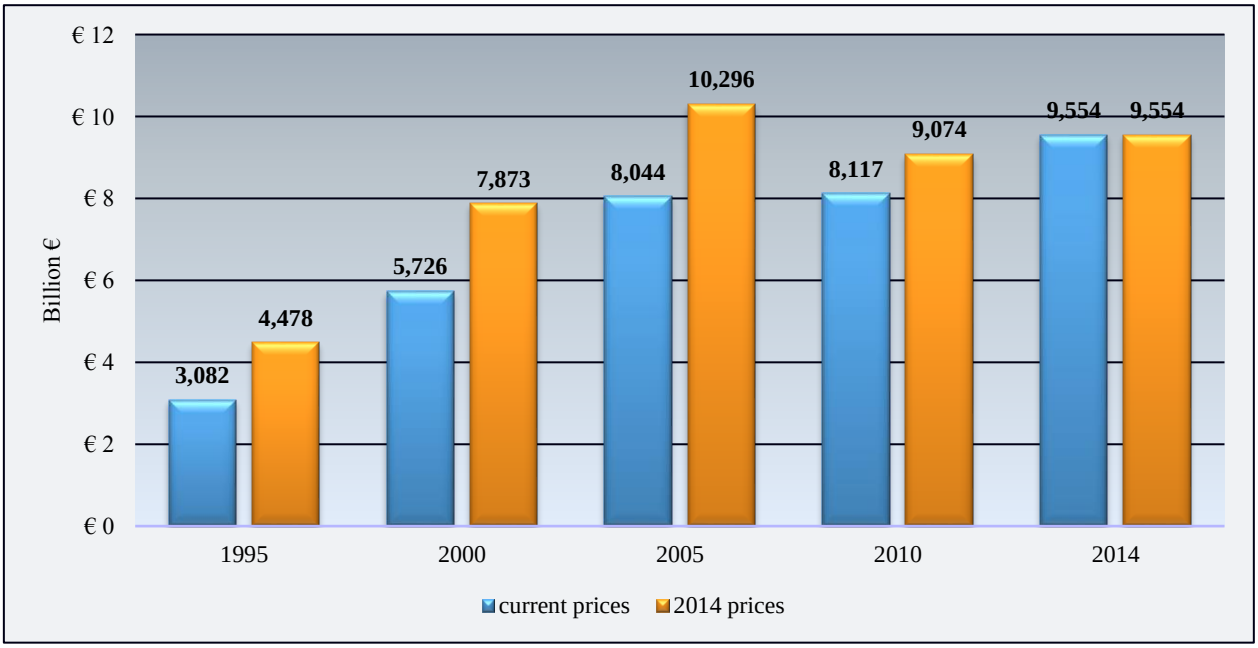


Figure 19: Direct health care cost of cancer in the UK 1995 - 2014

Source: Estimated based on data from NHS England [13]

Whilst expenditure on cancer has increased during the period, indirect costs (productivity losses) due to early mortality have decreased as can be seen in **Figure 20**. This was estimated using the human-capital approach by calculating the years of productive life lost combined with annual earnings and adjusted for the employment rate. The pattern is similar across Europe, but per-capita costs associated with mortality loss are higher in the UK due to higher annual earnings.

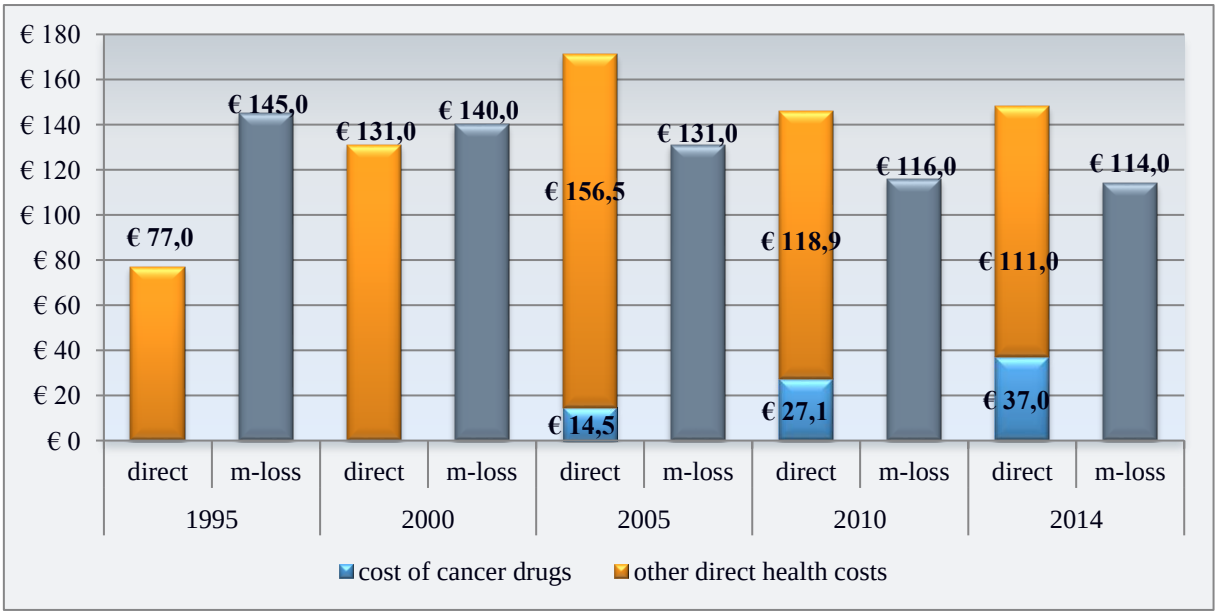


Figure 20: Change in per capita cancer costs in the UK 1995 - 2014

Notes: "direct" = direct health cost of cancer; "m-loss" = productivity loss due to premature mortality from cancer during working age. No separate data on pharmaceuticals 1995 and 2000.
Cancer is defined as ICD-10 C00-D48 for direct health costs, and C00-C97,B21 for productivity loss.

Based on data from IMS MiDAS, 8% of direct costs were due to pharmaceuticals in 2005, increasing to 25% in 2014. The European average was 12% in 2005 and 23% in 2014. It should be noted that these figures are based on list prices and do not take negotiated confidential discounts, common in many countries, into account. UK had among the lowest costs of cancer medicines among the wealthier European countries (**Figure 21**).

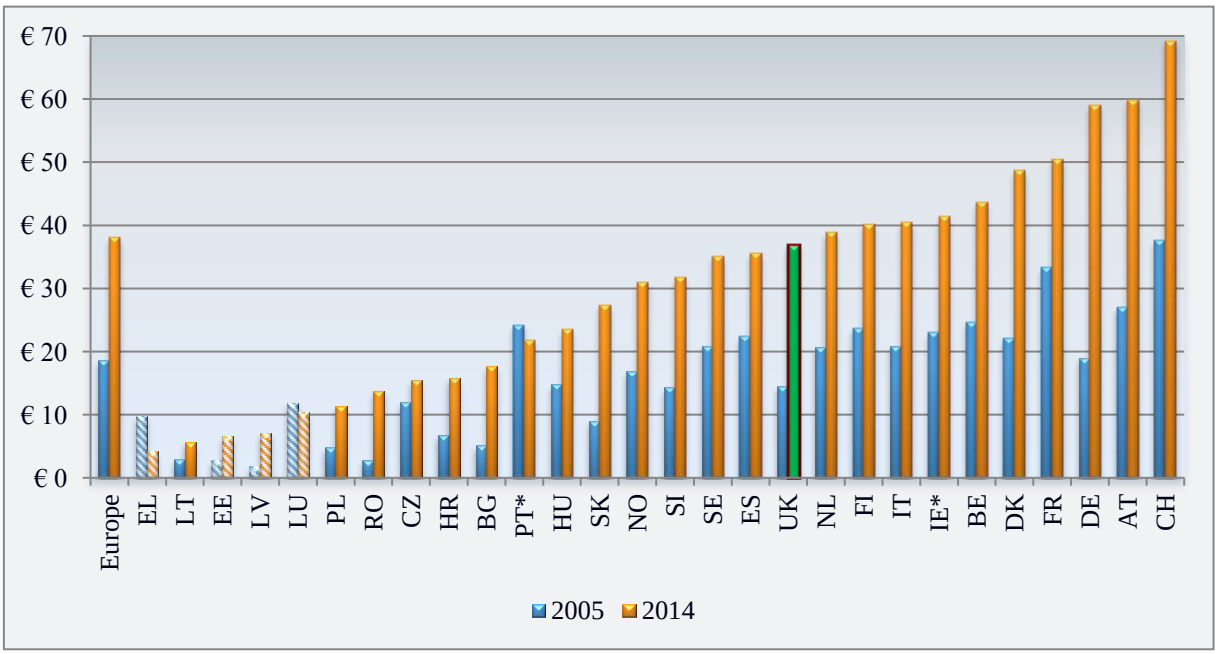


Figure 21: Development of per capita costs of cancer medicines in Europe 1995 - 2014

Source: IMS MiDAS [19]
Notes: *PT data from 2010, IE 2006.

It is possible to compare the expenditure on cancer discussed in this section to the previously described data on survival to get an indication of how efficiently resources are used. In **Figure 22**, spending and survival is compared for all cancers, breast cancer, CML, colorectal cancer, lung cancer and prostate cancer. It can be noted that with the exception of CML where the UK is on the efficiency curve, the UK achieves comparatively less survival in relation to what is spent on cancer per capita.

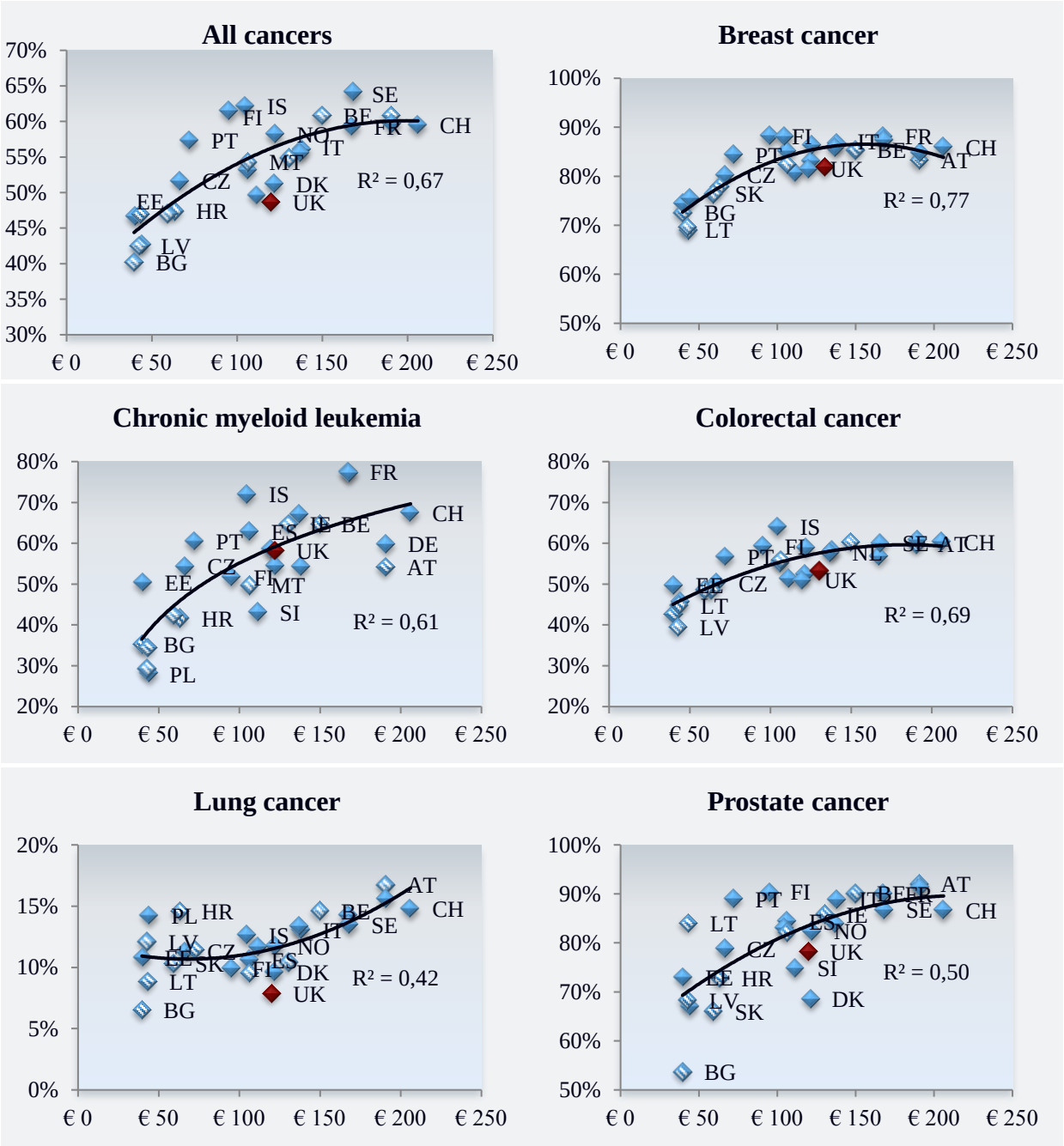


Figure 22: Relationship between cancer expenditure per capita (PPP-adjusted) in 2005 and 5-year relative survival rates for different cancer types during 2000–2007

Source EUROCARE-5 [9]
Notes: Hatched dots indicate that the national estimate for cancer expenditure is based on data from similar countries; see main report for methodology.

4 Uptake of new medicines

Between 1996 and 2015, 98 new medicines for use in oncology (defined as drugs belonging to ATC groups L1 and L2A or B) have been approved, 95 of them through the centralised procedure at the European Medicines Agency (EMA). As can be seen in **Figure 23**, the number of approvals has increased over time. Over time, there has been a shift from traditional molecules towards targeted therapies with the later making up the majority in later years (**Figure 24**). A recent development is the immunotherapies, with 4 drugs entering the market in recent years. There has also been an increasing focus on smaller orphan indications over time (**Figure 25**).

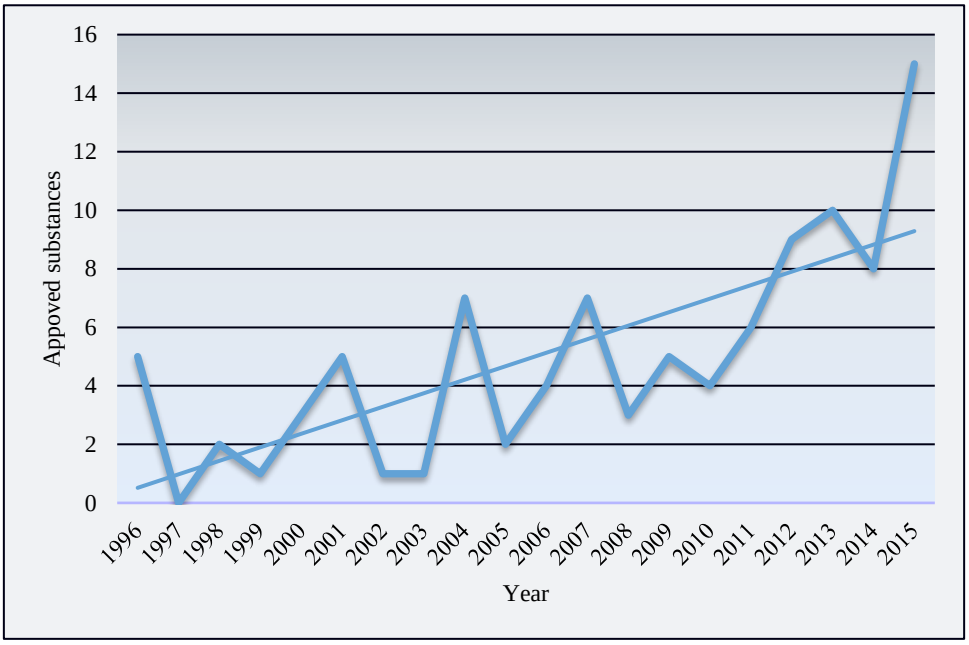


Figure 23: Number of approved drugs/indications over time.

Source. EMA. [20]

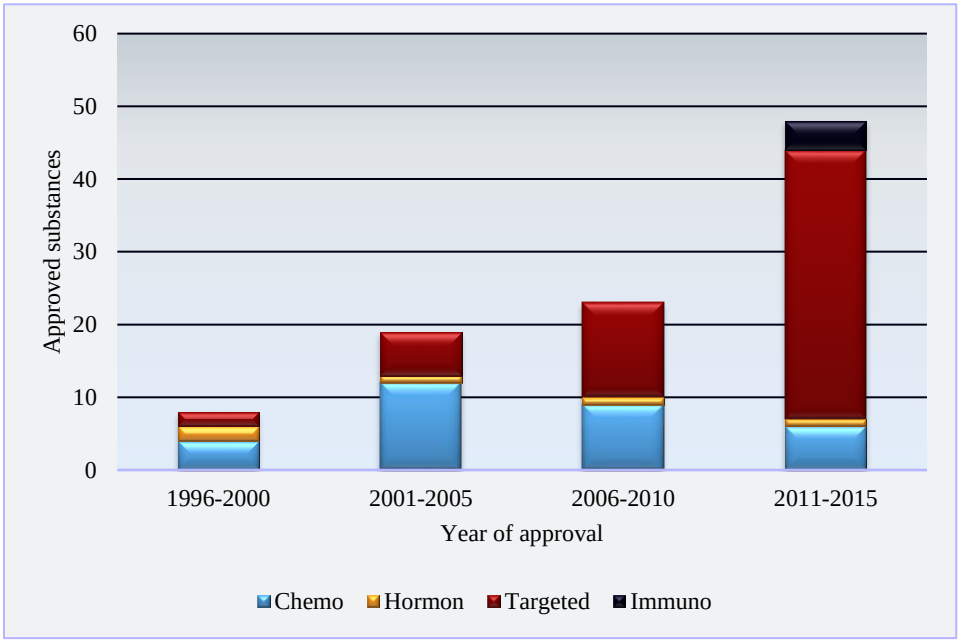


Figure 24: Number of approvals by type of therapy.

Source. EMA. [20]

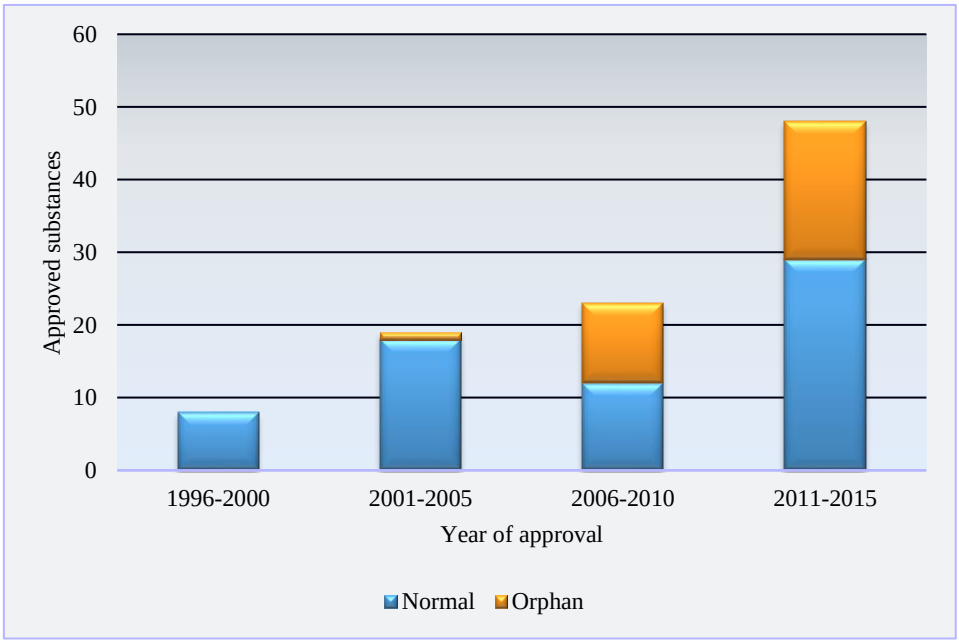


Figure 25: Number of approvals by approval pathway

Source. EMA. [20]

4.1 Vintage

The newest drugs (launched within the last three years) make up only 8% of the total average sales across Europe, varying between 4% and 11% per year in different countries, with the higher share in richer countries. As can be seen in **Figure 26** the UK has, except for the last two years, had a lower share of sales for these newer drugs with figures typically lower than 5%. In 2013 and 2014 the proportion was higher (13% and 15%) but it should be noted that the sales figures are based on list prices and do not take confidential rebates into account which have been much more common in recent years. An increase in sales may have been driven by the cancer drugs fund. The development in the UK is different from that in the other G5 countries, where the share of sales for the newer drugs has fluctuated between 4% and 15% with no obvious increase in the share of newer drugs in later years.

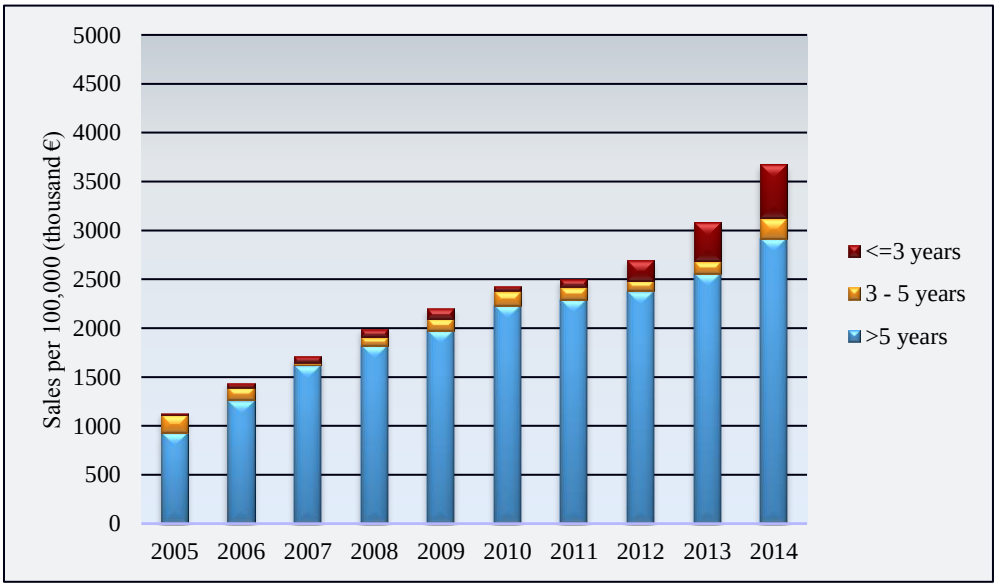


Figure 26: Sales of oncology medicines in the UK by year of marketing authorization

Source. IMS MiDAS. [19]

4.2 Comparison of uptake

In the previously published comparator report it was shown that there is substantial variation in access to medicines not only between countries with different economic status, but also between countries with similar circumstances. Below we show comparisons between the UK and the other four largest European countries (France, Germany, Italy and Spain) for six drugs: trastuzumab, imatinib, bevacizumab, erlotinib, ipulimimab and lenalidomide. They correspond to the most widely used new medicines in six different forms of cancer: HER2+ breast cancer, chronic myeloid leukemia (CML), colorectal cancer, lung cancer, melanoma

and multiple myeloma. We express uptake as grams per case, where cases have been defined as the number of deaths in the indication at hand.

Uptake of cancer medicines varies between countries but is generally slower for the UK compared to other G5 countries. The UK had the slowest uptake of trastuzumab (**Figure 27**), although uptake has continued to increase in later years when it has levelled off in the other four countries, leaving the UK with the second highest usage (after Spain) in 2014. A similar pattern was seen for lenalidomide (**Figure 32**). The UK had the slowest, and to date lowest, usage of imatinib (**Figure 28**), bevacizumab (**Figure 29**) and erlotinib (

Figure 30). In the case of ipulimimab, the UK was in the middle of the group (**Figure 31**). These figures are consistent with figures from the Office for Life Sciences which report that uptake is generally slower in the UK, with a usage that was only 15.3%, 56.7% and 76.9% compared to reference countries in year 1, 3 and 5 after launch for drugs approved by NICE. The corresponding figures for medicines not reviewed by NICE were 14.5%, 55.5% and 50.5%. [21] It can be noted that bevacizumab was not approved by NICE and the uptake is funded through the Cancer Drugs Fund (CDF).

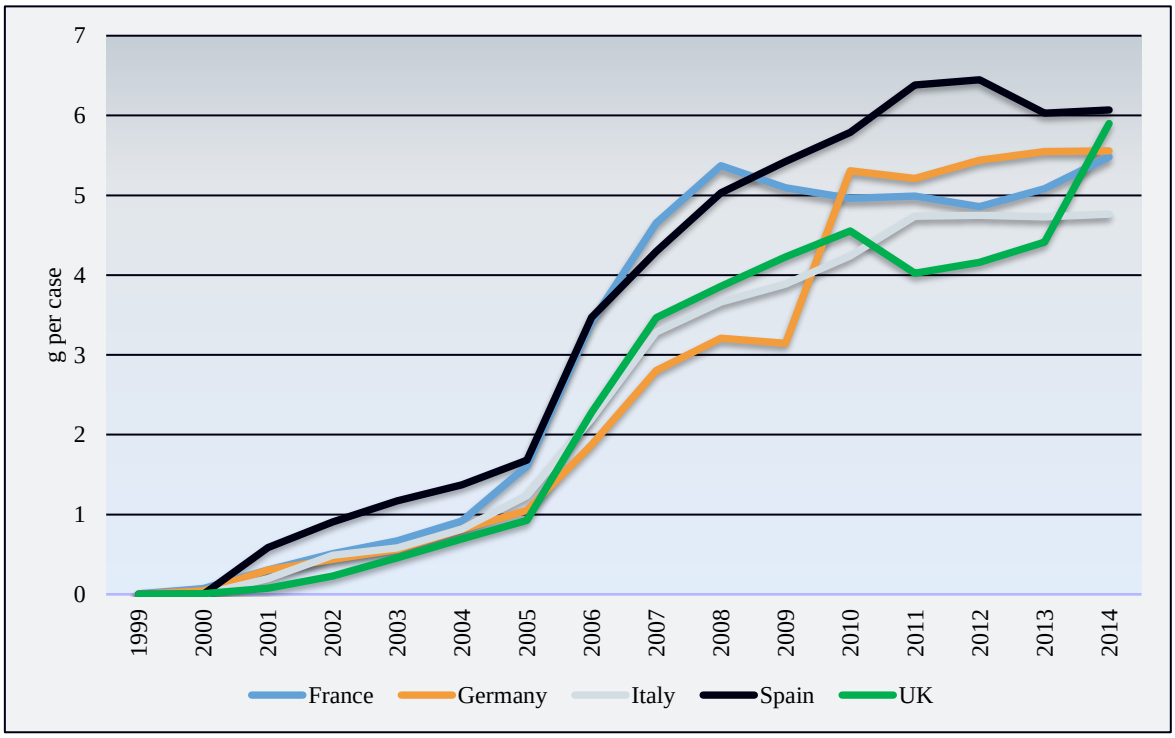


Figure 27: Uptake of trastuzumab expressed as g per breast cancer death

Source. IMS MiDAS. [19]

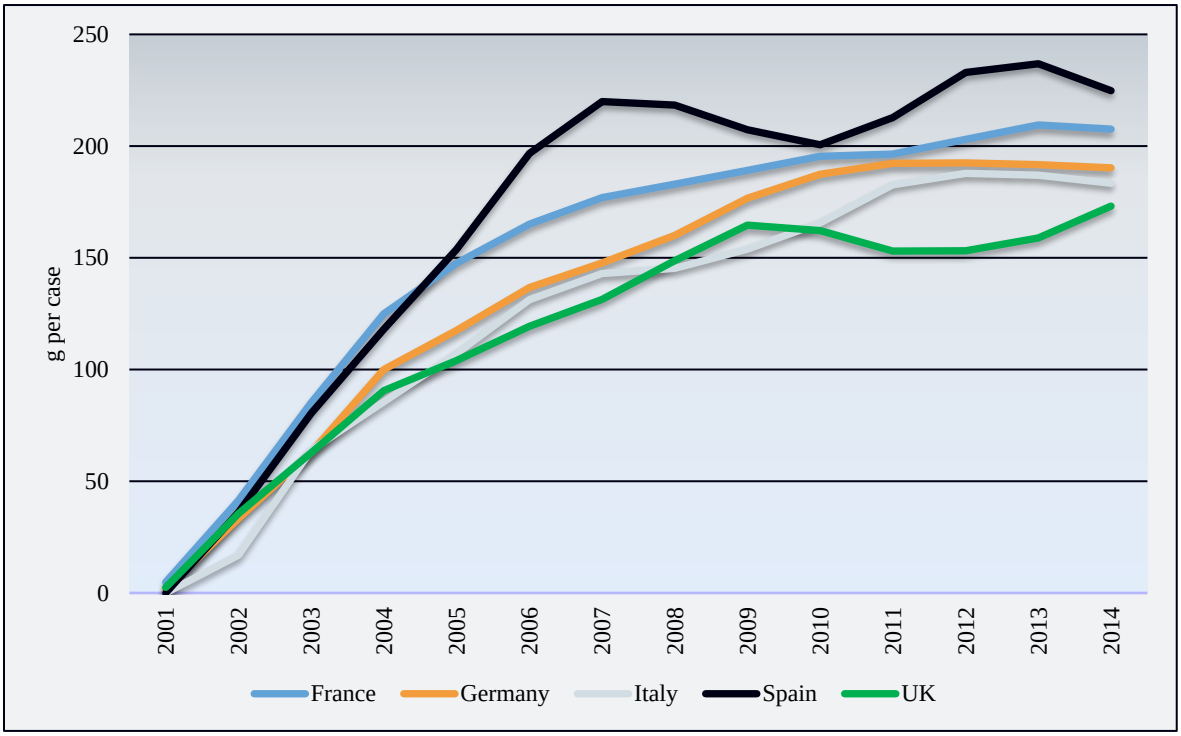


Figure 28: Uptake of imatinib expressed as g per leukemia death

Source. IMS MiDAS. [19]

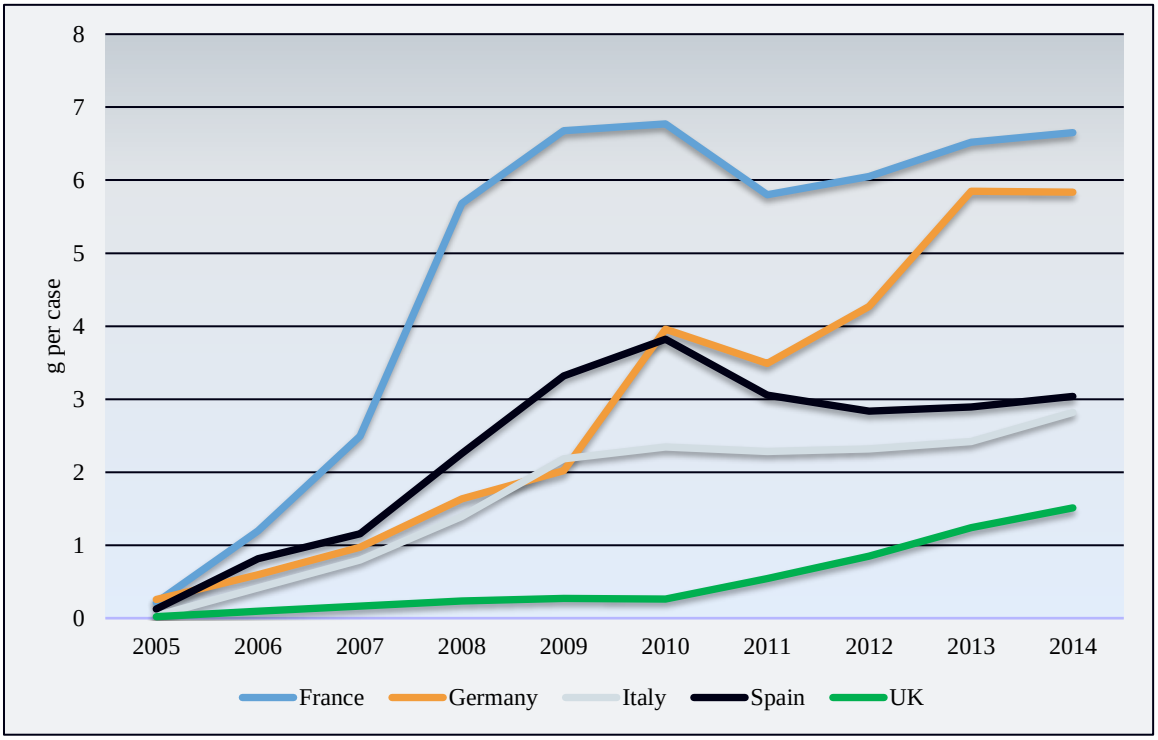


Figure 29: Uptake of bevacizumab expressed as g per death from colorectal cancer

Source. IMS MiDAS. [19]

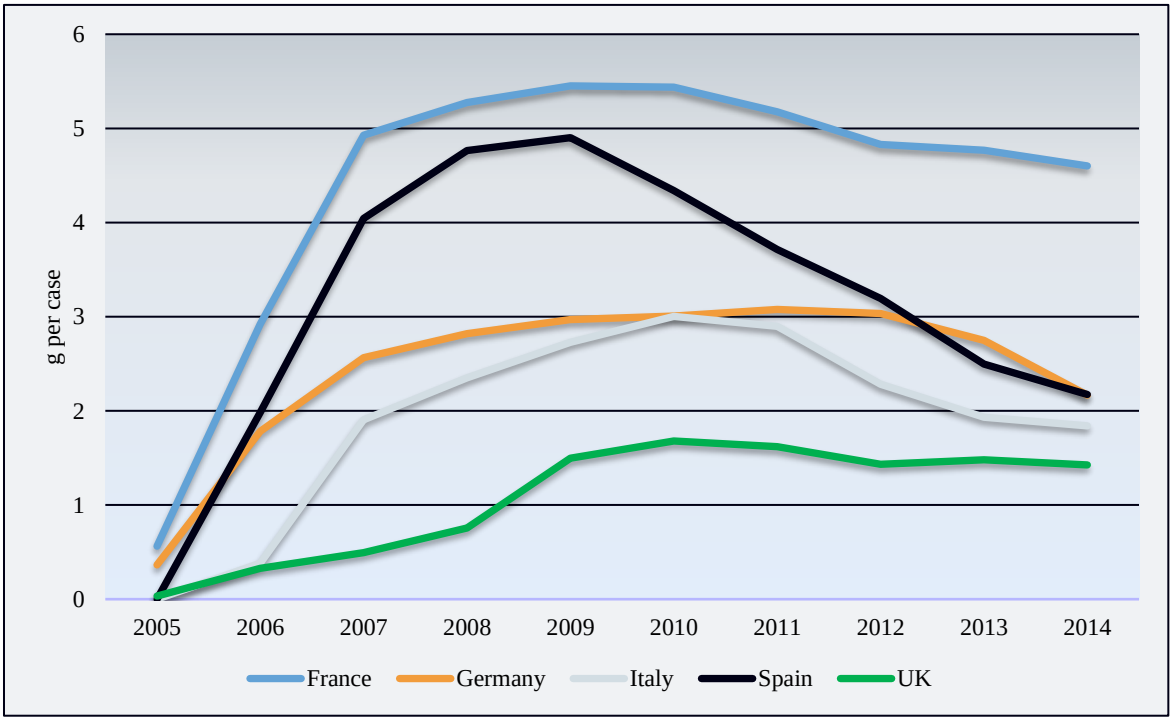


Figure 30: Uptake of erlotinib expressed as g per lung cancer death

Source. IMS MiDAS. [19]

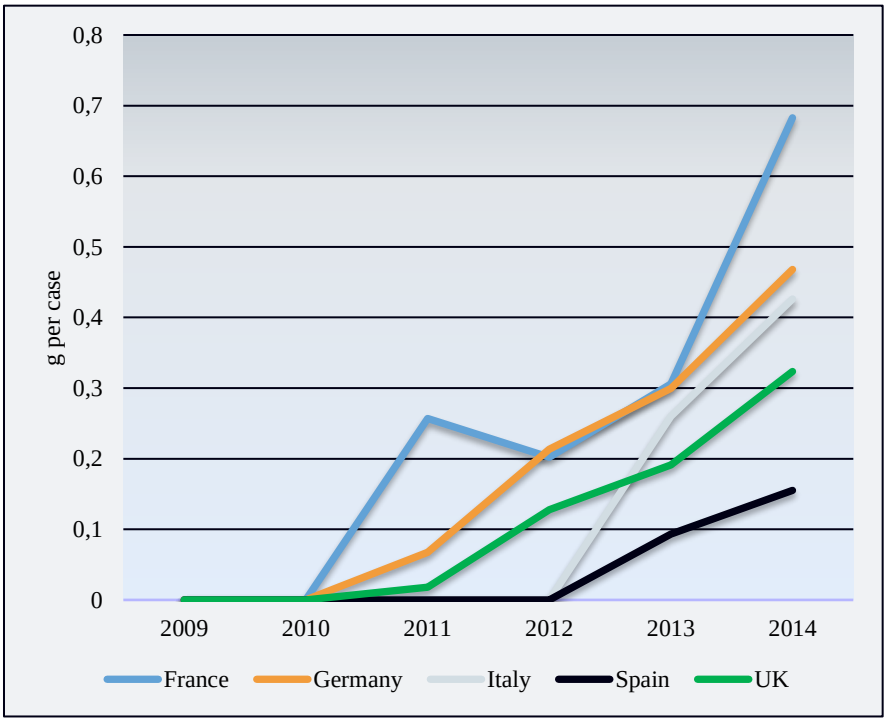


Figure 31: Uptake of ipulimimab expressed as g per melanoma death

Source. IMS MiDAS. [19]

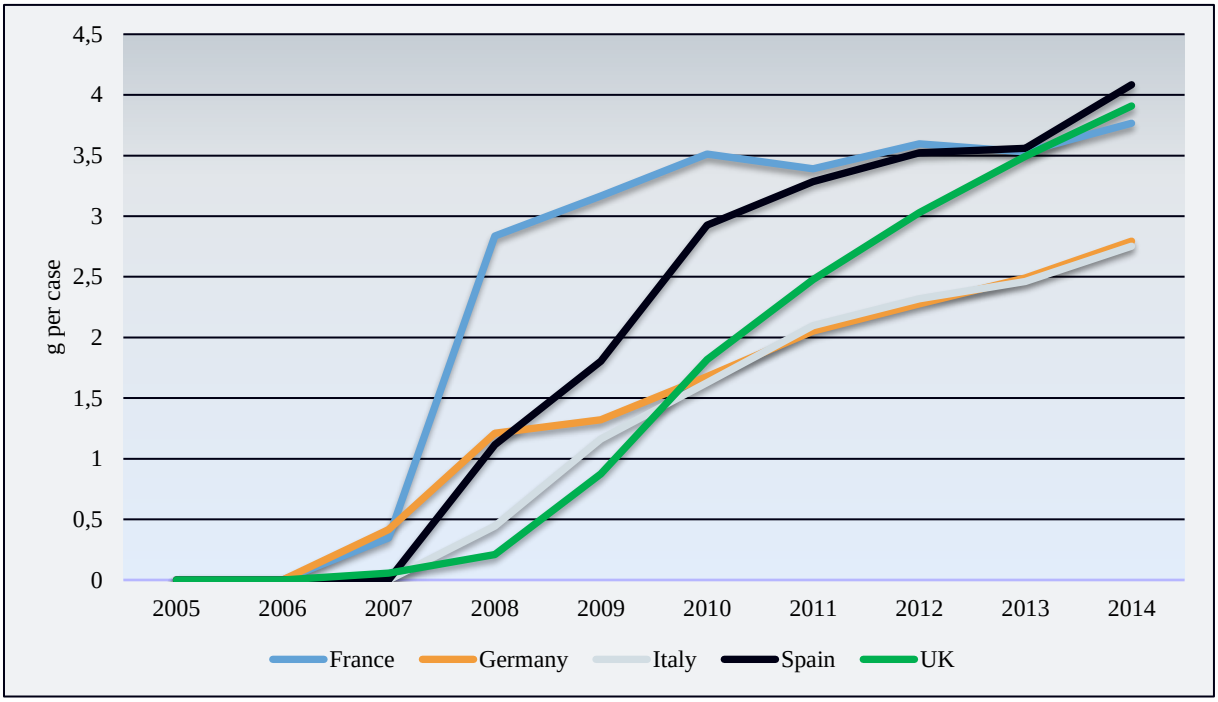


Figure 32: Uptake of lenalidomide expressed as g per myeloma death

Source. IMS MiDAS. [19]

A set of analyses was also conducted for two classes of medicines that are now off-patent: the aromatase inhibitors (used in breast cancer) and the taxanes (used in several different tumor types). In these two cases, uptake was defined slightly differently compared to previous analyses: uptake was expressed as units per 100,000 inhabitants. For the aromatase inhibitors daily defined doses, DDD, was used as the unit of measure to allow for the aggregation of medicines with different dosing and for the taxanes grams as no DDD has been defined for them due to their widely different usage across indications.

The uptake of the aromatase inhibitors (**Figure 33**) was similar in the five countries with the early exception of France where they were introduced somewhat later. An increase in uptake can be seen after 2004 when the drugs started to be used in the adjuvant setting as well. The usage has plateaued at different levels, with the UK in the middle. For the taxanes (**Figure 34** and **Figure 35**) uptake was much more varied, but for both it was markedly slower in the UK, and the UK has the lowest usage today.

As both aromatase inhibitors and taxanes are available as generics todays, the differences observed in the data in recent years is likely driven by differences in practice rather than by economic considerations.

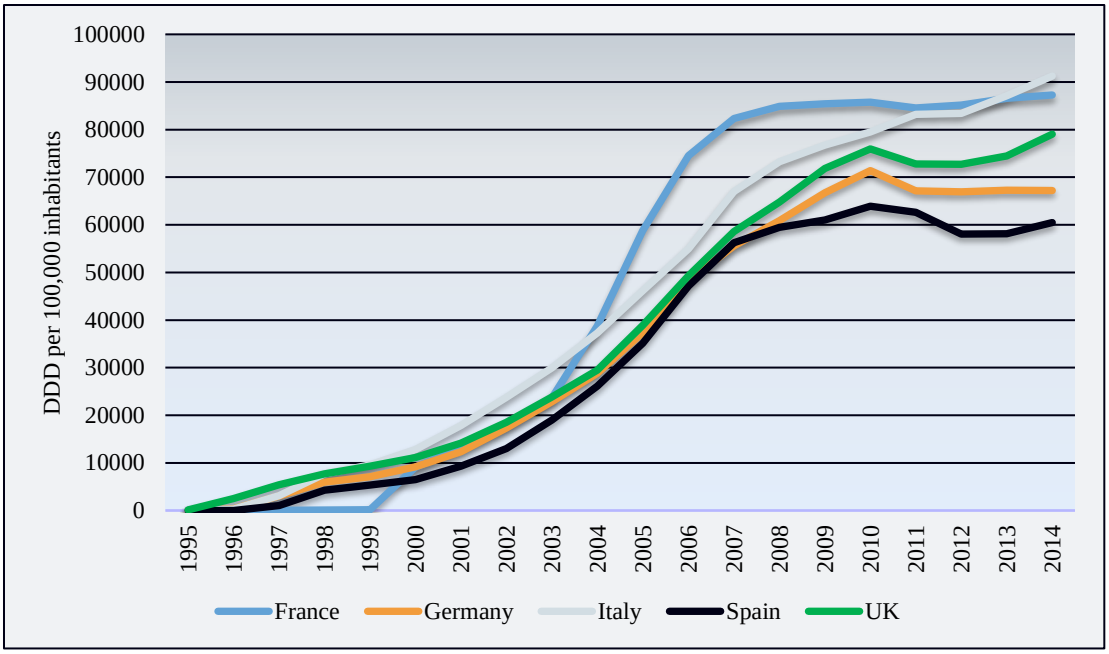


Figure 33: Uptake of aromatase inhibitors expressed as DDD per 100,000 inhabitants

Source. IMS MiDAS. [19].

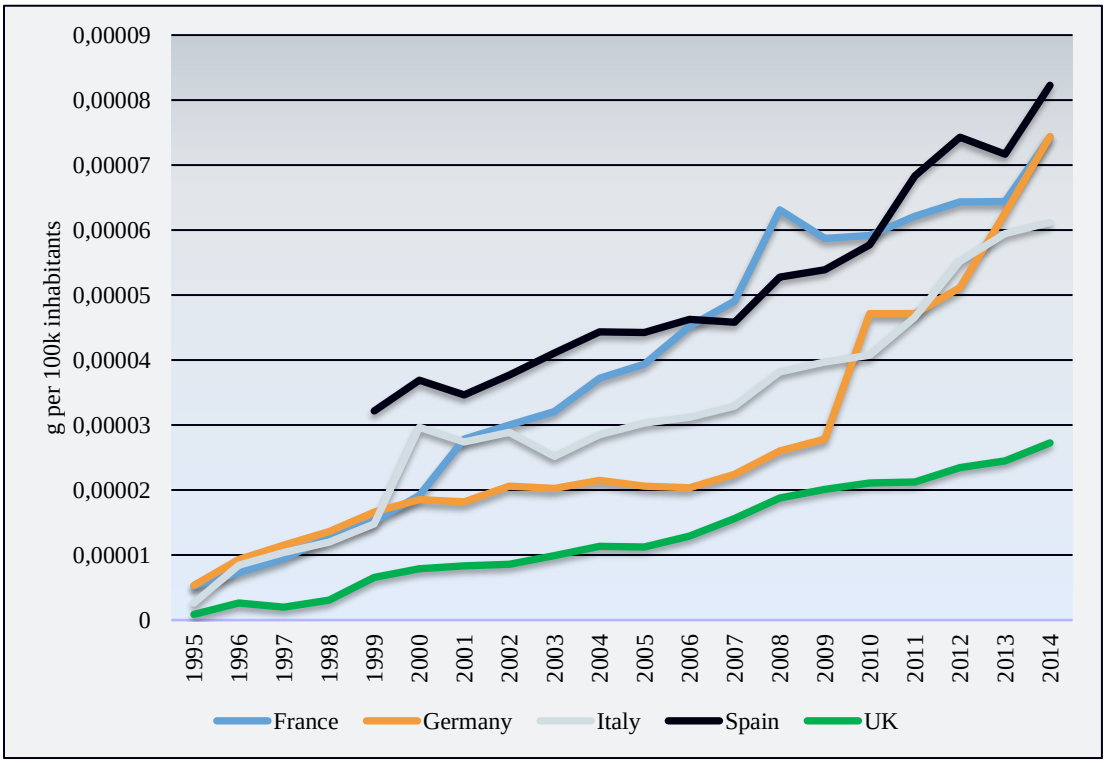


Figure 34: Use of Paclitaxel in gram per 100 000 population 1995-2014.

Source. IMS MiDAS. [19] Note: Data form Spain <1998 lacking.

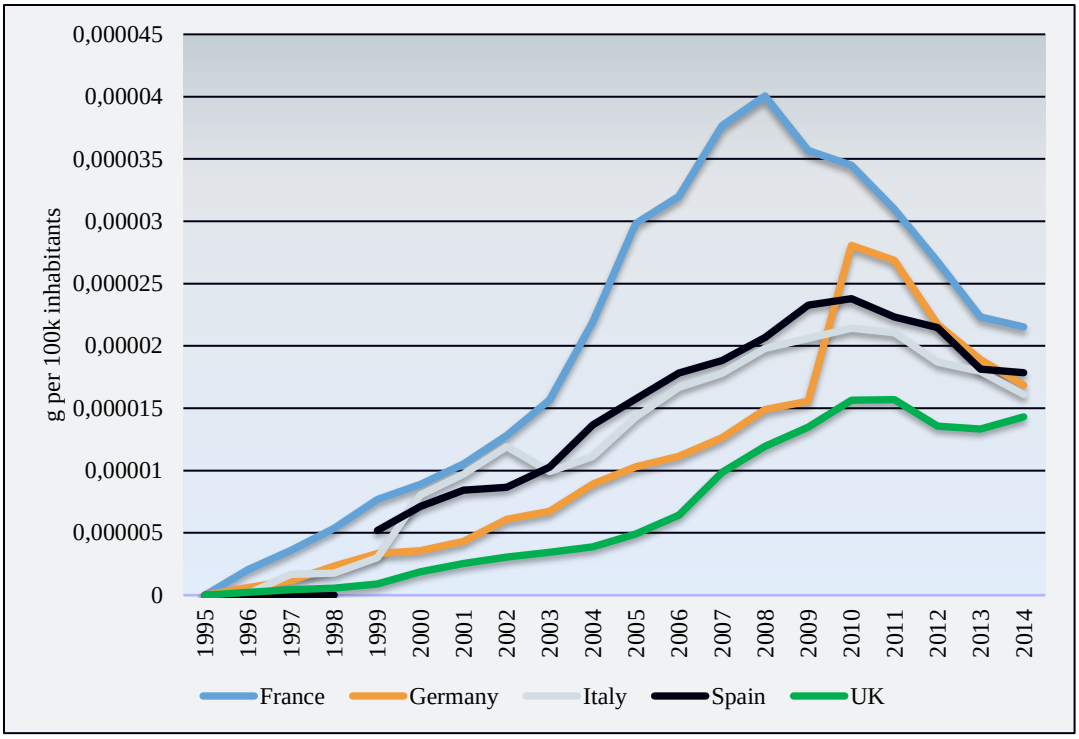


Figure 35: Use of Docetaxel in gram per 100 000 population 1995-2014

Source. IMS MiDAS. [19] Note: Data form Spain <1998 lacking.

5 Policy issues

Though the cost for cancer medicines has increased over the period in absolute terms, only a small number account for the majority of cancer medicines expenditure at any point in time, and this constantly changes as new innovation replaces older medicines. Notably, the share of cancer out of total health care expenditure in the UK has not increased over the last twenty years despite the introduction of over 100 new cancer drugs during this time. One factor is that older drugs have gone off patent or been replaced by newer therapies. But more importantly is the shift from inpatient care to outpatient care of cancer which has been supported by these therapeutic advances. The spending on new cancer medicines may not be a threat to the financial stability of health care systems as long as a solid methodology for assessing the value that new drugs bring is maintained and resources allocated accordingly.

Though we have an overall picture of the total cost of cancer, significant gaps still exist that prevents a detailed estimate of health care expenditure on cancer. In many European countries, we still lack data on the direct costs outside the hospital setting as well as the indirect costs linked to morbidity. In the UK, there is a lack of data on the total spend on medicines due to the use of confidential patient access schemes and the uptake of medicines

with multiple indications. The latter is a problem that is likely to increase as the current industry pipeline comes to the market.

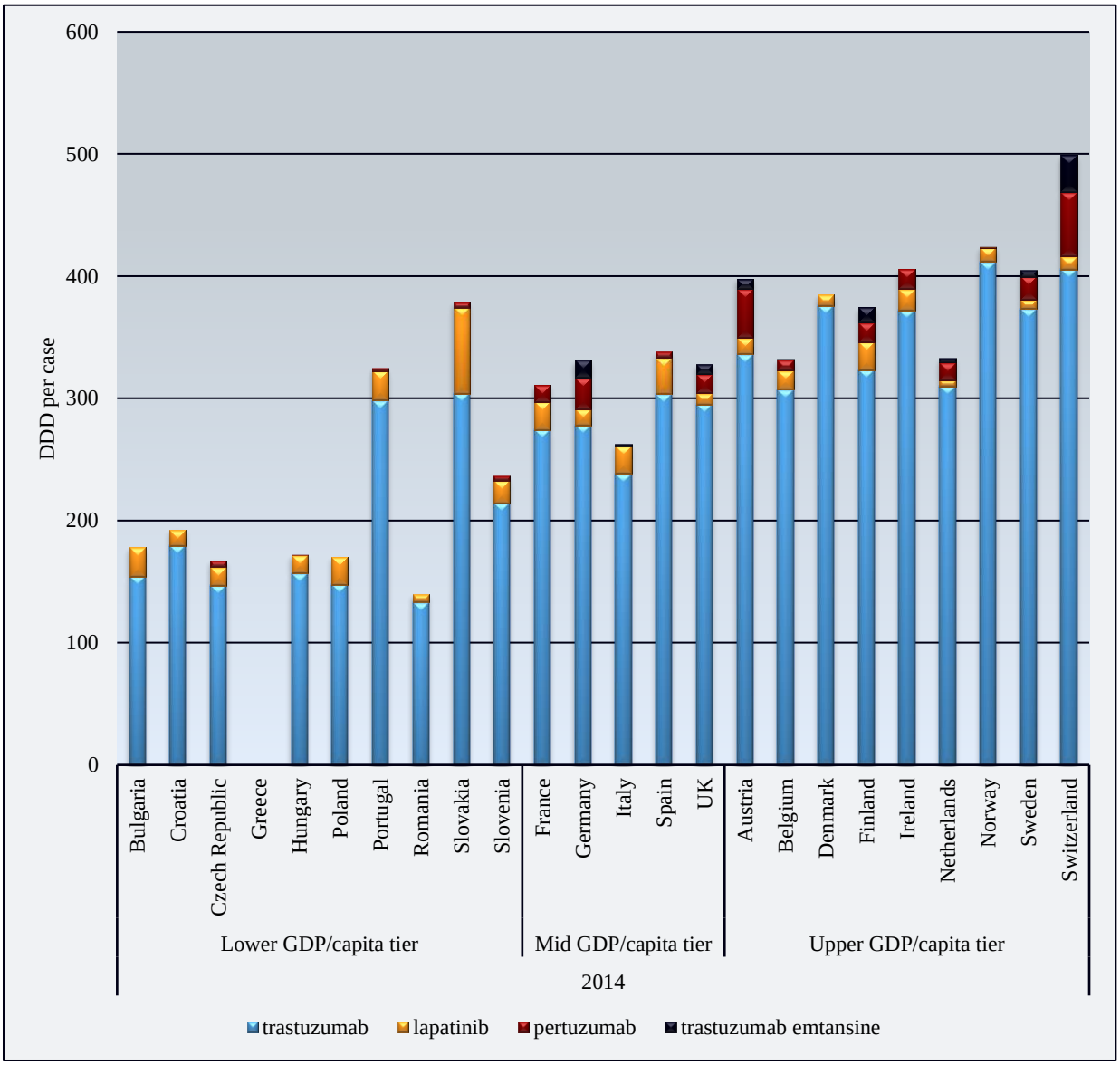


Figure 36: Use of therapies in HER2+ breast cancer in 2014

Source. IMS MiDAS. [19]

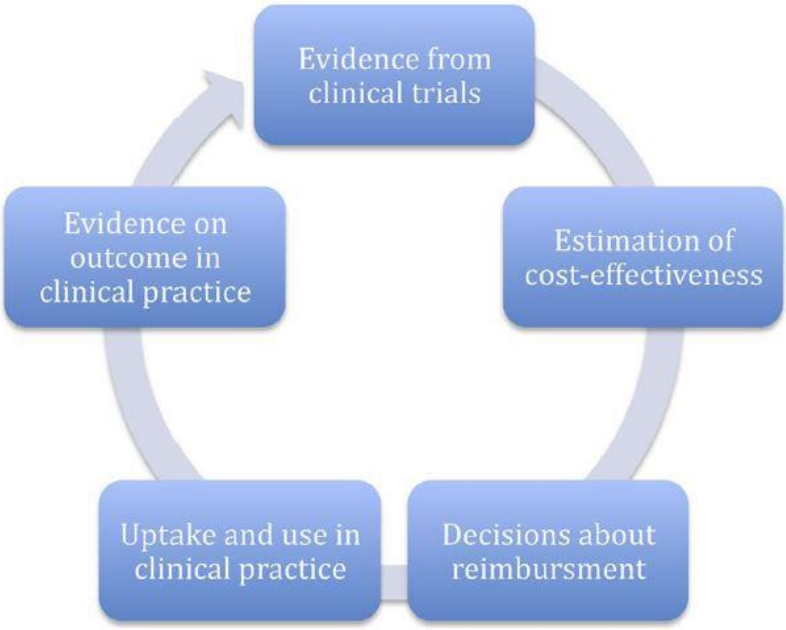
Cancer medicines introduced during the last five years account for less than ten per cent of total cancer medicine costs in a given year (**Figure 26**). In the UK that figure has historically been lower than 5%. In 2013 it started to increase however, likely related to the introduction of the Cancer Drugs Fund. Though the investment in new medicines has increased, little effort has been made to monitor how the CDF expenditure has impacted patient outcomes.

Most new cancer medicines in the UK historically have had low sales and slow uptake (**Figure 36**), which normally is associated with countries with lower national income and low health care spending per capita. Access in the UK is slow primarily due to HTA processes and the resistance to implement recommendations by local providers.

The shift towards personalised medicines requires new pathways to assess and bring new medicines to patients. It is clear that they can only provide value if they are used appropriately in clinical practice. Also, with increasingly narrow patient populations, we will only know their real value after they have been used in clinical practice for some time. Furthermore, many innovative treatments develop over time, with new indications or patient groups added as the available body of real world evidence grows.

In response, significant efforts have been made in Europe and the UK over the last five years to provide a more flexible regulatory and access framework. “Adaptive pathways” is a new model for planning access to new drugs in areas of high unmet medical need. [22] An accelerated approval regime has been introduced by the EMA which has been undertaken for about 5% of cancer medicines. New access processes in the UK subsequently need to align to expedite access for patients via UK appraisal routes (CDF, AAR, EAMS). This model is based on early collaboration between companies, MHRA, NICE and the NHS. Another important feature of the model is the use of real world data as a complement to data from clinical trials. Real world evidence on safety and effectiveness heavily relies on the support of patient and clinical organisations, and processes should clearly define how output from these studies can be incorporated into HTA evaluation.

HTA was identified as an increasingly important determinant for access in the last comparator report. While HTA remains a cornerstone in the UK access framework, the environment becomes more challenging, when assessments are requested earlier and are based on limited long-term outcomes evidence. There is also an increased need to implement an iterative assessment process as new cost-effectiveness data becomes available (from post-authorisation trials or real world evidence) and the products develop during their life cycle (new indications, combination therapies etc).



There is a growing awareness of the access challenges due to the traditional method of financing pharmaceutical innovation by a single price per unit used of the drug for all indications. This challenge is not unique to the UK. Stakeholders need to align on processes that permit indication based pricing and that have the flexibility to consider situations where two branded cancer medicines are used in combination treatment.

Managed access agreements are a key part of a solution to deliver more sophisticated strategies to manage uncertainty, short-term affordability and to streamline access in all these situations.

Pure risk sharing agreements, aimed at controlling costs, have the advantage that the need for collection of data is minimal. In contrast, outcome based agreements demand collection of data that can be challenging to collect in practice. In the UK significant steps are being made

to improve the data collection infrastructure for cancer. Whilst historically commercial based schemes have been favoured, outcomes and service improvement schemes may become more attractive once governance and operational aspects of data collection are in place. The new, revamped Cancer Drugs Fund, and the managed access agreements it will necessitate, will carve a path for other similar data driven arrangements in other disease areas. It could also prove very useful as a test bed for new pricing arrangements for combination therapies and indication based pricing. However, the use of the new CDF needs to be properly monitored to ensure that the right evidence is generated to inform future cost-effectiveness assessment, to improve access and patient outcomes.

Further HTA and access reforms may be needed in the UK to fully adapt to the changing environment. For instance, EAMS and CDF are only in the infancy of clarifying the use of real world data collection and the feasibility of the infrastructure, governance, transparency and safety reporting will all be tested as medicines navigate these new pathways.

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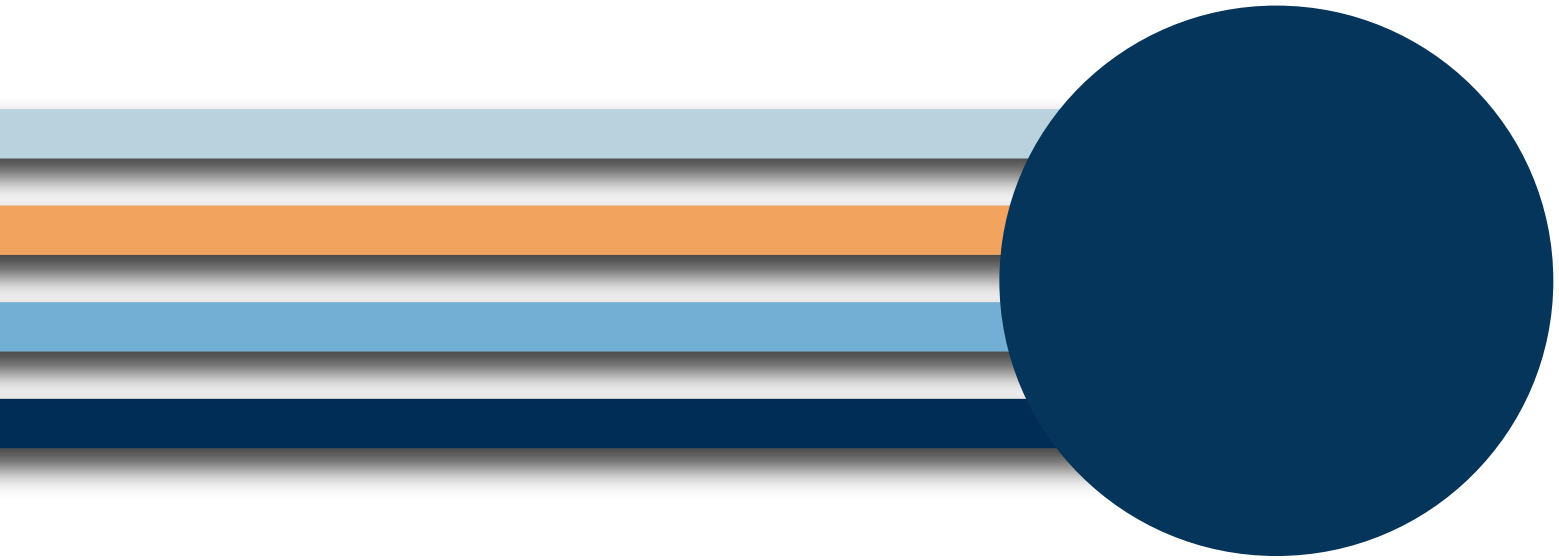

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