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Full Length Research Paper

Use of oncology drugs in Japan compared to France, Germany, Italy, Spain, Sweden, the UK and the USA: A comparison based on data from 1999 to 2009

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The development of new compounds over the past decades has provided a significant potential for improvements of cancer therapy and outcome. This study compares the use of oncology drugs in Japan with the use in the US and selected European countries (France, Germany, Italy, Spain, Sweden and the UK). The patterns of use of cancer drugs differ between the countries. Japan, France and the US spend more per capita than most other countries in the world on cancer drugs, but Japan spends a larger share on cancer drugs that were launched in 1999 or earlier ("mature" drugs). One of the main factors behind the slow introduction and uptake of cancer drugs in Japan is a lengthy process for approval of new drugs. Economic evaluations of new drugs are not as frequent in Japan as in the US and in Europe. The use of generic drugs is also low in Japan compared to the US and the European countries. A greater use of generics and more comprehensive assessments of the clinical and economic value of treatments may improve the efficiency in the use of health care resources and facilitate the introduction of newer drugs.

Key words: Oncology, drugs, generics, Japan, United States, France, Germany, Italy, Spain, Sweden, United Kingdom.

INTRODUCTION

In 2008, the International Agency for Research on Cancer (IARC) estimated that there were more than 12 million new cancer cases diagnosed worldwide. This number has doubled in the last 30 years, and in 2030, it is expected that 27 million new cases will be diagnosed (Boyle et al., 2008). In 2008, cancer caused about 7.6 million deaths globally (13% of all human deaths) (Garcia et al., 2007). In Japan, the estimated number of new cases was 2008 600,000 and the number of deaths 342,000.

Drugs constitute key elements in the treatment of solid tumours and in haematological malignancies. The development of new drug therapies has provided great opportunities for the improvements of cancer treatment leading to cure, extension of life, and reduction of pain and discomfort for the patient. Access to drug treatment is, however, constrained by a number of factors, such as organization of healthcare systems, resources available, policies and procedures regarding access and use of new technologies and economic prioritizations in healthcare. There are great variations in the use of drug treatments across countries. These differences indicate suboptimal use of existing treatment opportunities. This study analyzes the use of oncology drugs in Japan, the US, France, Germany, Italy, Spain, Sweden and the United Kingdom. Potential determinants of patient access to cancer treatment have been reviewed and assessed as explanations for the variations found between the studied countries.

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METHODS

Data on the burden of cancer in terms of incidence, mortality and costs have been collected from different sources and comparisons have been made between Japan, the US and selected European countries (France, Germany, Italy, Spain, Sweden and the UK). The comparisons are based on age standardized (world standard population) incidence and mortality rates as reported by the IARC (Tables 1 and 2).

The costs of cancer consist of direct and indirect cost. The direct costs are costs associated with the direct medical care and the indirect costs are the monetary value of the time and activities lost due to disease. The major components of the indirect costs are morbidity cost (the value of foregone earnings) and mortality cost (future loss of earnings caused by premature death). These costs were calculated using the human capital approach based on sex and age specific average earnings. The estimated direct and indirect costs are based on previously published studies indicated with references. The costs are based on national estimates where different methods may have been applied, but all of these estimates include direct and indirect costs specifically associated with the cancer disease. To facilitate comparisons between countries, the costs have been adjusted by using Purchasing Power Parity (PPP) in international dollars. The direct costs have also been adjusted to 2006 years prices using national inflation rates.

Access and use of oncology drugs was analyzed in the 8 countries over a 10 year period (1999 to 2009) based on sales data provided by IMS Health. Cancer drugs are defined as drugs under ATC (anatomical therapeutic chemical) code L1+L2A+B. The use of drugs was analysed by vintages; "mature" cancer drugs represent drugs first launched in any of the markets in 1999 or before and "new" cancer drugs are those available in any of the countries in the year 2000 or later. The "mature" drugs have been available for a long period of time and there is accumulated evidence based on clinical trials, epidemiological studies and clinical experience that they have had a major and clinically relevant impact on the outcome in different areas of oncology. "New" drugs include some of the new "targeted" drugs where the clinical data available may be limited at present. The cost of oncology drugs are measured in US$/capita. The relative cost of these drugs may differ, but this does not necessarily have an impact on the distribution of mature versus new drugs.

RESULTS

Burden of cancer

Incidence

The cancer incidence in Japan and the age standardized cancer incidence rate in Japan in 2008 was estimated to 201 per 100,000 inhabitants, which is significantly lower than in the US (300) and in the EU (264). Among the most common types of cancer, the incidence in breast and prostate cancer is significantly lower in Japan, while the incidence rate in stomach cancer is substantially higher (Table 1). The trend over the past four decades shows an overall increase in cancer incidence in all countries, both for men and for women, although most countries see a slower increase or even a decrease in cancer incidence in the past two decades (National Cancer research Institute, 2011; American Cancer Society, 2009; European Cancer Observatory, 2011).

The long term increase in incidence may have several explanatory factors such as an ageing population, which is clear in Japan.

Mortality

In 2008, the age standardized mortality in Japan was estimated to 95 deaths per 100,000 inhabitants, compared to 104 per 100,000 in the United States and 115 in the EU (Table 2). Cancer mortality and the age standardized overall mortality rate in Japan have increased to a level almost as high as in the US and in Europe. In Europe and in the US, the trend in the past 20 to 25 years has been a decline in mortality.

The decline in mortality is, most likely, a result of better treatments, but also better diagnostic methods leading to earlier detection and treatment. The European countries and the US have seen a large decline in the mortality in stomach cancer. The stomach cancer mortality in Japan has also been declining, but not at the same pace as in the US and in Europe. The mortality in prostate cancer is still substantially lower in Japan compared to the US and Europe. In the US a decline in colorectal cancer and male lung cancer mortality has been seen in the past two decades. In Japan, the trend has in contrast, been increasing (National Cancer research Institute, 2011; American Cancer Society, 2009; European Cancer Observatory, 2011). An important factor in the increasing trend in Japan is the ageing population.

Disability adjusted life years

Cancer causes 2,400,000 disability adjusted life years (DALY) lost in Japan each year. This is almost one fifth of all DALYs lost in Japan each year. Of these, 44% are caused by either stomach, colorectal or lung cancer. Stomach cancer is responsible for a much higher share of the total cancer related DALYs lost in Japan compared to the other countries. In contrary the relative burden of cancers of the lung, breast and prostate is lower in Japan than in the US and in Europe (Table 3).

Cost of cancer

In Japan, more than $ 23 billion in total, or $ 188 per capita, is spent on direct cancer treatment (Koinuma et al., 2007). Colorectal cancer consumes the largest share of resources followed by stomach cancer and lung cancer. In the US, the total direct costs of $ 314 per capita (American Cancer Society, 2009) is 67% higher than in Japan. The cancer treatment costs in Japan is lower than in France ($ 226 per capita) (Institute National de Cancer; 2007), Germany ($ 249) (Wilking et al., 2009) and in Sweden ($ 202 per capita) (Wilking et al., 2009). The Japanese direct per capita expenditures on cancer is

Table 1. Age standardized (world age standard) cancer incidence, 2008.

Country	All cancer	Prostate	Breast	Lung	Colorectal	Stomach
Japan	201	23	43	25	32	31
United States	300	84	76	42	29	4
France	300	118	98	30	29	5
Germany	282	83	82	28	36	8
Italy	274	58	86	27	37	11
Spain	241	57	61	29	30	8
Sweden	252	95	79	17	28	4
UK	267	64	89	31	31	6

Source: GLOBOCAN, IARC 2010.

Table 2. Age standardized (world age standard) cancer mortality, 2008.

Country	All cancer	Prostate	Breast	Lung	Colorectal	Stomach
Japan	95	5	9	17	12	14
United States	104	10	15	30	9	2
France	107	13	18	30	11	3
Germany	106	12	82	28	12	5
Italy	109	9	16	22	12	7
Spain	110	11	13	24	13	6
Sweden	100	20	15	18	11	3
UK	116	14	19	26	11	3

Source: GLOBOCAN, IARC 2010.

higher than in Italy ($ 168), Spain ($ 99) and the UK ($ 158) (Wilking et al., 2009) (Table 4). The differences are related to the total expenditures on health, and the share spent on cancer is not different in Japan from many of the countries in the comparison, where the low share for the US is most notable.

In addition to the direct treatment costs, cancer is also associated with large indirect costs due to due to loss of production. The vast majority, more than 90% in Japan, of the indirect costs of cancer is due to premature mortality. The total cost of cancer in Japan including both direct and indirect costs amounts to $ 88 billion or $ 691 per capita (Vital statistics, 2005). The indirect costs in Japan are thus almost three times as high as the direct costs.

The total cost of cancer per capita is lower in Japan compared to the US ($ 784) (American Cancer Society, 2009), but higher than in France ($ 582) (Institute National de Cancer, 2007) and in Sweden ($ 504) (Wilking et al., 2009) per capita (Table 5).

The use of oncology drugs

There are significant variations in the use of oncology drugs in the countries studied. The total use of anti cancer drugs in relation to the population (ATC code L1+L2A+B in USD/capita;) in 2009 is highest in France ($ 61 per capita) followed by USA ($ 60 per capita) , Japan ($ 56 per capita) and Spain ($ 49 per capita). The lowest use is found in the UK ($ 23 per capita) (Table 6). As share of total expenditures on cancer, drugs account for a larger share in Japan (30%) than in, for example, the US (19%) and UK (15%). There may be differences in relative costs between countries, but there are still large discrepancies not explained by different price levels.

While Japan spend nearly as much on cancer drugs that the US and France spends, there is a marked difference in the distribution of spending on “new” and “mature” cancer drugs. Japan spends only $ 12 on new drugs, while the US and France both spend $ 21. On the other hand, Japan spends most ($ 44 per capita) of any country on “mature” drugs. There may be two explanations for this, either the volume of drugs prescribed or the relative price of the “old” drugs, or a combination of these factors. Taking into account the relatively low incidence of cancer in Japan (Table 6), it is a safe conclusion that the price effect dominates.

The use of the most recent drugs may have an impact on the survival in cancer. Studies have indicated a correlation between the use of new drugs and cancer survival (Jönsson et al., 2007). In the UK where the use of the newest drugs is lower, the survival in cancer is also lower compared to other western European countries (Berrino

Table 3. Estimated total disability adjusted life years (DALYs) per country, 2004.

Country	All causes	Cancer share of DALYs lost (%)	Stomach share of all cancers (%)	Colorectal share of all cancers (%)	Lung share of all cancers (%)	Breast share of all cancers (%)	Prostate share of all cancers (%)
Japan	12,997	18.5	14.5	14.2	15.5	6.5	2.1
US	41,372	12.3	2.1	10.7	24.5	12.0	4.4
France	7,434	18.2	3.2	11.1	19.9	10.7	4.3
Germany	10,358	16.9	5.1	13.1	19.2	11.3	4.3
Italy	6,575	18.3	6.2	11.4	19.8	10.2	3.2
Spain	4,858	16.7	5.7	13.2	20.3	8.6	4.0
Sweden	1,033	14.6	3.8	12.4	15.2	9.8	7.7
UK	7,718	15.6	3.6	11.5	19.6	12.2	5.2

Source: WHO Global burden of disease 2009.

Table 4. Estimated direct costs of cancer 2006, (US$ PPP-adjusted).

Country	Total expenditures on health, MUS$	Health expenditure share of GDP (%)	Total expenditure on health per capita	Cancer share of health expenditures (%)	Direct costs of cancer per capita
Japan	328,897	8	2,581	7.3	188
US	2,074,861	15	6,719	4.7	314
France	223,830	11	3,420	6.6	226
Germany	208,856	11	3,465	7.2	249
Italy	155,346	9	2,631	6.4	168
Spain	113,409	8	2,466	4.0	99
Sweden	29,535	9	3,162	6.4	202
UK	174,647	8	2,815	5.6	158

et al., 2007; Verdecchia et al., 2007). Further studies are however needed to establish the impact of treatment on mortality at the population level.

The use of generic drugs is in general, low in Japan. In 2009, the generic share of the total drug volume was 20%. There are however efforts to increase the use of generic drugs in Japan. Since 1999, the generic share of the total drug volume has increased from 10%, and the government has set a target at 30% in 2012. Still, this is in contrast to the US, Germany and the UK where the generic share of drug volume is 60% (Iizuka et al., 2010).The price of generic medicines are, since 2004, regulated in Japan by limiting the prices to 70% of the original drug (Simoens, 2009). Still, the price of generics in Japan is higher than in the US and in Europe. While the public prices of branded drugs in general are similar to the prices in the US, the price of generics was in 2005 more than twice as high (Danzon et al., 2008). This is however not data specific for oncology drugs, but indicates that there is less of a price incentive in Japan compared to the US and In Europe. Although the price incentive to use generics is not as high as in other countries, there are still large potentials for savings in an increased use of generics, which could free resources for the use

of newer drugs.

Regulatory approval and health economics of cancer drugs

The introduction and use of new drugs is dependent on marketing approval. Approval times for new drugs are in general shortest in the US, while they are longer in the EU and in Japan (Jönsson et al., 2007; Ono et al., 2005). With respect to oncology drugs, these are approved later in Japan than in the EU and in the US. In Table 7, approval dates for oncology drugs launched in Japan in 2007 to 2010 are presented (EMA, 2011; FDA, 2011; Pharmaceutical and Medical Devices Agency, 2011). The average delay in Japanese approval is 33 months compared to the US, and in some cases, for example, ibritumomab and cetuximab, the delay was almost five years. Compared to Europe, the oncology drugs were approved in average 22 months later in Japan compared to the EU. Cancer drugs were thus approved 11 months later in Europe compared to the US (Table 7).

Similar observations were made in a recent study in which the date of approval of 65 new biopharmaceuticals were compared between the US, EU and Japan. Of the 65 new drugs approved in 2002 to 2006, 59 (91%) were approved in the US, 52 (80%) in EU and only 22 (34%) in Japan (Tsuji et al., 2008). The mean approval lag, measured by the time from first approval to approval in each of the countries/regions, was 3.7 months in the US, 7.5 months in EU and 52.6 months in Japan. Among drugs mainly used in oncology, trastuzumab was approved in the US in September 1998, but not until August 2000 in the EU and April 2001 in Japan. The delay of rituximab in Japan compared to the US was three and a half years. Later marketing approval naturally delays the introduction and, at least in the short term, limits the access and usage.

Decision makers in the healthcare sector need to balance a short term need to keep within a limited budget and economic benefits in the long term of introducing and using new technologies. To handle this, different methods have been introduced to fund and introduce new drugs. Cost-effectiveness is one of several factors guiding different types of decisions related to the introduction and uptake of new drugs. Cost-effectiveness has also increasingly been applied as a criterion for reimbursement and/or treatment guidelines in Europe. New treatments which often come at significantly higher costs may need evidence on cost effectiveness to be introduced. Leading countries in Europe in using health economic evidence as a basis for reimbursing new drugs are the UK and the Scandinavian countries (Wilking et al., 2009).

In the US, there are no requirements for the submission of cost-effectiveness data for new and existing medicines to obtain formulary listing under the national health insurance programmes (Medicare and Medicaid). In the private sector, the demand of such evidence by managed care organisations is growing, but the impact of such information, particularly cost-per-QALY data, is not widely or consistently accepted by decision-makers and third-party payers (Redwood, 2006).

In Japan, economic assessments are not currently used in the allocation of drug budgets (Nishimura et al., 2002). The governments approach to cost containment has generally focused on fees reduction in the complex fee-for-service schedule of the Japanese healthcare organisation. Drug pricing is highly regulated in Japan but the influence of economic evaluations in the price setting is limited (Ikegami et al., 2002).

Generic substitution of drugs when the patent has expired is an opportunity to reduce the cost of drugs. As mentioned earlier, generic substitution has traditionally played a minor role in Japan. Hospitals in Japan often both prescribe and dispense drugs (Riku et al., 2005). This creates an incentive to prescribe more expensive non-generics. Escalating drug expenditures has led the government to introduce new policy measures to increase the use of generics. Among the reforms are financial incentives for the hospitals if physicians pre-scribe generics and for pharmacies to substitute branded drugs with generics (Iizuka et al., 2010).

DISCUSSION

The objective of this study was to highlight the differences in patient access to cancer drugs in Japan, the US and selected countries in Europe, and to discuss the potential causes and consequences of the observed variations.

The analysis shows that USA has a faster uptake than Europe, with the exception of France, while Japan has a slow uptake, both when compared to the US and the EU. While Japan spends more money on cancer drugs than all other countries in this report, except for France and the US, most are spent on older branded drugs, where often generic alternatives are available. Differences in the use of the newest therapies across countries indicate that patients are not given the most optimal treatment available.

One of the main reasons for the slow uptake in Japan during the last ten years seems to be a lag of several years in the regulatory approval of new cancer drugs. The tradition in Japan to prescribe branded generic drugs also consumes resources that could be used for newer drugs giving patients access to more innovative treatments.

A large share of the total direct treatment costs of cancer is used for drugs. They may therefore be an easily identified target for cost-containment policies. Scarce resources and limited budgets are important hinders for the introduction and use of new drugs. It is therefore important to consider how healthcare systems and especially hospital budgets should be organized, to accommodate the introduction of new cancer drugs.

Table 5. Direct and indirect cost of cancer in Japan, US, France and Sweden.

Country	Direct cost		Indirect cost			Total		
	Direct cost (MUS$)	Per capita (US$)	Morbidity MUS$)	Mortality MUS$)	Per capita (US$)	Total cost (MUS$)	% of GDP	Per capita ($)
Japan	23,431	188***	4,966	59,711	508**	88,108	0.0214	691
USA	99,000	314***	19,600	124,800	470****	243,400	0.0176	784
France	13,506	226***	657	21,047	359*	35,210	0.0173	582
Sweden	1,890	202***	486	1,772	251*	4,530	0.0138	504

*2004; **2005; ***2006 ****2009.

Table 6. The use of cancer drugs by maturity.

Per capita spending	"Mature drugs" ($/capita)	"New drugs" ($/capita)	Total spending ($/capita)	Age standardized incidence
France	40	21	61	300
Germany	28	13	40	282
Italy	26	11	37	274
Japan	44	12	56	201
Spain	32	17	49	241
Sweden	25	9	34	252
The UK	19	4	23	266
USA	39	21	60	300

Cancer patients are dependent on reimbursement and publicly funded healthcare that function well and allocate appropriate budgetary resources to existing and new drug therapies. The ageing population and increasing incidence of cancer in Japan will lead to new demands for health care and needs for an optimal use of resources.

Variations in the use of new drugs in different countries have increased the focus on the development of policies regarding the use of new medical technologies and, in particular, new drugs. Existing and new treatments need to be assessed on the value both in terms of benefits to patients and their costs. HTAs and economic evaluations are therefore growing in importance in the decisions making process for market access and reimbursement. This does raise the question about the role of economic evaluation on the availability of new innovative cancer drugs. The evidence of any systematic impact of such studies on uptake of new drugs is still lacking. In the UK, National Institute for Clinical Excellence (NICE) and Scottish Medical Consortium (SMC) are the most active producers of HTA reports in Europe. Their recommendations are also, often positive regarding cancer drugs. Nevertheless, the uptake of cancer drugs in the UK is far below the European average. In Japan, there are opportunities for improvement in resource allocation to cancer through collaboration between different stakeholders, the Ministry of Health, Labour and Welfare, national agencies, the medical profession and the industry in order to obtain maximum benefit for patients of available cancer therapies. Apart from the mentioned barriers to treatment access, there are also other factors behind the data on variations in the drug use between countries. For example, there are differences in the relative prices of drugs between countries. Also within countries, the relative price between mature and new drugs may influence the introduction and use of new drugs. The differences in terms of volume may thus not be the same as the differences in the monetary value.

The characteristics of patients and varying treatment practices applied are other factors that may explain part of the variations. Still, the data presented in this study points at the need for

Table 7. Approval dates in Japan and in the US of cancer drugs launched in Japan 2007 to 2010.

Drug	Japan	United States	EU	Approval delay (Japan vs. United States)	Approval delay (Japan vs. EU)
Panitumumab	Apr.2010	Sep. 2006	Dec. 2007	43 months	28 months
Lenalidomide	Jun. 2010	Jun. 2006	Jun. 2007	48 months	36 months
Temsirolimus	Jul. 2010	May 2007	Nov. 2007	38 months	32 months
Lapatinib	Apr. 2009	Mar. 2007	Jun.2008	25 months	10 months
Thalidomide	Oct. 2008	May 2006	Jan. 2008	29 months	9 months
Nilotinib	Jan. 2008	Oct. 2007	Nov. 2007	3 months	2 months
Dasatinib	Jan. 2008	Jun. 2006	Nov. 2006	19 months	14 months
Sunitinib	Apr. 2008	Jan. 2006	Jul. 2006	27 months	21 months
Cetuximab	Jul. 2008	Feb. 2004	Jun. 2004	53 months	49 months
Ibritumomab	Jan. 2007	Feb. 2002	Jan. 2004	59 months	36 months
Sorafenib	Jan. 2008	Dec. 2005	Jul. 2006	25 months	18 months
Nelarabine	Oct. 2007	Oct. 2005	Aug. 2007	24 months	2 months
Bevacizumab	Apr. 2007	Feb. 2004	Jan.2005	38 months	27 months
Erlotinib	Oct. 2007	Nov. 2004	Sep. 2005	35 months	25 months
Average delay				33months	22 months

discussions on how patients should benefit from the advancements of new treatments.

REFERENCES

American Cancer Society (2009). Cancer Facts & Figures.

Berrino F, Atlanta GA, De Angelis R, Sant M, Rosso S, Bielska-Lasota M, Coebergh JW (2007). Survival for eight major cancers and all cancers combined for European adults diagnosed in 1995-99: results of the EUROCARE-4 study. Lancet Oncol., 8(9).

Boyle P, Levin B (2008). IARC World Cancer Report. Lyon: International Agency for Research on Cancer.

Danzon PM, Furukawa MF (2008). International prices and availability of pharmaceuticals in 2005. Health Aff (Millwood) Jan; 27(1): 221-33.

EMA (2011). www.ema.europa.eu.

European cancer observatory, http://eu-cancer.iarc.fr/.

FDA (2011). Drugs@FDA, http://www.accessdata.fda.gov.

Garcia M, Jemal A, Ward E, Center M, Hao Y, Siegel R (2007). Global cancer facts and figures. Atlanta: American Cancer Society.

Heinz Redwood (2006). The Use of Cost-Effectiveness Analysis of Medicines in the British National Health Service: Lessons for the United States.

Iizuka T, Kubo K (2010). The generic drug market in Japan: will it finally take off? Health Econ Policy Law, Dec, 21: pp. 1-21.

Ikegami N, Drummond M, Fukuhara S, Nishimura S, Torrance GW, Schubert F (2002). Why has the use of health economic evaluation in Japan lagged behind that in other developed countries? Pharmacoeconomics, pp. 20-22.

Institute National de Cancer (2007). Analyse Économique des Coûtes du Cancer en France. Paris: Institute National de Cancer.

Jönsson B, Wilking N (2007). A global comparison regarding patient access to cancer drugs. Ann. Oncol., 18(Suppl. 3).

Jönsson B, Nils Wilking, Daniel Högberg, Nahila Justo (2009). Comparator Report on Patient Access to Cancer Drugs in Europe: Accessible at www.comparatorreports.se.

Koinuma N, Ito M, Monma Y (2007). The estimated national cost of cancer in japan. Proceedings from the 66th Annual Meeting of the Japanese Cancer Association. National Cancer Center Research Institute, Japan, http://www.ncc.go.jp/en/nccri/index.html.

Nishimura S, Torrance GW, Ikegami N, Fukuhara S, Drummond M, Schubert F (2002). Information barriers to the implementation of economic evaluations in Japan. Pharmacoeconomics, 20(2): 9-15.

Ono S, Yoshioka C, Asaka O, Tamura K, Shibata T, Saito K (2005). New drug approval times and clinical evidence in Japan. Contemp. Clin. Trials, 26(6).

Pharmaceutical and Medical Devices Agency, Japan http://www.pmda.go.jp/english/service/list_s.html. 2011.

Riku J (2005). Current situation for generic drugs in Japan. J. Generic. Med., 2: 219-31.

Simoens S (2009). Developing the japanese Generic Medicines Market: What Can We Learn from? Eur. J. Gene. Med., 6: 129-35.

Tsuji K, Tsutani K (2008). Approval of new biopharmaceuticals 1999-2006: comparison of the US, EU and Japan situations. Eur. J. Pharm. Biopharm., 68(3): 496-502.

Verdecchia A, Francisci S, Brenner H, Gatta G, Micheli A, Mangone L (2007). Recent cancer survival in Europe: a 2000-02 period analysis of EUROCARE-4 data. Lancet Oncol., 8(9).

Vital Statistics, National Census (2005). National medical care expenditure, patient survey and labor force survey.

Wilking N, Jönsson B, Högberg D, Justo N (2009). Comparator Report on Patient Access to Cancer Drugs in Europe: Accessible at www.comparatorreports.se.