THE BURDEN OF CANCER AND MARKET ACCESS FOR NEW ONCOLOGY DRUGS IN EUROPEAN COUNTRIES

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Abstract

Objective: Aim of the study is to show the burden and cost of cancer, to overview the resources available for cancer treatment in European countries including Romania, and see how these relate to the countries market access for new oncology drugs.

Methodology An analysis of burden of cancer in European countries was performed by looking at various disease indicators from international studies, with a comparison per types of cancer for Romania based on local market research and a retrospective descriptive study on data from National Hospital database for 2008.

Results: The incidence of cancer in European countries is increasing, top three cancers as number of cases are breast, colorectal and prostate cancer. There are wide variations between European countries regarding resources allocated to cancer therapy and absorption of new oncology drugs. Romania is among countries with the lowest spending for cancer treatment in EU although cancer incidence is comparable with other Eastern European countries. The most frequent types of cases hospitalized are for breast, colorectal and lung cancer. Cases are treated in day hospital and inpatient settings, and they are usually associated with intravenous chemotherapy and surgical procedures, resulting in a large number of episodes of care.

Conclusions: In Romania, case-mix data can be used to show the real burden of cancer, in terms of evolution of volume of cases per types of cancer and per diagnoses. Costs of care for cancer patients are high, but most part (2/3) represent indirect costs, such as costs with loss of productivity due to disease, which generate an important economic burden for the society. In this holistic perspective, high costs of new therapies are in most of cases outweighed by future benefits from prolonging life and increased quality of life for cancer patients. Based on the analysis, important issues to be addressed in near future are the inequity in access between different regions to specialized oncologic care, and the delays in market uptake of new oncology drugs due to delayed reimbursement decisions following market authorization. Also, a functional National Cancer Registry (still under development) and additional resources for treatment in outpatient settings could improve patient access to treatment.

Key words: burden of cancer, cost evaluation, market acces for new oncology drugs

Introduction

The main purpose of this article is to show the burden and cost of cancer, to overview the resources available for cancer treatment in European countries including Romania, and see how these relate to the countries market access for new oncology drugs.

Metodology

An analysis on the burden of cancer in European countries was performed using data used from Karolinska Institute Comparator Report on Patient Access to Cancer Drugs in Europe (2009) and two international studies (GLOBOCAN 2002, Ferlay 2006).

Additionally, an analysis of cancer indicators and a comparison per types of cancer for Romania based on local market research (CEGEDIM, 2009) was made. In the same time, a retrospective descriptive study was performed, using data from National Hospital database for 2008 (NSPHHSM).

Data regarding hospital utilization for cancer is from NCOIISB (data available for 2007).

Absolute numbers and percentages were used to compare distributions stratified per age group, sex, type of residence, type of admission, average length of stay, the surgical procedures performed on these cases, and for comparison of different types of cancer.

NCOIISB= National Center for the Organization and Insurance of the Informational and Informatics System Bucharest

Results

Cancer incidence is increasing worldwide. In Europe 30, in 2006, over 2.4 million new cancer cases were diagnosed, which means a 10% increase compared to 2002 incidence.

In the same time, all-cancers mortality rate is slowly starting to recede, with only a 0.37% increase between 2002 to 2006 (GLOBOCAN 2002, Ferlay 2006).

This is due to progress in screening and better available treatments, both reflected in a positive trend in cancer survival.

1. The burden of cancer in European countries

Research of available studies showed that the highest volume of cases in EU 25, Switzerland, Iceland and Norway is registered for breast cancer, followed by prostate and colorectal cancer, with over 300,000 cases each. The first two cancer types are not only frequent, but also show the highest increase of incidence rate between 2002 and 2006: 18.51% for breast cancer and 54.25% increase for prostate cancer. An increasing incidence rate (by 21.46%) for the same period was noted for lung cancer in female, which also presents an increase of the mortality rate (by 21.11%). Causes for evolution of incidence and mortality for types of cancer are documented in literature (such as extensive screening for prostate cancer, or increased tobacco consumption among women for lung cancer); however, there are significant differences in incidence and mortality developments between cancer types, and this is the first divergence noted in the Comparator Report on Patient Access to Cancer Drugs in Europe, from Karolinska Institute (Wilking et al., 2009).

The Comparator Report on Patient Access to Cancer Drugs in Europe (from now on *Karolinska Report 2009*) also shows the geographical divergence across Europe. Hungary's incidence rate is almost double of that of Bulgaria or Romania, and the difference between male and female incidence is much smaller in the Nordic countries such as Denmark, Iceland or Sweden, than among eastern and Southern Europe (Belgium, France, Italy, Greece or Spain). With regard to mortality rates due to cancers in 2006, the Report shows higher than Europe average rates for the Central and Eastern Europe countries.

The most common measurement of the cancer burden used by WHO is Disability adjusted life years (DALYs), which combines both mortality and disability. In 2002, WHO estimated that more than 10 million DALYs were lost in the European countries due to cancer (third most prominent in terms of burden, after mental illnesses and cardiovascular diseases), which accounts, on average for about 16% of all DALYs lost in each country. For the same year, WHO estimated that in Romania about 12% of all DALYs were lost due to cancer.

Besides the burden of cancer on those suffering from cancer and their relatives, there is also an economic burden associated with the disease, in terms of costs of treatment and losses in productivity. Overall, in Europe the expenditure per capita for cancer in 2005 was 148€ (Eurostat, 2007) compared to 124€ in 2004, representing 6.3% of total healthcare expenditure. The health care expenditure for cancer for European countries is between 4-7% of the GDP, significantly lower than the share of the burden of cancer, which, as previously showed, accounts for 16.7 percent of all 'healthy' years lost in the European Union. From the economic burden of cancer, indirect costs (with losses of productivity, informal care from relatives and other non-medical services) account for two-thirds. Direct health care costs and drugs account for approximately 7% and 13% respectively, of all health care costs for cancer.

Country comparisons are difficult, due to different percentages of GDP allocated overall to healthcare, as well as to the different share allocated to cancer treatment. However, lower expenditures (direct costs of cancer) can be observed in the countries with lower percentage of GDP allocated to healthcare (Karolinska Report, 2009). France, Germany, Luxembourg, Austria, Norway, Sweden and Switzerland spend more than 200€ per capita for cancer treatment, followed by Iceland, Ireland, Denmark, Belgium with 180-195€, and with some lower values, but still over 100€, Netherlands, Spain, Italy, United Kingdom, Portugal and Greece. At the lower base, a cluster of countries spend less than 50€ per capita for treatment cancer, such as Poland, Slovakia, Estonia, Latvia, Lithuania and Bulgaria. Romania, with 22€ per capita in 2005, represents the country with the lowest spending for cancer treatment in EU, although cancer incidence compares with other Eastern European countries.

Hospitalization is the largest single item of the direct costs in cancer care in European countries, although the number of patients hospitalized is increasing, and the number of bed days is decreasing (Karolinska Report, 2009). The decrease in number of bed days does not necessarily represent savings, since it is a common trend in most countries to shift care to outpatient settings. Also, there is an increase in availability of new treatments.

Cost of drugs represents an increasing share in the total direct cost of cancer, due to new indications for already approved drugs, as well as introduction of new ones. In the same time, improved treatment may lead to improvements in survival and therefore longer periods of treatment.

In 2004 the estimated cost of drugs reached approximately 13% of total cancer costs in the EU (Jonsson and Wilking, 2007), and this is rising.

Total sales of oncology drugs in Europe have increased substantially over the period 1998-2007 from €4.3 per capita to €26.3 per capita, mainly due to introduction of new innovative drugs. Sales in 2007 in different countries reveal highest values (over 3 million € /100,000 inhabitants) for France, Switzerland, Austria, Denmark and Czech Republic, and lowest (under 500,000€ /100,000 inhabitants) for Latvia, Lithuania, Bulgaria and Romania.

Most of cancer drugs sold (68%) were introduced on the market before 1999, 17% were introduced between 1999-2002, 11% between 2003-2005, and only 3% were introduced in 2006-2007.

Comparison of proportion of new cancer drugs (introduced in 2006-2007) from total cancer drug sales in EU 28 countries in 2007 indicate the lowest uptake for Romania and Bulgaria; almost 80% of sales were for drugs introduced before 1998, and about 5% for those introduced in 2003-2005.

Main barriers in uptake of new oncology drugs are in most countries financially driven, due to the budgets constraints; however, delays between market authorization of new drugs and reimbursement decisions are often very long, as most countries treat these two processes separately. Examples are France, Hungary, Italy, Slovakia, Belgium, Austria, Greece and Spain with almost 1 year or more delay between approval and market access (much longer than the 180 days stipulated by EU regulation), whereas in Central-East European countries delays are more than 200 days (Poland - 214 days, Czech Republic - 270 days and Slovenia - 281 days).

In some countries, as shown in Karolinska Report 2009, delays are dependent on the way of administration, as, for example, cancer drugs in hospital use become readily available in hospitals once approved. Exceptions are Germany and United Kingdom where approval of drugs and reimbursement occur simultaneously; however, some barriers in access arise from limited budgets for drugs at prescribers level (Germany), or strict evaluations from technology assessment bodies (such as NICE in UK) which may generate delays.

2. Case study - the burden of cancer in Romania

A study for the research of local oncology market was conducted by Cegedim in April-May 2009, and involved 60 oncologists from Bucharest, some large towns (>250,000 inhabitants, assimilated with university centers) and medium towns (50,000 - 250,000 inhabitants, assimilated with capitals for districts), the sample being statistically representative for national level.

The results of the study show that an oncologist has on average for follow-up 2,140 patients with any type of cancer. Every month he has about 230 cancer patients for treatment, most of them having breast cancer, followed by those with colorectal and lung cancer.

While for breast cancer and colorectal cancer the ratio between pre-metastasis stages and metastasis stages for new patients is 2/1 and 4/3, for lung cancer most of the patients (3/2) are diagnosed when they already are in a metastatic stage.

Additionally, for breast and colorectal cancer only about 15% of patient in pre-metastasis stage develop metastasis during the first year after the diagnosis.

Not the same profile of evolution for the lung cancer, where 45% of the new patients in pre-metastasis stage develop metastases.

3. Analysis of cancer pathology hospitalized in 2008 in Romania

The analysis was performed for 118 diagnoses of cancer reported as principal diagnosis for day-hospital patients and inpatients discharged from Romanian hospitals (covering both acute and chronic care).

The study refers to patients with breast cancer, colorectal cancer, lung cancer, non Hodgkin lymphoma, lymphatic chronic leukemia, pancreas cancer, brain cancer, gastric cancer, renal cancer, prostate cancer, cervix and ovarian cancer.

These categories account for 202,949 cases, which represents 4% of all discharges at national level in 2008. Out of total number of cases, 88% were treated as inpatients (57% acute, 43% chronic cases), and 12% were treated as day-hospital, in hospital ambulatory settings.

From all cases of cancer reported by hospitals in 2008, one quarter are over 70 years old and 53.6% are men. Most of the patients (over 60%) are from urban areas, 70% of cases are treated in hospitals located in their district of residence, while 30% of them have to travel in another district for receiving care. The majority of patients (98.3%) are treated in acute care facilities.

The average length of stay (ALOS) is about 7 days for acute care patients, and 11 days for chronic care patients. Regarding the type of admission (Figure 1), about half of the cases are admitted with referral from the specialist physician.

The costs of hospital treatment for cancer cases are high, since 87.6% of cases have also a secondary diagnosis (complications and/or co-morbidities), and for 95% of patients at least one medical procedure was reported. Unfortunately, the lack of cost data on hospital services for these patients sets some limits for the analysis of burden of cancer related to hospital services.

Distribution of number of cases per type of cancer (Figure 2) shows that on first places are colorectal, lung and breast cancer, each of them accounting for almost 20% of all inpatient cancer pathology.

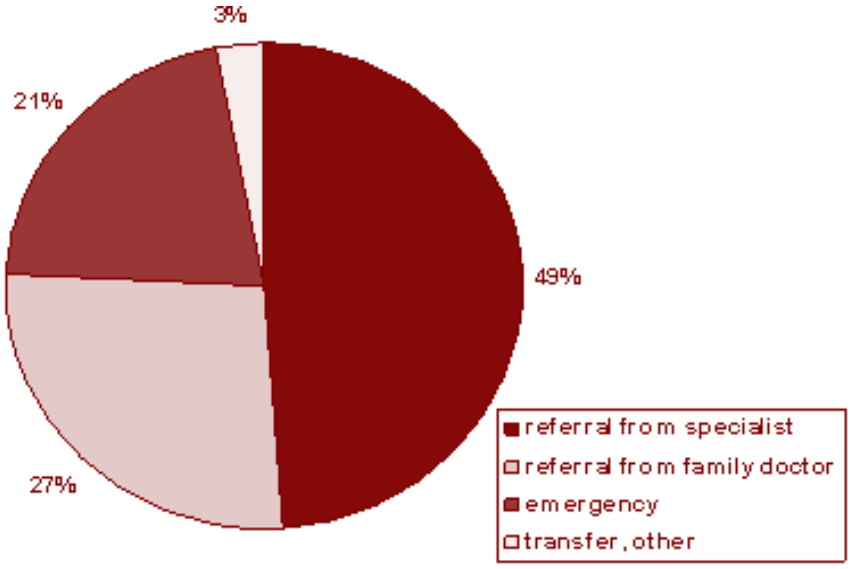
Almost 40% of inpatient cases with cancer have one of the following diagnoses:

- *Malignant breast tumor*, unspecified - 14,329 cases, representing 8.4% from all cancer cases;
- *Malignant rectal tumor* - 11,224 cases, which represent 6.6% of all cancer cases;
- *Malignant ovarian tumor* - 10,944 cases*Malignant tumor of bronchial and lung, unspecified* - 10,202 cases, which represent 6% of all cancer cases;
- *Malignant tumor in upper-external quadrant of the breast* - 9,711 cases, representing about 5.7% of all cancer cases;

- *Malignant tumor upper lobe, bronchial and lung* - 9,545 cases;
- *Malignant tumor of prostate* - 8,729 cases, representing 5.1% of all cancer cases;
- *Malignant tumor of cervix* - 5,781 cases.

In day-hospital care 23,614 cases were treated, totalizing 40,976 episodes, with a mean of more than 15 days care services to an episode.

Figure 1 – Distribution of cancer cases by type of admission to hospital in 2008



Data source: NSPHHSM, 2008

Breast cancer

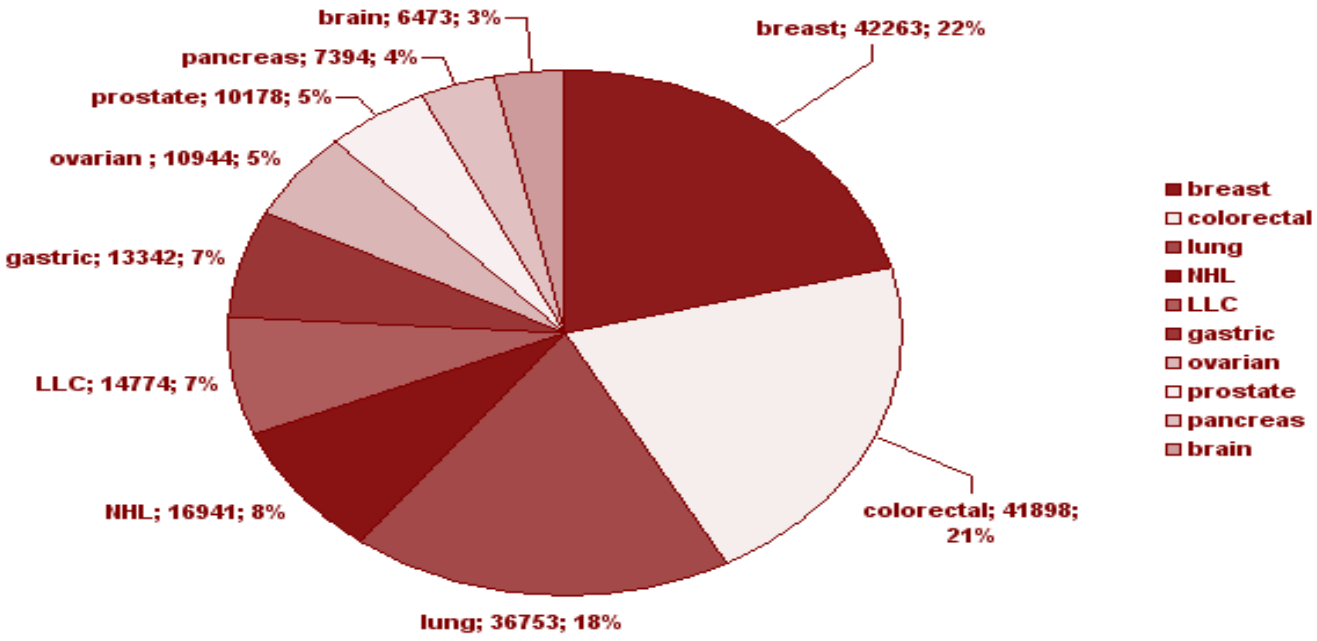
From the total of 42,263 cases, some 9,070 cases were treated in day hospital settings, accounting for 17,442 services, with an average of 15.2 visits or services per case treated.
From all inpatients with breast cancer, the 70 years old and over represent 15.7% of the cases, which is lower comparing to the percentage when considering all cancer types (25%).
The ALOS is 6.6 days, slightly lower than the mean for all cancer cases (7 days).
A difference in type of admission to hospital could be noticed, almost 70% from breast cancer patients are admitted with referral from specialist, while for all types of cancer 49% of patients have a specialist referral.

Only to 16% of breast cancer patients were performed some surgical procedures, and the most frequent was simple mastectomy, unilateral and excision of breast injuries. Intravenous chemotherapy (1-6 hours) was reported as secondary procedure for 12,645 cases (about 30% of total number of cases with breast cancer).

Colorectal cancer (CRC)

A total of 37,641 cases were treated for CRC, out of which 4,257 cases treated in day-hospital settings, accounting for 7,858 services, with a mean of 11.3 sessions/case.
A higher percentage (28.6%) are patients over 70 years old, than the mean for all cancers (25%); 56.4% from cases are men. Most of cases (55.3%) are admitted with a referral from the specialist (comparing to 49% for all cancer types).

Figure 2 – Distribution of number of cancer cases by localization of disease for all discharges in 2008



Data source: NSPHHSM, 2008

From all inpatients with CRC, to 23.2% were performed some surgical procedures, and the most frequent was the right hemi-colostomy with anastomosis and the limited excision of large bowel with anastomosis.
Intravenous chemotherapy (1-6 hours) was reported as secondary procedure for 9,667 cases.

Lung cancer (LC)

For this pathology 34,059 inpatients were reported. In addition 2,694 were treated as day-hospital, with a mean of 10.1 sessions per case. 20.9% from inpatient cases are over 70 years old.
An important finding is that lung cancer is more frequent in men than in women, 81.5% of discharges are men, comparing to 53.5% for all cancer cases. For this type of cancer an important percentage come from rural areas (42.8%).
From all inpatients with LC, to 5.2% were performed some surgical procedures, and the most frequent were lung lobotomy and fibro-bronchoscopy with biopsy. Nevertheless, a large number of cases (12,413) have intravenous chemotherapy (1-6 hours) reported as secondary procedure, and 11,020 cases have injections with steroids.

Non-Hodgkin lymphoma (NHL)

There was a total of 16,941 cases hospitalized (about 9% from all cancer cases), from which 1,721 NHL cases were treated in day-hospital settings, with a mean of 7 sessions per case.
For this type of cancer more patients have to travel for receiving hospital care, since 42.9% are residents in other districts than the one where hospital is located. The ALOS is 5.6 days, shorter with 1.4 days than the average for all cancer types.
Most of the patients (54.5%) are admitted with referral from the family doctor, and not from the specialist, as expected according to situation for other types of cancer.
Only 2% of cases with NHL have surgical procedures, like the biopsy of lymphatic node and the excision of cervical lymphatic nod.
Over 5,000 cases have reported intravenous chemotherapy (1-6 hours) as secondary procedure, and over 5,800 cases injections with steroids.

Chronic Lymphatic Leukemia (CLL)

A total of 14,774 cases (7.3% of all cancer cases) were hospitalized in 2008. A number of 2,357 cases were treated as day-hospital, accounting for 2,900 services, with a mean of 2.7 sessions per case.
The majority of cases have no surgical procedures. Intravenous chemotherapy (1-6 hours) was reported for 2,214 cases.

Pancreas cancer

A number of 6,789 cases were treated as inpatient and 605 cases as day-hospital, with a mean number of 10.5 sessions per case. More men (60.7% of cases) were hospitalized for this type of cancer and the ALOS is slightly higher than the mean for all cancers – 7.2 days comparing to 7 days.
The percentage of cases admitted on emergency basis is higher than the mean for all cancer types, with 36.8% versus 21%.
From all cases with pancreas cancer, 22.6% have a surgical procedure.
For 18% of cases intravenous chemotherapy (1-6 hours) was reported as secondary procedure.

Brain cancer

Although with lower volume of cases than for other types of cancer (6,093 inpatients and 380 cases treated in day-hospital), this type of cancer could be very important since the inpatients are obviously younger than for other types of cancer (only 10.9% are over 70 years old, comparing to 25% the mean percentage for all cancer types).
Additionally, more patients need to travel in other district for hospitalization (48.7%).
ALOS is longer (8.2 days) than for other types of cancer.
Another important aspect is the high percentage of cases admitted as emergencies, 38.5% versus a 21% for all cancers. From all inpatients, 21.4% underwent surgical procedures, the most frequent being the ablation of cerebral tumor and ablation of cerebellums tumor. CT scan was performed for 1,940 of cases with brain cancer.

Renal cancer

A total of 4,215 cases (2.3% of all cancer cases) were treated as inpatient and day-hospital care.
A smaller percentage (19.5%) are over 70 years old than for other types of cancer, so patients tend to be younger.
ALOS was 8 days, and 34.5% of cases were admitted with referral from the family doctor versus the average of 27% for all types of cancer.
This is a type of cancer with a high rate of surgical procedures, with 30.5% of cases having a surgical procedure.
The most frequent are radical nefrectomy and total unilateral nefrectomy.
Fewer than 10% of these cases have intravenous chemotherapy (1-6 hours) as secondary procedure.

Gastric cancer

A total of 13,342 cases (7.4% of all cancer cases) were hospitalized for gastric cancer, for which the majority were treated as inpatient (12,583) and 759 as day-hospital care.
The total number of services received was 1,205, with a mean of 5.8 sessions per case.
An important percentage of cases (32.9%) are over 70 years old. This cancer type affects men more than other cancers, as 66, 2% from all discharges are men.
The ALOS is higher than the mean (8.3 days comparing to 7), and the number of emergency admissions is also high (30.4%).
For the 21.8% of cases with surgical procedures, more often were performed procedures like total gastrectomy and exploratory laparatomy.
About 1/3 of cases had intravenous chemotherapy (1-6 hours) recorded as secondary procedure.

Prostate cancer

From a total of 10,178 cases (5.1% of all cancer cases), 8,729 cases were inpatient and 1,449 cases were treated as day-hospital. Patients with prostate cancer appear to be older than the average for all types of cancer, since 56.7% are over 70 years old. They are more often admitted as emergency than other patients with cancer, and they stay less in hospital (ALOS of 6 days). The most frequent surgical procedures performed on these patients were bilateral orhidectomy and transurethral resection of prostate. About 39% of patients underwent a surgical procedure.

Cervix and ovarian cancer

In 2008, a number of 19,506 cases having a diagnosis of a cervix cancer were hospitalized, and 10,944 of cases had a malignant ovarian tumor.

Distribution of hospital resources for cancer care

In 2007 a number of 3,420 hospital beds were available in oncology wards, nationwide. In spite of this apparently large number of beds, an analysis of geographic distribution pointed out that there is a wide inequity among districts in the available number of beds. Although all districts have at least one oncology ward in hospitals, some districts have a very small number of oncology beds (for example Giurgiu with 5 beds), some others, as the university centers, have the highest number of oncology beds. Bucharest has a number of 775 beds, highest of all districts. There was an average of 81 beds per district, with a median of 50. A large variation among districts from the point of view of volume of oncology beds is shown by the 41.5% coefficient of variation. The university centers, like Bucharest, Cluj, Timisoara, Iasi have the highest number of beds, with Bucharest having 7 oncology wards.

As a general feature, most hospital facilities designated for oncology are concentrated nearby university centers, mostly in the middle of the country and in Bucharest. People with cancer diseases from remote areas, peripheral districts, need to travel often long distances at regular intervals to receive specialized care in hospitals.

Conclusions

In Romania, case-mix data can be used to show the real burden of cancer, in terms of evolution of the volume of cases per types of cancers, and for various diagnoses, and could be used in further studies for the estimation of the economic burden associated with the disease. A profile of the patient with a certain type of cancer can be drawn. Available data shows that the most frequent types of cancer are breast, colorectal and lung cancer. Prostate cancer, currently on the third place as volume of cases in the European countries, is placed only on the eight place in Romania.

A quarter of cancer patients are over 70 years old, with higher percentages of this age group for colorectal, gastric and prostate cancer. Brain cancer, kidney and lung cancer affect more the younger population. Colorectal cancer, pancreas, breast cancer, brain and kidney cancer are very often associated with higher volumes of surgical procedures performed (over 20% of cases). Intravenous chemotherapy is most common procedure reported among all types of cancer patients.

Analysis revealed some important issues that need to be addressed in future. One of them is the inequity in access of patients from various regions of the country, especially the remote zones, to the specialized oncology care in hospitals. For these patients day-hospital care is not accessible, and most of them need to be hospitalized even for short periods, so that services like chemotherapy, administration of cancer drugs could be accessed by these patients. Especially for this category, newly available oral drug therapies may represent a viable alternative to improve access to care.

Another issue is the high cost of cancer treatment, including cost of hospitalization, drug therapies, but even more important, the non-medical and indirect costs such as transportation, time of caregivers, loss of productivity due to disease. Some studies estimated that 2/3 of cancer costs arise from indirect costs, showing this is the main burden on society. For this matter, costs of new drug therapies, which are often quite high, can offset the long term cost of disease and societies should be aware of the benefits of such therapies in the long run. Other barriers in patient access to new oncology drugs come from delays with the reimbursement process, following introduction of new drug on the market.

The cost of medical care in hospital might be high, considering the length of stay and procedures delivered. However, the lack of data on costs of hospital services at national level makes difficult an estimation of the economic burden of cancer in Romania. A functional National Cancer Registry (still under development) and additional resources for treatment in outpatient settings can provide evidence for resource allocation and even reduce costs in hospitals, and most important, improve accessibility of patients to treatment.

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