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- H. 知的財産権の出願・登録状況
1. 特許取得
なし
 2. 実用新案登録
なし
 3. その他
なし

Ⅱ. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

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Ⅲ. 研究成果の刊行物・別刷

Review Article: Strategy for drug discovery at pharmaceutical companies

Proposal for the Breakdown of Increased Cancer Healthcare Cost and Its Improvement

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Technological progress in the field of cancer treatment can be expected to accelerate in the future, giving hope to such patients. At the same time, there is concern that cancer care will become more expensive. It is indispensable to minimize the economic burden of patients to deliver technological advances in treatment. It is important for the physician engaged in cancer care to recognize the economic burden of patients and to reduce this burden as much as possible. The Cancer Control Act was enacted in 2007 to promote work on cancer control using all the resources of the nation, and this should surely entail financial support. In order to take advantage of innovations in cancer care, reform of the payment system to lighten the economic burden of the patient would be a pressing necessity.

Key words: economic burden – cancer economics – cost of cancer – molecular targeted drugs – healthcare reform

EXPANDING MEDICAL EXPENSES OF CANCER

The national medical care expenditure in fiscal year 2010 in Japan announced at the end of September 2012 was 37 420 200 million yen, an increase of 3.9% compared with the previous fiscal year. The national income ratio, which was 8.1% in 2000, became 10.7%. The medical expenditure tends to increase sequentially when a slump in economic growth is prolonged. As for the medical care expenditure by age group, it was 55.4% for those 65 years old and older, 45.1% for those 70 years old and older and 33.3% for those 75 years old and older. These were 48.3, 37.4 and 25.1%, respectively, in 2000. Rapid aging of the population was found to be the major factor in the increase in medical care expenditures.

The medical care expenditure per capita was 292 200 yen, a record high. This generally represents an increase in each age group, and it is thought that technological progress is a major factor in the increase. The medical care expenditure

for cancer in 2010 was 3 031 200 million yen. In total, 498 800 million yen were spent for colorectal cancer, 381 100 million yen for cancer of the trachea, bronchus and lung, 323 900 million yen for stomach cancer, 252 900 million yen for breast cancer and so on. The ratio of the cancer expenditure to the total medical expenditure was 11.2%. The growth rate of expenditures for cancer was 45.7% from 2000 to 2010, while that of the national medical care expenditure was 24.1% (Fig. 1). The increase in the cancer care expenditure is really remarkable.

In order to tackle with the high price of new technology and new therapeutic drugs, Central Social Insurance Medical Council in Japan has begun to discuss the possibility to introduce technology assessment in the actual public health insurance system. The point at issue is how to reduce healthcare cost and to improve the quality at the same time. Some indicators such as cost-effectiveness and quality-adjusted life years is taken up for the discussion.

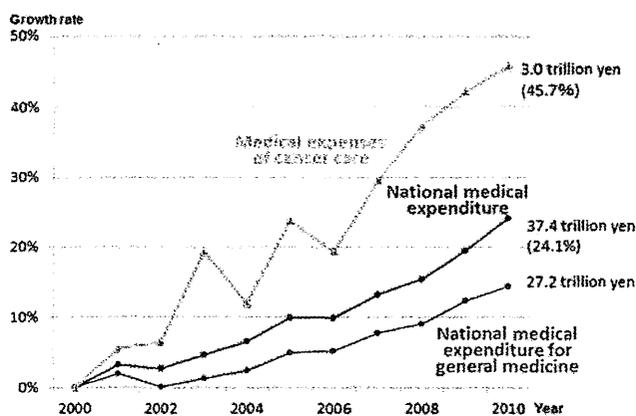


Figure 1. The trend of increase of cancer care expenses from the year 2000. The growth rate of expenditures for cancer was 45.7% from 2000 to 2010, while that of the national medical care expenditure was 24.1

INCREASING ECONOMIC BURDEN OF PATIENTS

Along with the increase in the national medical care expenditure, the economic burden of patients as well as the financial burden of the country became heavier. The co-payment for patients was raised from a fixed charge to 10% in 1984. The ratio of the patient's co-payment was raised from 10% to 20% in 1997 and from 20% to 30% in 2002. Thereafter, the co-payment of 30% (~15% for all ages) has continued. Since the medical care expenditure continued to increase and the co-payment ratio is always 30%, the actual economic burden for the patient increases constantly.

The increase in the cancer care expenditure largely resulted from the increase in the number of cancer patients along with the aging of the population. Simultaneously, rapid technical progress influences the increase in the cancer care expenditure to a great extent. Aging factor and other factors including technical progress have contributed in 46 and 54%, respectively, to the increase in the national medical care expenditure from fiscal year 2007–2008 according to the statistics of Ministry of Health, Labour and Welfare.

The cancer care expenditure per patient increased 9% for 5 years from 2002 through 2007, whereas the average annual salary has decreased 11% from 4.61 million yen in 2000 to 4.12 million yen in 2010 according to National Tax Agency 'Private salary investigation'. This means that the economic burden of patients has become heavier.

The actual situation of the economic burden of patients with cancer is not fully grasped. Therefore, we investigated 40 institutions such as university hospitals and cancer centers through the country (2010 through 2011). This was a self-completed survey asking patients with cancer to list the expenses related to cancer based on a household account book or on the receipts. Moreover, we got clinical information from physicians upon the approval of the patients and conducted a data linkage of the patient survey (1).

As a result, the average annual out-of-pocket expenses for cancer were 864 000 yen ($n = 2022$). The direct expenses of hospitalization, ambulatory care and transportation were 294 000 yen (applicable patients: 68.2%), 259 000 yen and 56 000 yen, respectively. For indirect expenses, the premium of private insurance and cost of alternative medicine were 380 000 yen (applicable patients: 55.0%) and 213 000 yen (32.3%), respectively (Fig. 2).

On the other hand, the refunds and benefits were 624 000 yen on average. The benefits from private insurance, medical refunds and tax refunds were 1 140 000 yen (applicable patients: 43.3%), 242 000 yen (48.2%), 62 000 yen (22.3%), respectively. The substantial economic burden when refunds and benefits were deducted from out-of-pocket expenses was 240 000 yen. Private insurance in Japan complements public insurance, and many patients are aided by this benefit.

For gastric cancer ($n = 158$), the out-of-pocket expenses and the refunds/benefits were 724 000 yen and 664 000 yen, respectively. These were 931 000 yen and 636 000 yen for colorectal cancer ($n = 244$), 1 102 000 yen and 681 000 yen for lung cancer ($n = 302$), 687 000 yen and 496 000 yen for breast cancer ($n = 773$), and 489 000 yen and 246 000 yen for prostate cancer ($n = 102$), respectively. The out-of-pocket expenses and the refunds/benefits differ considerably by types of cancer due to the large variety of treatments and prognosis and so forth.

The out-of-pocket expenses and the refunds/benefits were 1 217 000 yen and 652 000 yen for molecular targeted treatment ($n = 494$), and were 1 156 000 yen and 615 000 yen for the treatment of hematological malignancies, respectively. The out-of-pocket expenses (direct and indirect expenses) were 1 104 000 yen for chemotherapy using Trastuzumab ($n = 206$), 1 160 000 yen for Gefitinib ($n = 61$) 1 242 000 yen for Imatinib ($n = 213$), and 1 533 000 yen for Bevacizumab ($n = 160$), respectively.

DIFFERENCE IN BURDEN BY CLINICAL STAGE

The economic burden differs according to the clinical stage. The out-of-pocket expenses and the refunds/benefits were 610 000 yen and 509 000 yen in Stage I, 683 000 yen and 478 000 yen Stage II, 982 000 yen and 754 000 yen in Stage III, and 1 284 000 yen and 778 000 yen in Stage IV, respectively. The expenditures for alternative medicine and supplements tended to increase with the seriousness of the disease. The annual length of hospital stay was 20.6 days in Stage I, 23.3 days in Stage II, 37.1 days in Stage III and 44.3 days in Stage IV, respectively. The number of visits to hospital was 14.2 times in Stage I, 18.9 times in Stage II, 22.4 times in Stage III, and 24.9 times Stage IV, respectively. Looking at this according to the types of therapy, the length of stay was 27.8 days for surgery, 39.9 days for chemotherapy and 32.6 days for radiotherapy. The number of visits was 18.6 times for surgery, 24.6 times for chemotherapy and 29.3 times for radiotherapy.

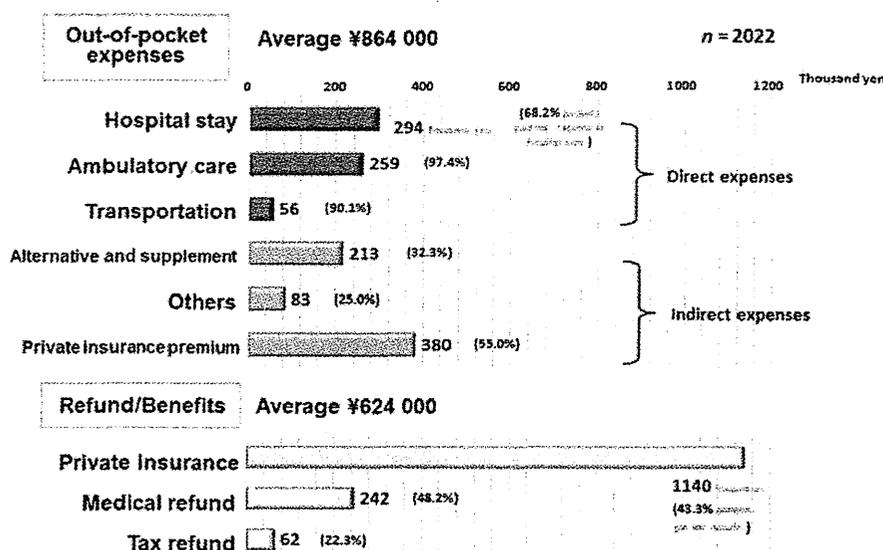


Figure 2. Annual economic burden of cancer patient. The average annual out-of-pocket expenses for cancer were 864 000 yen and the refunds and benefits were 624 000.

The economic burden also differed according to the ratio of the patient’s co-payment. The out-of-pocket expenses and the refunds/benefits were 934 000 yen and 746 000 yen with a co-payment of 30% ($n = 1443$ average age 58.5 years old), respectively. In other words, the actual burden was 188 000 yen. However, these were 672 000 yen and 275 000 yen with a co-payment of 10% ($n = 554$, 75.4 years old). In this case, the balance was 397 000 yen, which was heavier than burden with a co-payment of 30%. In case of a co-payment of 10%, the average benefit from private insurance (683 000 yen on average for 32.4% of the patients) and the medical refund (86 000 yen for 54.8% of the patients) are much smaller than that of a co-payment of 30%.

Around 69% of the patients had economic worries ($n = 2037$). The mean out-of-pocket expense (752 000 yen) of the patients without economic worries was three-fourths that of the patients (987 000 yen) with economic worries (Fig. 3). In the viewpoint of promoting work, if the length of stay is shortened and the number of hospital visits is decreased, the patients with cancer would have more working opportunities. For example, in patients with breast cancer ($n = 774$), the average length of stay was 14.1 days and the number of visits was 20.4 times. If the hospitalization included Saturday and Sunday for 4 days and ended on a half day, the suspension of work due to treatments would be almost equal to annual paid holidays.

DECLINING THE TREATMENT DUE TO ECONOMIC REASONS

According to our survey, three-fourths of the patients with colorectal cancer felt that the medical expenses under public insurance were heavy ($n = 232$). Half of the above patients

felt that the premium of private insurance and the costs of alternative medicine were also heavy. Many patients think that the indirect expenses are crucial. Sixty percent of patients with colorectal cancer were obliged to withdraw deposits and savings, and 10% managed to pay the medical costs by borrowing from a family member or relative ($n = 249$). In our survey, the average age of patients with colorectal cancer was 64.4 years and a pension was the sole regular income for many patients. For one-third of the above patients, the household income was between 1 million and 3 million yen. For 40% of the above patients, the household savings were less than 7 million yen.

Although medical treatment cannot be denied for economic reasons under Japanese universal health insurance system, patients who refused an expensive therapy have recently increased. According to our survey for physicians engaged in cancer care ($n = 1176$, clinical experience: 17.8 years), 1.6 inpatients and 1.5 outpatients per month gave up the most appropriate treatment due to some economic reason.

Sixteen percent of the above patients had to cancel the scheduled treatment, 56% could not avoid changing the treatment and 13% were obliged to interrupt the treatment. It is an extremely serious situation for patients, and also for their physicians, when patients must forego necessary treatments, especially considering that refunds are available expensive medical treatments. Since molecular-targeted drugs are expensive in general, it is not rare to modify or withdraw these drugs such as Bevacizumab or Sorafenib for the treatment of solid tumors and Rituximab or Imatinib for hematological malignancies. In the case of Bevacizumab, for instance, a planned regimen such as Bevacizumab + XELOX was modified to XELOX. In the same manner, some regimens were modified from Bevacizumab + mFOLFOX6 to mFOLFOX6, and from Bevacizumab + FOLFIRI to FOLFIRI.

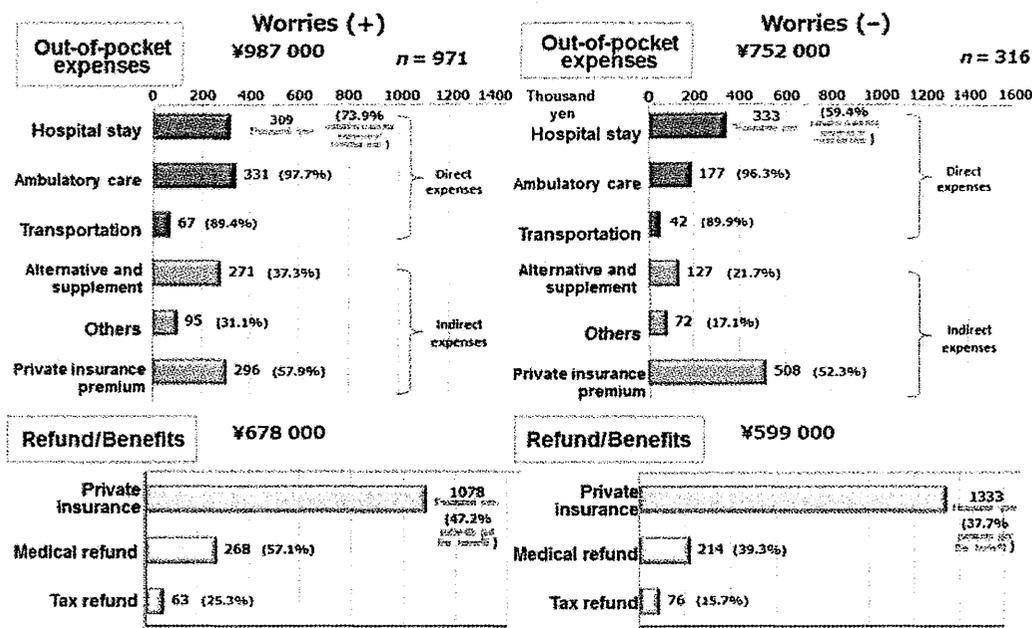


Figure 3. Annual economic burden of cancer patient by worries about economic problems. The mean out-of-pocket expense of patients without economic worries was three-fourths that of the patients with economic worries.

We calculated the change in drug costs on the basis of the payment system for medical services in 2011 (the standard treatment for a male patient of 60 kg and 165 cm) in the above three cases. Drug costs were decreased by 48.6%, from 468 000 yen to 228 000 yen, by 49.8%, from 299 000 yen to 149 000 yen, and by 35.4%, from 232 000 yen to 82 000 yen, respectively. Given the payment system, if one half of the current drug costs is supported by a second or third party, more patients would be able to undergo optimal treatment.

IMPORTANT ROLE OF MEDICAL REFUND SYSTEM

There are limits to the expenses patients must pay based on their income. The medical refund system is a safety net that complements the health insurance system (co-payment of 10–30% by the patient). The government expenditure for medical refunds has doubled during the 8 years from 2000 through 2008 (1713 billion yen), suggesting that the economic burden on patients has been increasing. The medical refund system was founded in 1973, and many regulations were introduced afterwards. User cannot easily understand this complicated system. However, the detailed rules of the system have come to be understood by patients, since this system is requested by the patients the number of users has increased. This system is explained in detail when required in the consultation support center of cancer center hospitals. Forty-eight percent of patients with cancer and 80% of patients administered molecular-targeted treatment applied

for this system, which has recently become indispensable. We examined how the medical refund system reduces patients' payments using the survey data. We found that this system lightens the patients' burden by 32.5% on average (n = 686) (Fig. 4). These are 35.4% in patients with colorectal cancer and 36.6% in patients from 40 to 49 years old.

MEASURES AGAINST RISING COST OF CANCER TREATMENT

There are many requests for relief from the economic burden from patients with cancer, who want the cost of anticancer drugs to be reduced, the ceiling for reimbursement to be lowered, the percentage of co-payment to be lower than for other diseases and that more information about the economic burden should be given to patients and so on (n = 236). Measures corresponding to the patients' suffering from the economic burden of treatment are very urgent. The problem of so-called 'economic refugees with cancer' (patients who cannot undergo the adequate treatment for economic reasons) might be addressed along with the accelerating technological progress.

These measures could be broken down into three levels: physicians' consideration in the clinical setting, better operation of the actual system and drastic healthcare reform. The first level includes the promotion of ambulatory care as an alternative to hospitalization, shortening the duration of hospitalization, reducing excessive testing and medication, the use of cheaper generic drugs and adequate explanation about the costs. The second level includes reductions in the ceiling

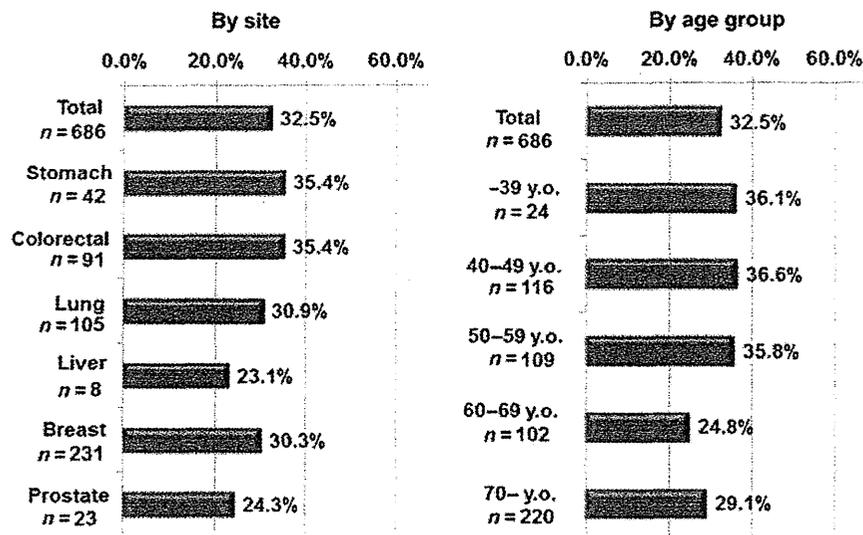


Figure 4. Percent reduce of the patients' payments with medical refund system. The medical refund system lightens the patients' burden by 32.5% on average. y.o., years old.

for reimbursement and improvement of the so-called 'drug lag' (shortening the approval process for new drugs) and 'device lag' (that of new technology). A few patients are obliged to the new drugs by way of the personal import on their own expense.

For the third level, it is necessary to review the proper percentage of co-payments depending not only on age but also on the seriousness or other characteristics of the disease to relieve the excessive economic burden of the patients. The national income has been decreasing while medical costs per person have been increasing for the past decade and there is surely a limit to the economic relief that can be provided by the medical refund system. This is because the payment of medical refunds has greatly expanded and the government will suffer from insufficient funds.

Information about patients' out-of-pocket expenses in other countries would be useful for our healthcare reform, although health insurance systems differ country by country and a simple comparison might lead to misunderstandings. Medical care is free of charge as a rule in such countries as the UK, Canada and Australia (excluding drug costs). The out-of-pocket expenses of a patient is 10 euros per day for hospitalization and 10 euros per quarter for ambulatory care (it is free of charge if there is a letter of introduction) in Germany. There is an upper limit of 80 krona per day (~9600 yen) for hospitalization and an upper limit of 900 krona per year for ambulatory care in Sweden. The economic burden of a patient is rather light in these countries.

The percentage of out-of-pocket payments is 20% for hospitalization and 30% for ambulatory care in France, whose system resembles that of Japan. However, some private insurance can bridge most of the payment gaps, and medical care for 30 diseases including cancer is free of charge. This is an important example of how the heavy economic burden of long-term and expensive treatments can be avoided by

patients. That is, it turns out that the out-of-pocket payments in Japan act at a particularly high level for developed countries. It is extremely important to secure necessary healthcare resources from and to drastically rationalize the distribution of medical expenditures. Such reform of the current insurance system is inevitable because of the need to cope with constantly advancing innovation. Healthcare systems in some western countries have introduced the concept of priority (so-called 'triage' not only in emergency medicine but also in general medicine), which serve as a reference for Japan.

The total sum of out-of-pocket payments by patients with cancer in Japan comes to 461 billion yen per year based on the data of our survey. Therefore, making cancer treatment free of charge would be possible in Japan if an additional 500 billion yen in public spending were made available. There is little risk of moral hazard (increase of the number of patients and medical expenditures caused by the lack of fee) since the diagnosis of cancer is concrete. Financial support depending on the type of disease is more rational than that depending on the age group (such as charge-free medical care for the elderly ~40 years ago), because the elderly vary in health status significantly even at the same age.

The average age of patients with cancer exceeds 60 years old. The income is restricted to a pension in many cases and the out-of-pocket expenses for cancer treatment are often covered by drawing on savings. When looking at the annual household income (tax included), 31% of the patients earned 1~3 million yen or less and more than half is <5 million yen (n = 2928, average age 61.7 years old). As for the amount of household savings, in 40% it was <7 million yen and in half it was <10 million yen. Many senior citizens tend to reduce daily living expenses on the preparation for the high probability suffering from serious illness in the future. The domestic demand is reduced if those of middle

and advanced age, which occupy the majority of the population, refrain from consumption because of worries about future illness. It is essential to stabilize the pension system, but the solution to this problem will likely take time before anxiety about the future is alleviated. Relief from the economic burden of cancer care must be a reasonable certainty for the elderly, and it would be one of the most cost-effective measures to implement.

CONCLUSION

Technological progress in the field of cancer treatment can be expected to accelerate in the future giving hope to such patients. At the same time, there is concern that cancer care will become more expensive. It is indispensable to minimize the economic burden of patients to deliver technological advances in treatment. The economic burden of the patient might influence the outcome of treatment, and the costs would therefore be an important element in high-quality cancer care, as ASCO (American Society of Clinical Oncology) noted (2). It is important for the physician engaged in cancer care to recognize the economic burden of patients and to reduce this burden as much as possible. The Cancer Control Act was enacted in 2007 to promote

work on cancer control using all the resources of the nation, and this should surely entail financial support. In order to take advantage of innovations in cancer care, reform of the payment system to lighten the economic burden of the patient would be a pressing necessity.

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Conflict of interest statement

None declared.

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