Chapter 1

Basic Concept of This Book

1 Purpose

How many cancer patients are there in our country? In this country, there exist no data that should be most fundamental in making future market projections for new anti-cancer drug development.

The reason is that no system has yet been established on a nationwide scale to get hold of the complete number of patients (full computerization of patient records, mandatory registration of cancer patients, etc.). To find a solution to this issue, our company have devised a calculation method of cancer patients.

It is a method to calculate the total number of cancer patients in our country and allow future projections (estimations) by using a combination of existing statistical data. To be more specific, the method takes advantage of the "Vital Statistics", "Patient Survey" and survival rates of various types of cancer (1- to 5-year survival rates) in calculating numbers of patients (new-onset patients and all-surviving patients) and estimating numbers of patients up to 10 years later.

This method, first announced in the "Number of Cancer Patients and Actual Drug Usage"[1] published in 1990, calculated numbers of patients for 20 types of cancer and the total number of cancer patients.

Subsequently, our company have published marketing books on cancer market projections [2-8] and released the calculation and estimation of numbers of patients by cancer types.

Additionally, our unique calculation method was given opportunities for presentation at the 112th meeting of the Pharmaceutical Society of Japan and for publication in the thesis later (Pharmaceutical Library Bulletin 37(3)195-201, 1992)[9].

This book, based on the up-to-date statistical data published subsequently, utilizes the calculation method of our company in calculating the numbers of new-onset patients for 19 individual types of cancer and the total cancer patients. Furthermore, the number of total surviving patients, which could not be grasped by using the hitherto available data only, has been calculated for each type of cancer for the first time in our country. Also, future projections for the numbers of new-onset patients and total surviving patients have become available, which provide indispensable data for projecting future market of

new anti-cancer drugs.

It is wished that as many parties concerned with anti-cancer treatments and development of anti-cancer drugs as possible will utilize this book to serve their purposes.

We are determined to further the accuracy in calculating the number of cancer patients upon renewing various statistical data and collecting new data presented at conferences and published in registered surveys.

2 Individual Types of Cancer

This book deals with the following 19 types of cancer (Table-1).

Classification codes used in the Table are identical with those in the International Classification of Diseases (ICD-10) used in the "Vital Statistics". Malignant neoplasm (cancer) belongs to C00-C97 classification. While ICD uses classification by sites, our book classifies by types of cancer, the reason being that in clinical practice treatments are administered not by finely defined sites but by regions or diseases such as malignant lymphocyte, since data such as treatment results or patient profiles are classified by types of cancer. Therefore, the 19 types of cancer in this book correspond to 31 sites according to the ICD classification.

The criterion of selecting types of cancer to be dealt with is whether the cancer accounts for over 1% of total deaths of cancer (malignant neoplasm) patients in the Vital Statistics. In specific terms, the cancer with deaths of more than 3,535 patients, which accounts for 1% of the total 353,499 cancer deaths in 2010. It ranges in 19 types of cancer from lung cancer with the most deaths (69,780) to multiple myeloma with the least deaths (4,237).

However, cancer of duodenal papilla is the only exception (with 993 deaths). Duodenal papilla cancer is largely classified as biliary tract cancer along with gallbladder cancer and bile duct cancer. In the Vital Statistics, these three cancers are not classified under biliary tract cancer, with each placed under separate classifications. Accordingly, the numbers of patients of these three classified under biliary tract cancer are calculated individually.

(Table-1) 19 Types of cancer dealt in this book

No.	Types of cancer	ICD classification	statistical data used as the basis for estimating the number of patients
1	esophagus cancer	C15	Vital Statistics
2	gastric cancer	C16	Patient Survey
3	colorectal cancer	C18～C20	Patient Survey
4	liver cancer	C22	Patient Survey
5	gallbladder cancer	C23	Vital Statistics
6	bile duct cancer	C24.0	Vital Statistics
7	duodenal papilla cancer	C24.1	Vital Statistics
8	pancreatic cancer	C25	Vital Statistics
9	lung cancer	C34	Patient Survey
10	breast cancer	C50	Patient Survey
11	uterine cervical cancer	C53(C55)*1	Vital Statistics
12	uterine corpus cancer	C54(C55)*1	Vital Statistics
13	ovarian cancer	C56	Vital Statistics
14	prostate cancer	C61	Patient Survey
15	renal cell carcinoma	C64	Vital Statistics
16	bladder cancer	C67	Vital Statistics
17	malignant lymphocyte	C81～C 85、C96	Vital Statistics
18	leukemia	C91～C95	Vital Statistics
19	multiple myeloma	C88～90	Vital Statistics

*1 : Classification of C55 is “malignant neoplasm of uterus, site unknown”. Deaths of C55 were divided into deaths of uterine cervical cancer and uterine corpus cancer corresponding to the ratio of these two cancers’ deaths. (for details, “uterine cervical cancer” and “uterine corpus cancer” section, respectively)

3 Types of Data

In calculating the number of patients, a variety of data need to be used in combination. Available existing data are as follows:

① “Patient Survey” by the Ministry of Health, Labor and Welfare

② “Vital Statistics” by the Ministry of Health, Labor and Welfare

③ “Number of Affected Individuals” by grant-in-aid for cancer research subsidized by the Ministry of Health, Labor and Welfare

④ “Comprehensive Survey of Living Conditions” by the Ministry of Health, Labor and Welfare

⑤Registration survey for each type of cancer

In utilizing each datum, specific characteristics and issues (scope and limitation) must be taken into account (Table-2, omitted).

4 Calculation Method

There are two types in the number of cancer patients.

The number of new-onset patients— The number of patients who suffered from cancer within a given year. It is so-called the number of affected individuals.

The number of total surviving patients— The number of patients who are suffering from cancer at the present time. It includes individuals who were affected in the past.

Each number has a different meaning and its calculation method differs. In the following, the calculation method devised by our company is shown.

①Number of New-Onset Patients

It refers to individuals who suffered from cancer within the year. It calculates the number of new-onset patients of 19 types of cancer in a single year. The data to be used are the number of deaths* in the Vital Statistics and the 5-year survival rates.

As for the 5-year survival rate, it is calculated by using such data collected by our company as various academic documents, registration surveys, papers presented at conferences, etc. Its accuracy stays within an uncertainty of ±5% (for details, refer to the "1. Accuracy of 5-year survival rates" section in the "Chapter 3, Calculation Basis of Number of Patients").

The method calculates the number of new-onset patients by dividing the total number of deaths in a given year by the death rate. The death rate is sought in inverse operation from the 5-year survival rate of each type of cancer (Figure 1). The year adopted for the number of deaths is the year when the 5-year survival rate was settled (detailed later**).

Figure 1 Calculation Method of Number of Patients (single year: 2000)

(Number of deaths ÷ Death rate = Number of patients)

↑ (1 − 5-year survival rate)

[Example of calculation for gastric cancer]

50,650 patients	÷	0.3346	=	151,375 patients
(Deaths in 2000)		(Death rate: 1 − 0.6654)		(Number of patients)

This calculation method has been devised independently by our company and is detailed in our documents (Document 3, p17-19) and Pharmaceutical Library Bulletin

(Document 9, p198).

* Number of deaths in Vital Statistics

For cancers that have extremely few deaths, the number of deaths varies greatly from year to year, and adoption of a given year's number of deaths may prove problematical. In such case, it is calculated by reviewing and estimating the increase-decrease tendency of the figures for around 10 years at the settled year.

** Settled year

It means the subject year (which year of cases are used) of the adopted 5-year survival rate. If the subject year spans a several years, the mean year is set as the settled year.

②Number of total surviving patients

The number of total surviving patients means the number of patients suffering from cancer at present. In other words, it means the total number of patients who are currently under treatment or examination.

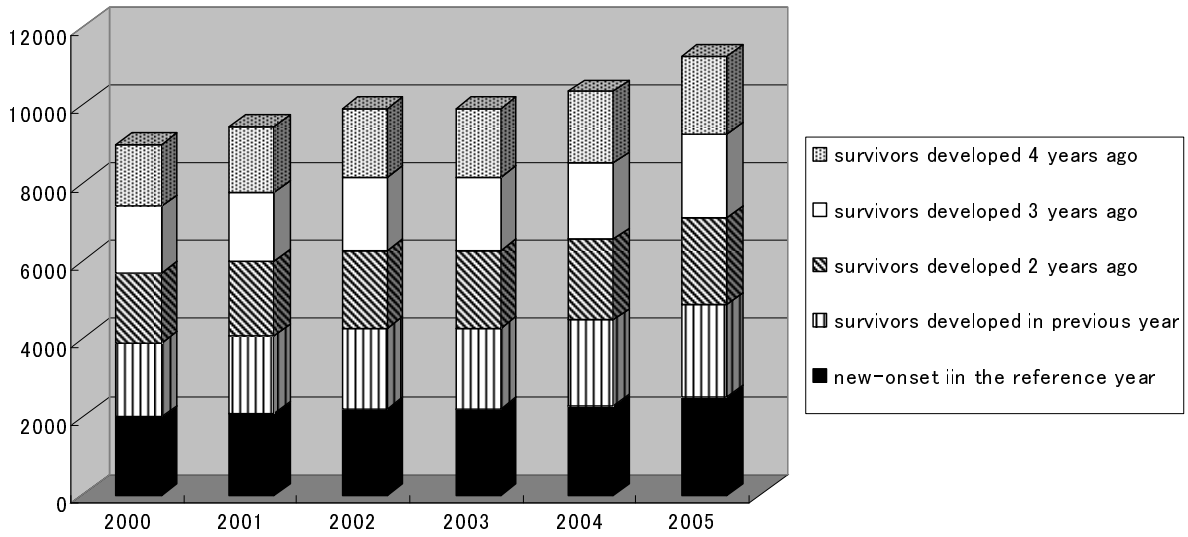
1) Concept of Calculating the Number of Total Surviving Patients

Assumption is that patients receive continued treatment for 5 years after onset, and numbers of patients for these 5 years are summed up. The period of 5 years means that 5 years are the guideline for determining if the cancer has been fully healed or not. If it does not relapse within the 5-year period, the cancer is considered healed. Even if it relapses, in case the patient survives the 5-year period by retreatment, and then the cancer is considered healed. For most cancers, the survival curve slides almost into a plateau after 5 years, suggesting that 5-year is one conclusive term[*3].

Consider the number of patients for 5 years in a given year, then the number of surviving patients for that year corresponds to the aggregate total of surviving patients for 5 years minus the numbers of deaths in the first, second, third, fourth and fifth years (Figure-2).

Note[*3] In certain types of cancer such as breast cancer, hepatic cancer, etc., relapses and treatments can repeat after the 5-year term. In such case, a 10-year or 15-year period is used, adopting the 10-year or 15-year survival rate.

(Figure-2) The number of total survivng patients



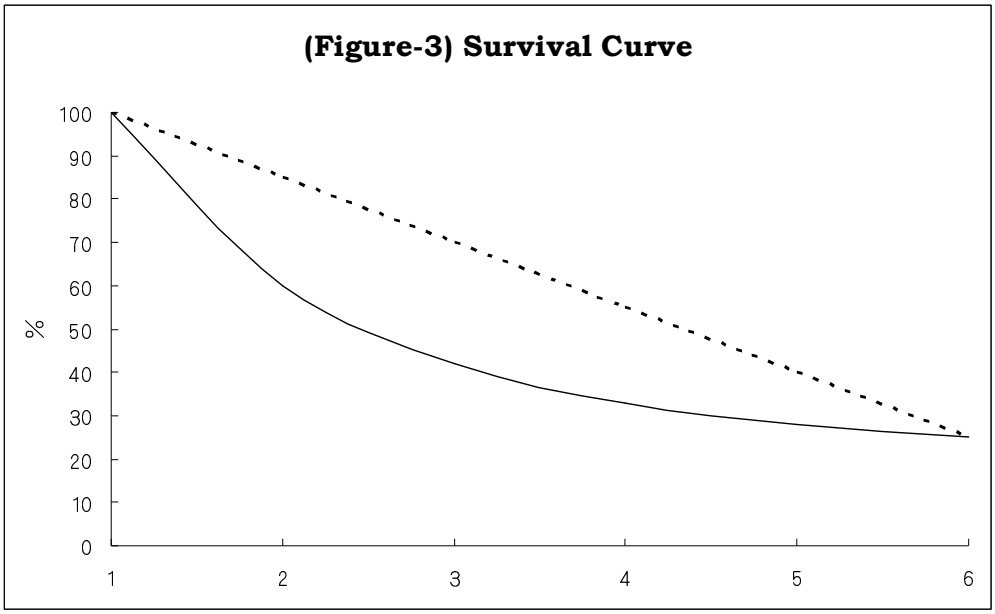
2) Survival Rate of Each Year

The number of total surviving patients is calculated for the first, second, third… fifth year, using the survival rate of respective year. The survival rate data of each year required for such calculation, however, is quite limited for certain types of cancer. Sometimes, the data are non-existent. In fact, there are no data available for the most up-to-date 5-year survival rate on a nationwide scale, and the current status is such that we are obliged to combine various data collected by our company from sources like academic documents, published lectures at conventions, registration surveys for each type of cancer, etc. in calculating the 5-year survival rate. In the following, we will discuss how to process all these data.

a) When there are little survival data available for each year

As for the survival rate for each year, whatever little data available are processed and utilized as follows:

Supposing that the calculated 5-year survival rate is 25%, the survival curve does not decrease (at the same rate of decrease for each year) in a straight line ($y = ax + b$) from 100% in the first year to 25% in the fifth year (Figure-3, dotted line). This differs from the actual survival curve (Figure-3, solid line).



Therefore, the rate of decrease in survival rate for each year, from the first to the second year, from the second to the third year, and so forth is calculated by using whatever survival rate is available for each year. For example, if the existing data show the survival rates of 63%, 45%, 35%, 30% and 27% respectively for the first, second, third, fourth and fifth years, the decrease rates are 37%, 18%, 10%, 5% and 3% respectively for periods from the first to second, from the second to third, and so forth. According to these decrease rates, the survival rate for each year that corresponds to the 5-year survival rate of 25% is calculated.

(For concrete calculation equations, refer to the "Survival Rate for Each Year" section in each type of cancer.)

b) When there are no survival data available for each year

When 5-year survival data are available but no survival data is available for each year, the processing method is based on over 1,000 survival data for each year owned by our company for various types of cancer. For details, refer to the "3. Calculation method in case no yearly survival rate data are available" section in the "Chapter 3, Calculation Basis of Number of Patients".

3) Concrete Calculation Method of Number of Total Surviving Patients

The method to calculate the number of total surviving patients is based on summing up the total numbers of survivors for five years (survivors in the first, second…and fifth years) as calculated for the first year through the fifth, using the survival rate for each year.

In this process, two numbers of total surviving patients can be obtained depending on which survival rate is to be adopted:

a) Adopt the maximum number of patients for each year

b) Adopt the number of patients at the intermediate time for each year (by definite integration)

a) Adopt the maximum number for each year

The maximum number is used in the calculation of the number of total surviving patients in this book.

Taking lung cancer in 1994 as an example, the number of total surviving patients is calculated as follows:

The number of new-onset patients for the first year (1994) was 56,661 (with the survival rate of 100% at this time).

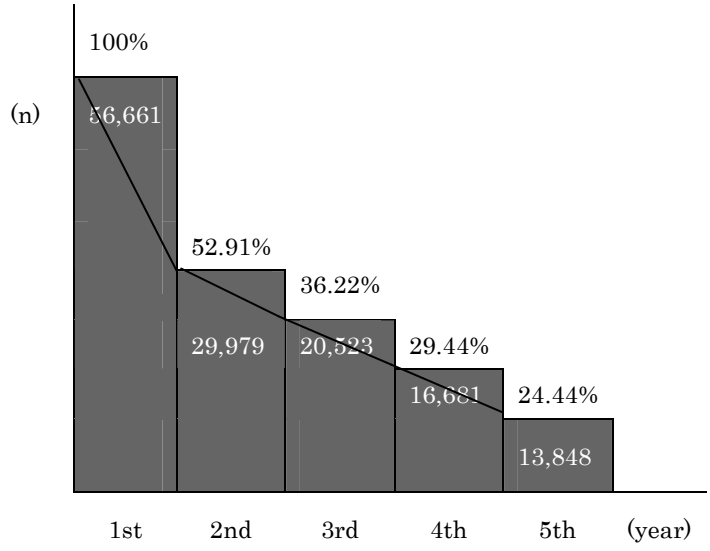
In the second year, the number of patients means the number of new-onset patients in the first year who were surviving in 1994, equaling to 56,661 x 52.91% (1-year survival rate) = 29,979. Likewise, using the 2-year, 3-year, 4-year survival rates, the number of new-onset patients in the second, third and fourth year who were surviving in 1994 are calculated. Summing up these yearly totals, the number of total surviving patients will add up to 137,692 (Table-3).

(Table-3) Calculation of the number of lung cancer patients (1994 year)

	1st year	2nd year	3rd year	4th year	5th year	total*1
Survival rate of each year (%)	100	52.91	36.22	29.44	24.44	23.27
The number of patients in each year	56,661	29,979	20,523	16,681	13,848	137,692

*1: total of total surviving patients for 5 years

(Figure-4) Breakdown for the number of lung cancer patients



The number of surviving patients for each year adopts the maximum value for respective year. The patients in the first year (new-onset patients) are all affected individuals, equaling

to 100% of 56,661. This is the maximum for the first year. The second year patients (new-onset patients in the first year) will be maximal at the 1-year survival rate of 52.91%. As shown in Figure-4, the survival curve drops gradually as years pass. In the second year, the survival rate goes down from 52.91% and ultimately reaches 36.22% (2-year survival rate). The number of patients in the second year is calculated by using the maximum at 52.91%.

Similarly, numbers of patients for the third, fourth and fifth year are calculated using the maximum values.

b) Adopt the intermediate number of patients for each year (by definite integration)

Just for reference, the calculation method using definite integration is shown below.

1-year through 5-year survival rates are usually on a continuous curve. By definite integration in calculating, the numbers of patients for each year for 0-1-year, 1-2-year, through 4-5-year periods can be shown as in Table-4. Equations used are as follows:

$$\int f(\chi)\mathrm{d}\chi = \int (a\chi + b)\mathrm{d}\chi = \frac{a\chi^2}{2} + b\chi + C$$

(Table-4) Calculation of the number of lung cancer patients (by definite integration)

	0～1-year	1～2-year	2～3-year	3～4-year	4～5 -year	total for 5 years
The number of patients in each year	43,320	25,251	18,602	15,264	13,516	115,954

The number of surviving patients for each year adopts the intermediate value for respective year (results by definite integration of first-order equation). The patients in the first year (new-onset patients) are calculated by performing integration between 100% and 52.91%. The number of patients in the second year (new-onset in the previous year) is calculated by performing integration between 52.91% and 36.22%. This way, by adopting the intermediate value of surviving rate for each year, the number of patients is bound to be less than that calculated on maximum values as shown in Table-4.

c) Concept of two numbers of total surviving patients

Two numbers are obtained for total surviving patients (one using the maximum values and the other by definite integration).

In this book, the purpose of calculating the number of patients is to estimate the number of patients obtainable by marketing new anti-cancer drugs. Projections of future market are based on assumptions of the maximum possibility.

As long as that is our purpose, in this book we calculate the maximum number of patients for each year and accumulate the totals to adopt as the number of total surviving patients.

5 Estimation Methods

Thus, the numbers of new-onset patients and total surviving patients have been calculated. From this point on, estimation of these numbers will be made.

The method of estimation will use the rate of increase/decrease in the number of patients in the Patient Survey.

①Reason for using Patient Survey in estimation

As touched upon earlier, while the Patient Survey provides estimated data from one-day surveys and is not complete in probing into the substantive number of patients, it has high values in tracing the transition. The Survey (conducted once in three years) is carried out each time on the identical method and offers valuable fixed-point data to pursue transitions (increase/decrease) in the numbers of patients. Especially for types of cancer such as gastric, lung and colon cancers with relatively large numbers of patients, it provides trends in increase or decrease.

Also, the Patient Survey is a large-scale research conducted nation-wide and covers hospitals with substantially high rates (with extraction rates in 2008 Survey: 7.5/10 for inpatients and 3.9/10 for outpatients). For cancer patients who are likely to be treated basically at hospitals, potentially accompanied by hospitalization, rather than at clinics unlike patients of hypertension or diabetes, the Patient Survey has high utility with rich hospital data.

②Reason for not using Vital Statistics

Meanwhile, the Vital Statistics records numbers of deaths each year and is useful in learning increase/decrease in fatality. Also, it provides actual figures and has the merit of no errors as seen in estimates. However, the Vital Statistics has one issue to be addressed in using its number of deaths for estimating the numbers of new-onset patients and total surviving patients.

The issue relates to improvements in treatment results (5-year survival rate). As diagnostic technology advances and medical examination diffuses, discovery of cancer at early stages and improvement in excision rates result in fundamentally bettering treatment results. Accordingly, in estimating the number of patients on the basis of the Vital Statistics, data of the 5-year survival rate for each respective year are essential, because the number of deaths varies as the 5-year survival rate changes.

Notwithstanding, however, the 5-year survival rate data are not published unless 5 years have passed since contracting the disease. Ordinarily, publications at conventions and in academic theses, etc. take shape 6-7 years later at the soonest, and registration

survey reports even take 10 to 15 years before publication. After the year in which 5-year survival rate was settled for calculating the number of new-onset patients, there is no means of getting yearly data for the 5-year survival rate.

Under the circumstances where data for the yearly 5-year survival rate are lacking that correspond to the yearly number of deaths, it should be concluded impractical to make estimation on the basis of the Vital Statistics.

③Cancer types where Vital Statistics is used exceptionally

Estimation is fundamentally based on the Patient Survey. Sometimes, however, there are types of cancer where it cannot be applied. Namely, the types of cancer with not large patient size (13 cancer types. Refer to Table-1). In these types of cancer with fewer patients, there are cases one-day surveys cannot discover, resulting in ups and downs in the number of patients from year to year. Since estimation of the yearly number of patients is made from one-day surveys, tracing the yearly transition is difficult (depending on the size of samples, the number goes up and down erratically).

In concrete terms, for types of cancer that have less than 50,000 new-onset patients, the Patient Survey is considered not applicable.

For these types of cancer, estimation is based on the number of deaths in the Vital Statistics. As stated earlier, where the number of deaths is used, there is a need to take into consideration the variation in treatment results (5-year survival rate). For cancer types with small patient sizes, data for the 5-year survival rate are extremely few, and in statistical processing the 5-year survival rate has to be treated as unchanged. Should there be any change, its rate of change is considered so minimal in the total number of all cancer patients that the impact on the total number of patients would be little.

6 Reference

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