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# Large-scale questionnaire survey to assess doctors' attitudes toward package inserts for prescription drugs in clinical practice

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We conducted a survey to assess doctors' attitudes toward package inserts for prescription drugs in clinical practice. The questionnaire consists of respondent basic information such as age and sex, and assessment of each package insert content, e.g. warning, clinically significant adverse reactions, conditional contraindications and conditional contraindications for coadministration, and conditions for approval. As a result, we received responses from 2827 doctors (including hospital doctors and medical practitioners) from all prefectures.

In the investigation on the necessity for improvement of the "warning", 26.4% of the doctors answered "Needs improvement" regarding the written method and the contents of warning. Meanwhile, in the investigation on the necessity for improvement of "clinically significant adverse reactions", 35.8% of the doctors answered "Needs improvement". Compared with the section of warning, there were numerous opinions which described that the section of clinically significant adverse reactions needs improvement.

Regarding the attitude toward conditional contraindications and conditional contraindications for coadministration, 54.1% of the doctors answered "Equivalent to contraindications". On the other hand, 41.2% of the doctors answered "Equivalent to careful administration or precautions for coadministration". Thus, the opinions of doctors about "conditional" of conditional contraindications and conditional contraindications for coadministration were split down the middle.

The visibility of conditions for approval was low at approximately 20%, and it was revealed that there are many doctors who do not know the conditions for approval. However about 90% of the doctors who do know the conditions for approval answered that there are some drugs with conditions for approval which affect their adoption in their institution or there are some drugs with conditions for approval listed on their prescription.

These study results show the necessity for package inserts to provide true useful information quickly in clinical practice. In Japan, the package insert for a prescription drug is the only drug information that has been legally approved. Drug usage based information other than package inserts is highly risky and may lead to serious consequences. The results of a comprehensive review of package inserts shows that we need to consider the manner of presenting the information which is actually used by many doctors in clinical practice.

**Key Words:** doctors' attitude, package inserts for prescription drugs, questionnaire survey

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## Introduction

In Japan the package insert for prescription drug is the only drug information that has been legally approved. It is drawn up on the basis of Pharmaceutical Affairs Bureau No.606 [1] and No.607 [2] in 1997. More than ten years have passed since the Guidelines for the Package Inserts of Prescription Drugs was revised; various problems have arisen regarding the quality and quantity of information on the package inserts used in clinical practice. Surveys for pharmacists on the utilization of package inserts have been undertaken[3][4], but few studies have surveyed the prescribing physicians. Thus we conducted a questionnaire survey on the use of package inserts for doctors. Doctors were classified as hospital doctors and medical practitioners, and there was a variety of diagnosis and treatment departments included. In order to minimize the deviation of the investigation candidate by these factors, the following research studies were planned: a survey for hospital doctors covering all diagnosis and treatment departments of each institution, and a survey for medical practitioners covering all prefectures. By conducting a comprehensive investigation of doctors of all prefectures, it seemed to be possible to minimize the impact on the investigation from factors such as scale, policy, information technology environment for facilities.

## Methods

We carried out a large-scale questionnaire survey for doctors (including hospital doctors and medical practitioners). The aim of the study was to assess doctors' attitudes toward package inserts for prescription drugs in clinical practice. The survey was conducted from September to November in 2009. The questionnaire was mailed to the director of the hospital and it was returned via a self-addressed envelope. In the survey for hospital doctors, we sent out 14404 questionnaires to 929 institutions. The institutions are listed in Table 1. In the survey for medical practitioners, we randomly selected 10 institutions from the two most populous cities in each prefecture for a total of 940 institutions from the homepage of Japan Medical Association and mailed a questionnaire to each institution. The questionnaire consisted of respondent basic information such as age and sex, and assessment of each item (e.g. warning, clinically significant adverse reactions, conditional contraindications and conditional contraindications for coadministration, conditions for approval).

## Results

### 1. Respondents basic information

We received responses from 2827 doctors (including hospital doctors and medical practitioners; comprising 19.6% of the total number of questionnaires). Table 1 shows the basic information of the respondents. Although the male-to-female ratio was 10:1, there was not much difference in age[5]. The percentage of doctors who belong to the Drug Committee, which determines the adoption of prescription drugs, was 35.2%. Regarding the doctor respondents, the main departments of diagnosis and treatment were internal medicine (10.5%), orthopedic surgery (7.7%), surgery (6.6%) and pediatrics (6.6%).

### 2. The status, degree of consciousness and frequency of use

Regarding status or importance, 24.8% doctors answered the importance of the package inserts as drug information to be the "most important" (Table 2), on the other hand, 1.3% doctors answered "not important". And we found that 30.2% doctors responded having a high degree of consciousness, however 0.7% doctors had a low degree of consciousness regarding package inserts in clinical practice. Regarding the frequency of using package inserts for prescription drugs, 84.4% doctors answered "frequently" or "sometimes", whereas, 14.2% doctors answered "rarely" or "never".

### 3. Obtaining package inserts

In response to the question "Where do you get package inserts?", 62.9% of the doctors obtained inserts at the "Pharmaceutical department or Pharmacy" (Fig. 1), followed by 42.0% from Information Technology [Pharmaceuticals and Medical Devices Agency (PMDA) web site, Pharmaceutical company web site]. Other responses were "drug information on electronic health record" and "information from a medical representative".

■ **Institutions included**

| | | |
|---|---|---|
| Hospital doctors | University hospitals (National /Private) | 128 |
| | Prefectural hospitals | 218 |
| | Municipal hospitals | 431 |
| | National Center | 8 |
| | National Hospital Organization | 143 |
| | Private hospital | 1 |
| Medical practitioners | | 940 |
| | Total | 1869 |

■ **Basic information of respondents**

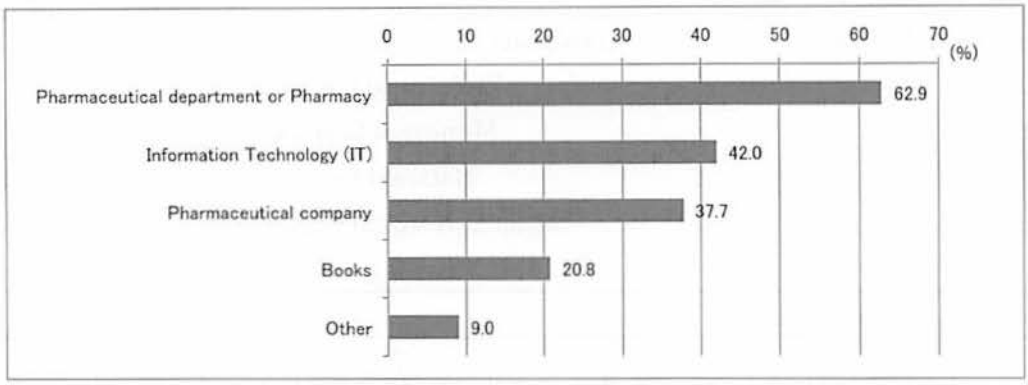
| | | |
|---|---|---|
| Age | 20's | 1.8% |
| | 30's | 18.5% |
| | 40's | 36.3% |
| | 50's | 34.1% |
| | Over 60's | 9.1% |
| | Unknown | 0.2% |
| Sex | Male | 89.0% |
| | Female | 9.4% |
| | Unknown | 1.6% |
| drug committee | Attending | 35.2% |
| | Not attending | 62.0% |
| | Unknown | 2.8% |
| | Total | 2827 |

Table 1 Institutions included and basic information of respondents

| "What is the status of package inserts related to drug information?" | | | | |
|---|---|---|---|---|
| Most important | Important | Not important | | Unknown |
| 24.8% | 73.3% | 1.3% | | 0.6% |
| "How often are you concerned about description in the package inserts in clinical practice?" | | | | |
| Always | Sometimes | Never | | Unknown |
| 30.2% | 69.0% | 0.7% | | 0.1% |
| "How often do you use package inserts in clinical practice?" | | | | |
| Frequently | Sometimes | Rarely | Never | Unknown |
| 19.7% | 64.7% | 13.8% | 0.4% | 1.4% |

Table 2 The status, degree of consciousness and frequency of use (N=2827)

Fig. 1 Question on obtaining inserts (N=2827、multiple answers allowed)

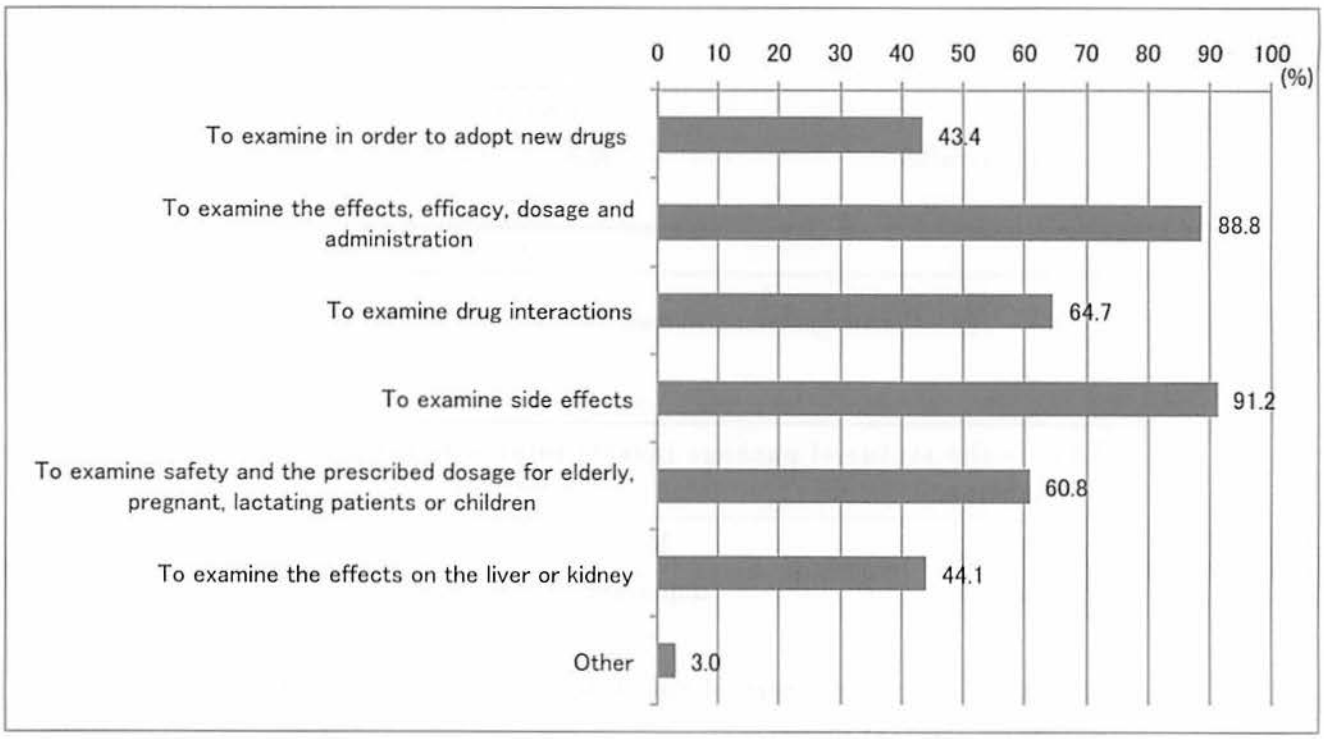



Answers for "Where do you get package inserts?"

## 4. Main use of package inserts

In response to the question "For what situation do you mainly use package inserts?", more than 85% responded "to examine side effects" or "to examine effects, efficacy, dosage and administration" (Fig. 2). Over 60 percent of the respondents answered "to examine the drug interactions" "to examine safety and the prescribed dosage for elderly, pregnant, lactating patients or children".

Fig. 2 Main use of package inserts (N=2827、multiple answers allowed)



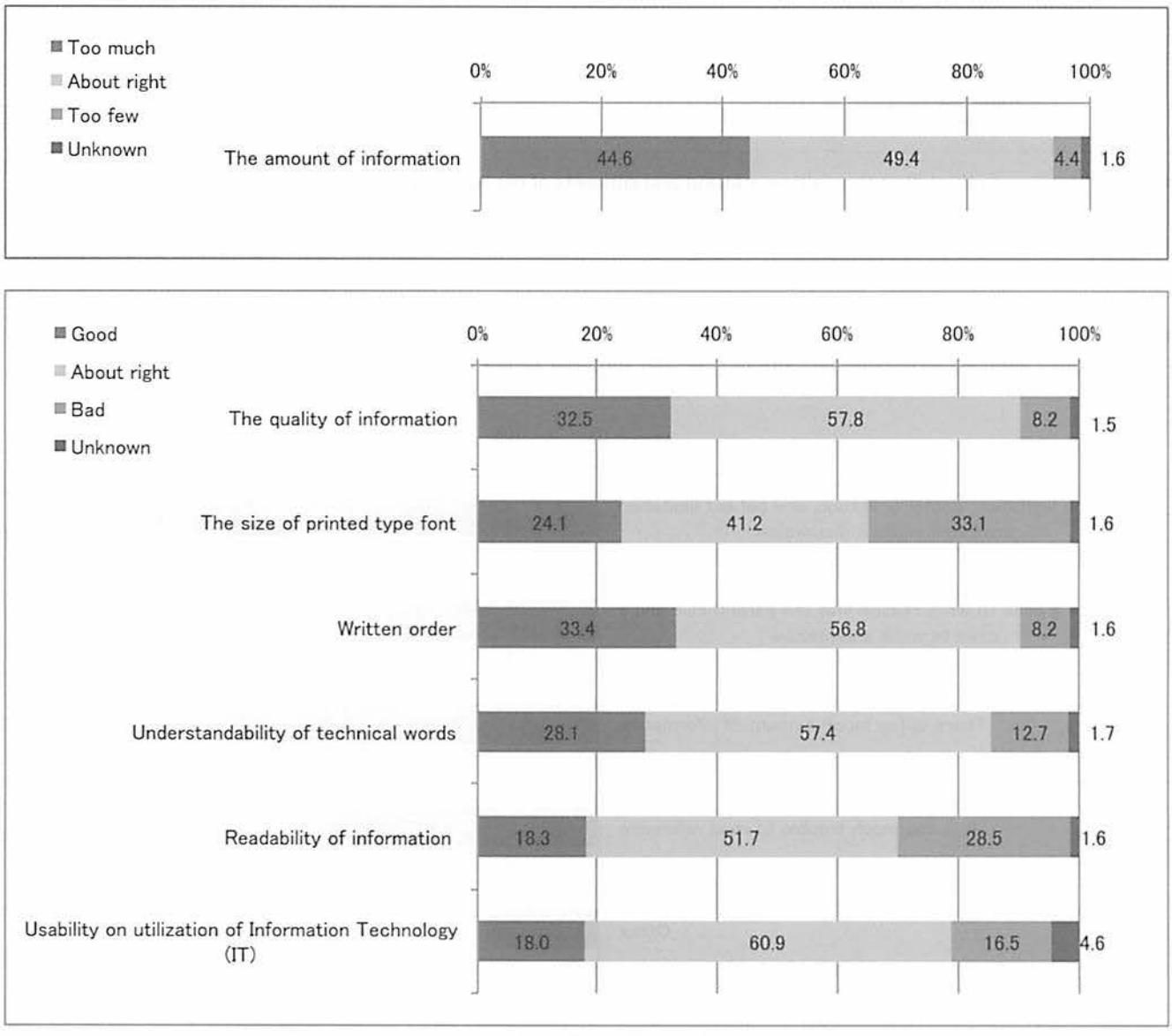

Answers for "Where do you get package inserts?"

## 5. Evaluation of overall package inserts

In the evaluation of overall package inserts, responders were asked to choose from among three choices in seven questions. Overall, the percentage of the doctors who answered "About right" was the highest (Fig. 3), those who answered "too much" was 10 times higher than doctors responding "too few" regarding the amount of information. In regard to "the quality of information" and "written order", the percentage of doctors who answered "Good" was about 4 fold those who answered "Bad". Meanwhile, in regard to

"the size of printed type font" and "readability of information", the percentage of doctors who answered "Bad" was about 1.4 fold those who answered "Good". Concerning "understandability of technical words", "readability of information" and "usability on utilization of Information Technology (IT)", the opinion "About right" accounted for 60 percent for these three questions, and the opinion "Bad" accounted for 12.7%, 28.5%, 16.5%, respectively.

Fig. 3 Evaluation of overall package inserts (N=2827)

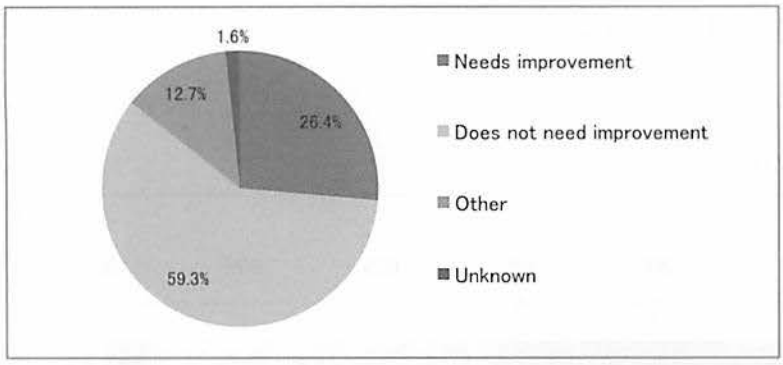



Answers for "Please select one of the four choices regarding overall package inserts."

## 6. The necessity and reason for an improvement of "Warning"

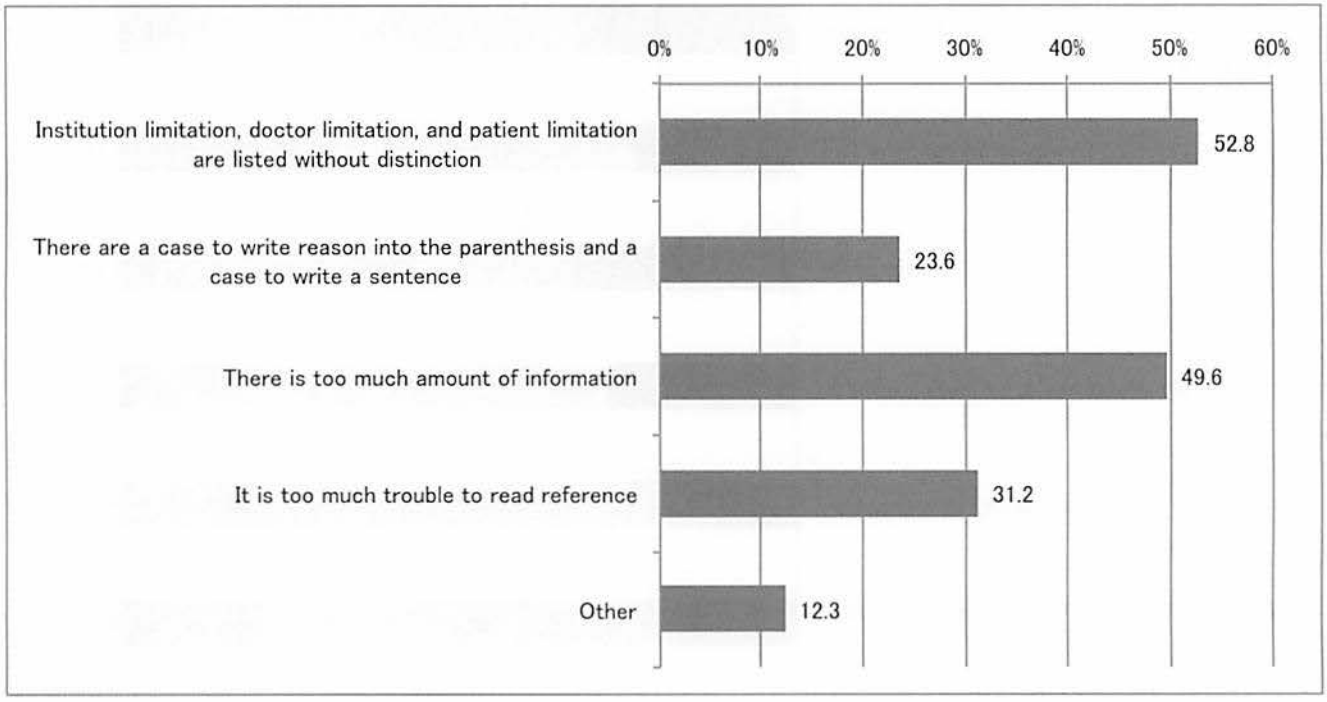
In response to the question "Do you think that the written method and contents of the warning need to be improved?" 26.4% of the doctors answered "Needs improvement" for the written method and contents of warning (Fig. 4). On the other hand, 59.3% of the doctors answered "Does not need improvement". For the doctor who answered "Needs improvement", "Institution limitation, doctor limitation, and patient limitation are listed without distinction" was the highest at 52.8% among options. And next the percentage of the doctors who answered "There is too much amount of information" was high (49.6%) (Fig. 5).

Fig. 4 The necessity for improvement of the warning (N=2827)




Answers for "Do you think that the written method and contents of the warning need to be improved?"

Fig. 5 The problem of the description of warning (Only those who answered "Needs improvement" in Figure 4 were asked to complete Figure 5: N=746, multiple answers were allowed)

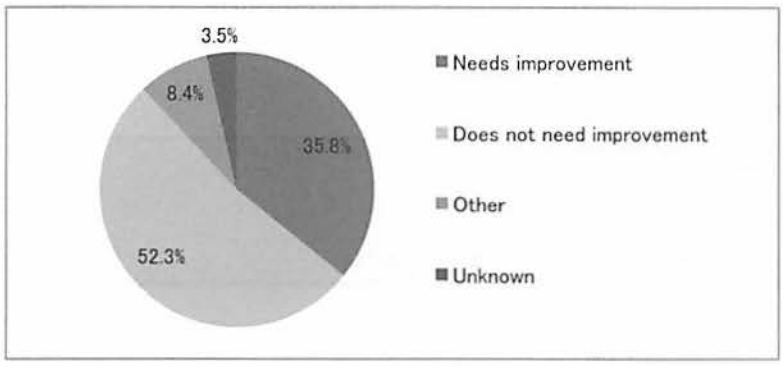



Answers for"Please choose from multiple options regarding the problem of warning."

## 7. The necessity and reason for an improvement of "clinically significant adverse reactions"

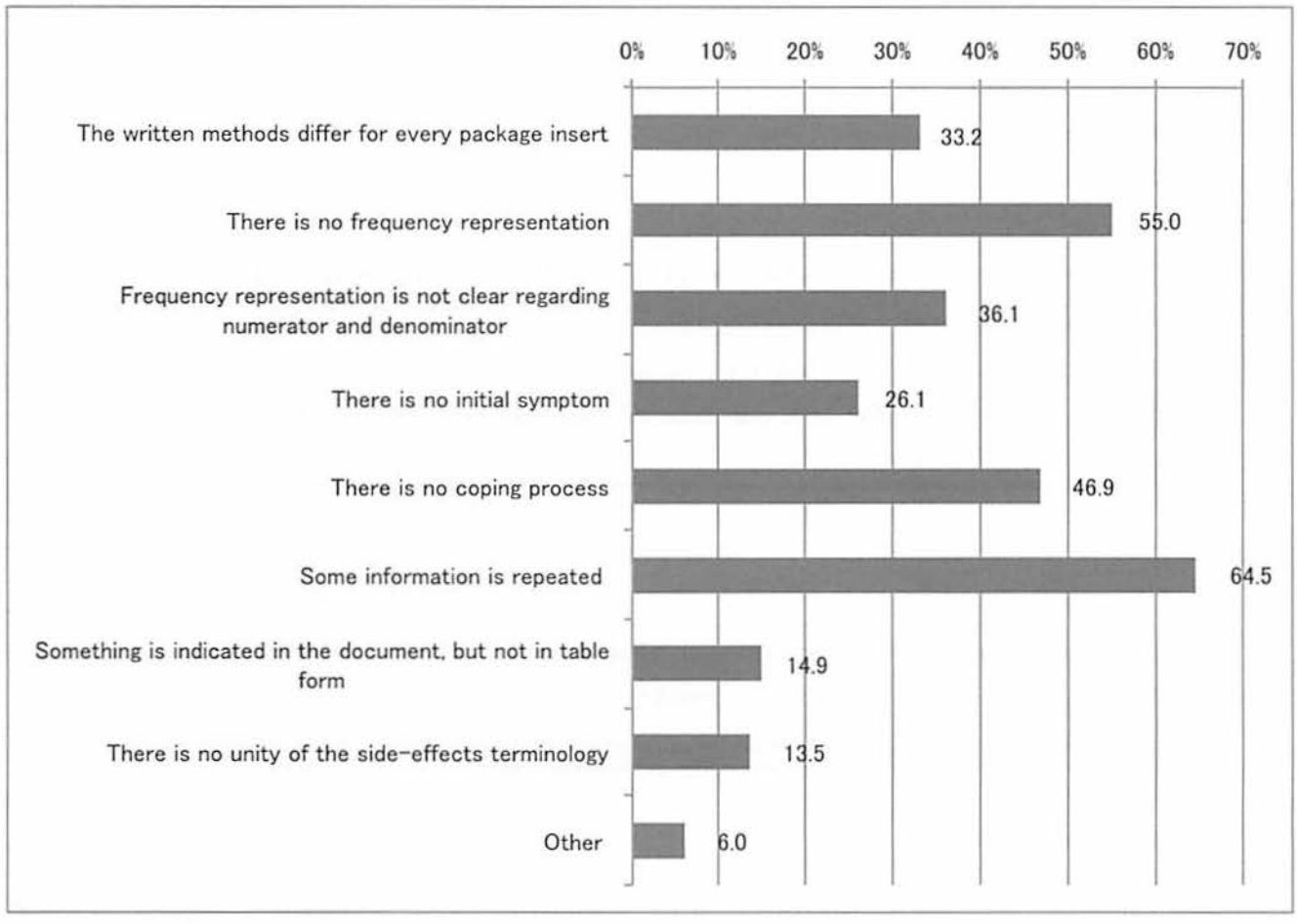
Concerning the written method and contents of clinically significant adverse reactions, 35.8% of the doctors answered "Needs improvement" (Fig. 6). In response to the problem of the contents of clinically significant adverse reactions for the doctors who answered " Needs improvement ", the reasons were " Something has been repeated in a similar writing" (64.5%), "Something has no frequency representation" (55.0%) and "Something has no coping process" (46.9%) (Fig. 7).

Fig. 6 The necessity for the improvement of clinically significant adverse reactions (N=2827)




Answers for "Do you think that the written method and the contents of clinically significant adverse reactions need to be improved?"

Fig. 7 The problem of description of clinically significant adverse reactions (Only those who answered "Needs improvement" in Figure 6 were asked to complete Figure 7:N=1013、multiple answers were allowed)




Answers for "Please choose from multiple options regarding the problem of clinically significant adverse reactions."

## 8. Attitude toward conditional contraindications and conditional contraindications for coadministration

In response to the attitude toward "conditional" of conditional contraindications and conditional contraindications for coadministration, 54.1% of the doctors answered "Equivalent to contraindications", whereas , 41.2% of the doctors answered "Equivalent to careful administration or precautions for coadministration". Moreover 1.5% of the doctors answered "Unknown" and 3.2% of the doctors answered other reasons were "case by case" or "in the middle of both".

## 9. The visibility and opportunity of utilization of conditions for approval

In response to the question "Did you know that the conditions for approval are described in the package inserts?", 20.3% of the doctors answered "I know it" (Table 3). On the other hand, 78.7% of the doctors

Table 3 The visibility and opportunity of utilization of conditions for approval

| | |
|---|---|
| **■The visibility of conditions for approval**<br>(N=2827)<br>"Did you know that the conditions for approval are described in package inserts?" | |
| Yes | 20.3% |
| No | 78.7% |
| Unknown | 1.0% |
| **■The effect of conditions for approval on the adoption of drugs**<br>(Only those answering "I know approval on prescription" : N=573)<br>"Are there any cases that drugs in which conditions for approval affect their adoption for your treatment facilities?" | |
| Strongly influence | 13.3% |
| Depending on contents | 77.3% |
| Never influence | 8.0% |
| Unknown | 1.4% |
| **■The difference in the information received from drug companies by the presence of conditions for approval**<br>(Only those answering "I know approval on prescription" : N=573)<br>"Is there any difference in information received from drug companies between drugs with conditions for approval and general drugs?" | |
| Yes | 52.9% |
| No | 45.2% |
| Unknown | 1.9% |
| **■The effect of conditions for approval on prescription**<br>(Only those answering "I know approval on prescription" : N=573)<br>"Are there any cases drugs with conditions for approval effect on your prescription?" | |
| Strongly influence | 10.8% |
| Depending on contents | 82.4% |
| Never influence | 5.8% |
| Unknown | 1.0% |
| **■Information provision to patients**<br>(Only those answering "I know approval on prescription" : N=573)<br>"Do you provide a patient with information about conditions for approval?" | |
| Yes | 24.8% |
| Depending on contents | 72.4% |
| No | 2.6% |
| Unknown | 0.2% |

answered "don't know". The subjects of subsequent questions were only doctors who answered to have known conditions for approval. In response to the question "Are there any cases that drugs in which conditions for approval affect their adoption for your treatment facilities?", 90.6% of the doctors answered "strongly influence "or "depending on contents". On the other hand, 8.0% of the doctors answered "never influence". And as a result of asking any difference in information received from drug companies between drugs with conditions for approval and general drugs, 52.9% of the doctors answered "There is a difference". Furthermore, as a result of asking the effect of conditions for approval on prescription, 93.2% of the doctors answered "It will strongly influence" or "It is influential depending on the contents, but "never influence" was only 5.8%. Table 3 shows the result of having investigated whether provision to patients about approval on prescription. As a result, 97.2% of the doctors provide "surely or depending on contents" a patient with information about conditions for approval.

## Discussion

We conducted a survey to assess doctors' attitudes toward package inserts for prescription drugs in clinical practice. As a result, we received answers from 2827 doctors from all prefectures. As for the background basis for this study and the fact that many doctors cooperated in this research concerning the package inserts, it appears that there has been no similar research concerning doctors' attitudes toward package inserts for prescription drugs in Japan.

Based on the answers regarding the status of package inserts, we further analyzed the degree of consciousness and utilization (Table 4). As a result, the doctors who answered status of the package inserts as "most important" were more likely to answer that they have been conscious of the description of package inserts and they use it. On the other hand, this analysis indicates that the doctors who answered status of the package inserts as "not important" had a low degree of consciousness and non-frequent use of the package inserts. From these results, the problem is presented that some doctors do not have concern for and do not use package inserts. The package insert for prescription drug is the only drug information that has been legally approved and it is a true reflection of risks and benefits associated with drug usage. Drug usage based on information other than package inserts is highly risky and may lead to serious consequences.

The result of the comprehensive review of package inserts indicates that we need to consider the way of presenting the information which is actually used by more doctors in clinical practice. Concerning the way to obtain package inserts, 62.9% of the doctors answered "Pharmaceutical department or Pharmacy ". Due to the separation of pharmacy and clinic, doctors tend to concentrate on the diagnosis and medical treatment, while pharmacists concentrate on pharmacy or the confirmation of drug compliance. We think that it is important to focus attention on the difference of the information which a doctor often uses, and the information which a pharmacist often uses when considering the state of the future package inserts.

Moreover, the IT environment has changed substantially from the time the 1997 notice of Guidelines for package inserts of prescription drugs. The package insert is a paper enclosed with medical supplies, but now it can also be accessed on the Internet. It seems that accessing package inserts on the Internet presents various problems which did not arise with the use of paper package inserts. We conducted general assessment of package inserts regarding the quality of information, the size of type font print, order, understandability of technical words, readability of information and usability on utilization of Information Technology (IT). But the percentage of the answer "good" to all contents was less than 35%, an overall low evaluation. To provide user-friendly information is the plan to promote the use of package inserts, and it is an important element which eventually will lead to the proper use of medical supplies. These findings suggest that the revision of Guidelines for package inserts of prescription drugs needs to reflect the present use in clinical practice.

In the investigation on the necessity for improvement of the "warning", 26.4% of the doctors answered "Needs improvement" regarding the written method and the contents of warning.

Meanwhile 59.3% of the doctors answered "Does not need improvement". Therefore the result shows that doctors' evaluations are reasonably good regarding the section of warning. In the light of pursuing improved readability, it is necessary to make changes according to the suggestions "Institution limitation, doctor limitation, and patient limitation are listed without distinction" and "There is too much information".

In the investigation on the necessity for improvement of "clinically significant adverse reactions", 35.8% of the doctors answered "Needs improvement". Compared with the section of warning, there were numerous opinions which described that the section of clinically significant adverse reactions needs improvement. Thus this finding suggests that there is some problem with the written description of clinically significant adverse reactions, especially many doctors feel that there is something that has been repeated in a similar writing.

Regarding the attitude toward conditional contraindications and conditional contraindications for coadministration, 54.1% of the doctors answered "Equivalent to contraindications". On the other hand, 41.2% of the doctors answered "Equivalent to careful administration or precautions for coadministration". Thus, the opinions of doctors about "conditional" of conditional contraindications and conditional contraindications for coadministration were split

Table 4 Analysis of the answers regarding status, degree of consciousness and utilization (N=2827)

| The status of package inserts | The degree of consciousness | | The degree of utilization | |
|---|---|---|---|---|
| Most important | | (%) | | (%) |
| N=700 (24.8%) | Always | 54.4 | Frequently | 37.7 |
| | Sometimes | 45.3 | Sometimes | 56.4 |
| | Never | 0.1 | Rarely | 4.4 |
| | Unknown | 0.1 | Never | 0.1 |
| | | | Unknown | 1.3 |
| Important | | (%) | | (%) |
| N=2075 (73.4%) | Always | 22.3 | Frequently | 13.8 |
| | Sometimes | 77.1 | Sometimes | 68.5 |
| | Never | 0.5 | Rarely | 16.0 |
| | Unknown | 0.1 | Never | 0.3 |
| | | | Unknown | 1.4 |
| Not important | | (%) | | (%) |
| N=36 (1.3%) | Always | 5.6 | Frequently | 2.8 |
| | Sometimes | 72.2 | Sometimes | 16.7 |
| | Never | 22.2 | Rarely | 69.4 |
| | Unknown | 0 | Never | 11.1 |
| | | | Unknown | 0 |
| Unknown | | (%) | | (%) |
| N=16 (0.6%) | Always | 43.8 | Frequently | 31.3 |
| | Sometimes | 50.0 | Sometimes | 43.8 |
| | Never | 6.3 | Rarely | 18.8 |
| | Unknown | 0 | Never | 0 |
| | | | Unknown | 6.3 |

Answers for "Please select one of the four or five choices regarding status, degree of consciousness and utilization."

down the middle. It is suggested that the way of thinking about "conditional" of conditional contraindications and conditional contraindications is not the opinion of each institution but rather the judgment of the individual medical staff members.

The visibility of conditions for approval was low at approximately 20%, and it was revealed that there are many doctors who do not know the conditions for approval. However about 90% of the doctors who do know the conditions for approval answered that there are some drugs with conditions for approval which affect their adoption in their institution or there are some drugs with conditions for approval listed on their prescription. Moreover, as a result of having investigated whether provision to patients regarding approval on prescription is necessary, it was revealed that 97.2% of the doctors provide, or depending on the contents, a patient with information about conditions for approval. From these results, it is suggested that the doctors who know conditions for approval provide information positively to the patient and that the contents includes the important information which should be provided to them.

These study results show the necessity for package inserts to provide true useful information quickly in clinical practice. We wish to thank all of the doctors who cooperated with this investigation.

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