Analysis of Questionnaire Data Concerning the Role of Printed Marks in the Safety of Using Transdermal Patches

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Abstract

Awareness of the safety of medication use has not been investigated from the perspective of medication users. This study focused on medical experts' opinions concerning the safety of using transdermal patches with printed therapeutic classification marks. We conducted a questionnaire study of cardiac transdermal patch users, including doctors, pharmacists, and nurses. In addition to traditional statistical analyses, we developed a pseudo-distance measure and applied an agglomerative hierarchical clustering algorithm to questionnaire data. Medical experts supported the validity of transdermal patches and therapeutic classification mark design. Opinions regarding displays on labels differed by occupation. Following the opinion of pharmacists and nurses, who deal directly with the medications, we conclude that the display of therapeutic classification marks and product names should be promoted.

Keywords: Safety of Medication Use, Therapeutic Classification Mark, Transdermal Patch, Clustering Algorithm.

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1. INTRODUCTION

Medication safety has attracted attention for a long time, with an emphasis on toxicity and side effects of drugs. The safety of drug use is attracting increasing attention from the perspective of medical accident prevention.

In a Japanese hospital, a medical accident occurred in which a patient suffering from a lung ailment and a patient suffering from heart disease were mixed up, and the operations were performed without modification. This incident happened despite a cardiac transdermal patch that was placed on the body of the heart disease patient, which was communicated when the patients were delivered for surgery. Surgeons in the operating room could not identify what the transdermal patch was, since placing marks or product name labels on it was prohibited. If they had known, they would have avoided performing the wrong surgery.

In fact, there are many near-miss reports showing that medications are misused or mixed up due to similarities in product name or shape of packaging [1]. It is therefore important to take countermeasures to ensure that medical experts and patients use medications properly.

Although there have been numerous studies discussing the safety of transdermal medication from the perspective of developers or investigating the safety of these products within an organization [2-4], there has never been a study estimating measures of safety from the perspective of medication users, namely, medical experts and patients. Therefore, we conducted a nationwide investigation using questionnaires to obtain feedback from doctors, nurses, pharmacists, and patients about the therapeutic classification mark (a white heart mark with a small white square representing the patch) [5] printed on transparent isosorbide dinitrate transdermal patches, a cardiac medication.

In this report, we applied traditional statistical analysis and a data-mining technique to questionnaire data, and clarified what medical experts think of the mark as a measure of safety. The questionnaire consisted of multiple-choice questions, in which respondents were able to choose more than one option for each question. In general, statistical analysis for multiple-choice questions is based on a majority vote for each option. However, combinations of selected options also have significant meaning, since respondents do not choose separately but by the set, and therefore they express their intent as a group of options. Hence, we proposed a method for finding option patterns in data that most answerers selected by using clustering algorithms. Based on these patterns, medical experts' opinions concerning the role of therapeutic classification marks in the safety of using transdermal patches were assessed.

2. METHODS

2.1 Target data

Target data were answers to multiple-choice questions listed in Table 1, which formed a part of the questionnaire used by TOA EIYO Ltd. in 2004 during development of the therapeutic classification mark and product name label to ensure the safe use of Frandol tape S. We conducted our questionnaire study by sending questionnaire sheets to medical experts by mail. A total of 7,078 doctors, 7,018 nurses, and 7,361 pharmacists answered each question. Although we also conducted a questionnaire study that targeted patients, here we focused on medical experts, who are responsible for medical safety.

A	**What systemic transdermal absorbent preparations do you usually deal with?**
1	*Cardiac medication*
2	*Hormone replacement*
3	*Asthma medication*
4	*Smoking-cessation medication*
5	*Cancer pain-relief medication*
B	**Why did you select the systemic transdermal absorbent preparation?**
1	*Burden is not imposed on the digestive tract.*
2	*First pass effect of the liver does not occur.*
3	*Effect lasts for many hours.*
4	*Administration can be terminated by peeling off.*
5	*Eating meals does not have an effect.*
6	*I can ensure good compliance.*
7	*I did not select.*
8	*Other reasons*
C	**What do you think about the design of the therapeutic classification mark and product name label of 'Frandol tape S™'?**
1	*The concept is valid for medical accident prevention.*
2	*More innovation of the concept is necessary to prevent medical accidents.*
3	*The mark is favorable for cardiac transdermal patches.*
4	*More innovation of the mark is necessary.*
5	*The print color, white, is easy to see and favorable.*
6	*The print color should be more vivid.*
7	*The mark, label, and layout are valid for medical accident prevention.*
8	*More innovation of the size of the mark, the number of labels, and layout is necessary.*
D	**What preventive measures against medical accidents are related to the systemic transdermal absorbent preparation?**
1	*Displaying the mark and the label is good enough.*
2	*The mark indicating the same efficacy should be integrated.*
3	*The mark indicating the same efficacy should not be integrated, but should be unique to each company.*
4	*The mark should be displayed for other systemic transdermal absorbent preparations.*
5	*Displaying the mark and the label is unnecessary.*
6	*The effort is necessary for product recognition by medical experts, patients, and their families.*

TABLE 1: Questions and Options (Originally Written in Japanese).

2.2 Agglomerative hierarchical clustering

In addition to traditional statistical analysis, we applied a clustering algorithm to find options that were selected together by respondents. This was not a straightforward task given that ordinal distance measures, such as Euclidean distance or Manhattan distance, are not suitable for our analyses. In this section, we illustrate the distance measure and clustering method that were used.

The vector was defined as the set of the elements each of which has the value 1 if a respondent selects the option and zero if not. To determine how options were selected, we applied an agglomerated hierarchical clustering algorithm to the vector. The algorithm provided us with a dendrogram, which provides information on groups formed by the data. By applying this to our target vectors, we were able to see the groups of options that respondents selected.

The Euclidean distance or Manhattan distance is usually adopted to measure the distance of the vectors. Their application to our target vectors is equivalent to counting the number of different vector elements. This results not only in the most simultaneously selected options, but also the simultaneously unselected options being judged as neighboring each other. Options unselected by most respondents therefore tend to have a short distance relative to each other.

The distance, however, should measure differences in the way options are selected by respondents. For vectors whose elements were either 1 or 0, their inner product counts the number of elements whose value is both 1. We take this into account and propose a distance-like measure that counts the number of elements whose value is not 1 in either vector:.

$$d'(a,b) = \sum_k (1 - a_k b_k).$$

Strictly speaking, d' does not satisfy one of the axioms of distance, namely, the value of d' for the identical selection of vectors is not equal to 0. The requirement of distance for agglomerative hierarchical clustering is, however, only to supply a measurement that allows us to compare the similarity.

Table 2 shows sample data we used to evaluate our method. Figure 1 shows the dendrogram for which the Euclidean distance is used, and Figure 2 shows that for our pseudo-distance measure. We can see that Options 2 and 5 are considered to be neighboring in Figure 1, although no respondents chose them simultaneously (Table 2). As expected, these options are considered to be far from each other in Figure 2.

We should also note that the traditional approach that only counts the number of respondents does not distinguish whether the options are chosen simultaneously or not. In Table 2, the number of respondents who selected Option 2 and Option 5 is the same, but these options were selected by different respondents as mentioned above. Therefore, we applied our pseudo-distance measure to the data rather than using the traditional approach.

	Option 1	Option 2	Option 3	Option 4	Option 5
Respondent 1	1	0	1	1	0
Respondent 2	1	0	1	1	0
Respondent 3	1	0	1	1	0
Respondent 4	0	0	1	1	1
Respondent 5	0	0	0	0	1
Respondent 6	0	1	0	0	0
Respondent 7	1	1	1	1	0
Respondent 8	1	0	1	0	0
Respondent 9	1	0	1	0	0

TABLE 2: Sample Data for Evaluation of the Clustering Method Using Our Pseudo-distance Measurement.
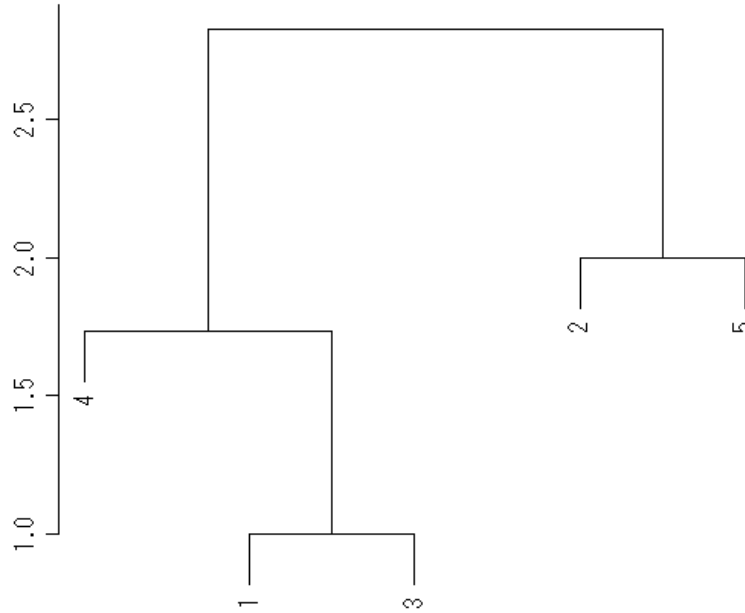
FIGURE 1: The Resultant Dendrogram Based on Euclidean Distance for Data in Table 2. Numbers in the Dendrogram Denote Each Option. The Vertical Axis Denotes the Merged Distance of Clusters..
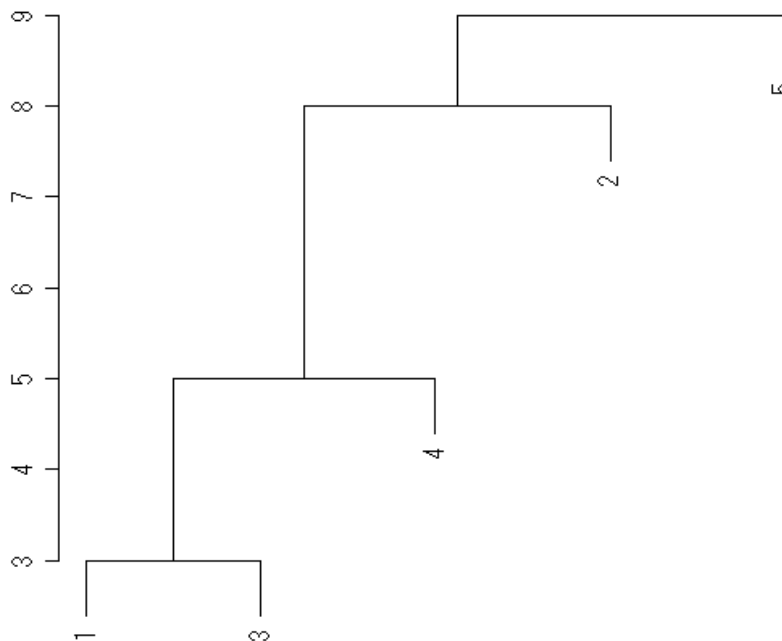

FIGURE 2: The Resultant Dendrogram Based on Our Pseudo-distance Measure for Data in Table 2. Numbers in the Dendrogram Denote Each Option. The Vertical Axis Denotes the Merged Distance of Clusters.

3. RESULTS

Figures 3 and 4 show results from Question A, which addresses the types of transdermal medication commonly encountered by medical experts. We can see that Options 1 and 3 were selected most frequently and were selected together. Although the frequency of co-occurrence is relatively lower, Option 5 can also be regarded as having been selected simultaneously with Options 1 and 3. This suggests that the systemic transdermal absorbent preparations that medical experts usually deal with are cardiac and asthma drugs, with some medical experts also using cancer pain-relief medications.

FIGURE 3: Bar Graph for Question A, Which Counts the Number of Respondents Selecting Each Option.
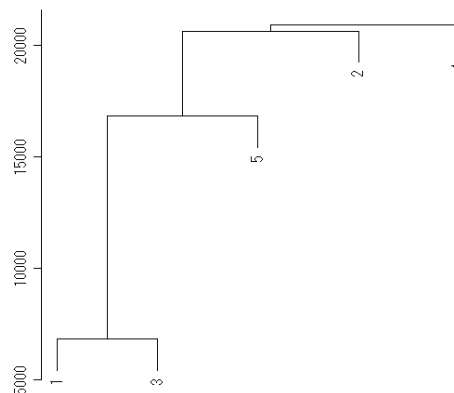

FIGURE 4: Dendrogram of Frequently Used Systemic Transdermal Absorbent Preparations (Question A).

The results for Question B, which focuses on reasons for choosing the transdermal preparation, are shown in Figures 5 and 6. Options 1 and 3 were selected together by many respondents, with Option 5 as the third option that was often simultaneously selected with these options. Interestingly, Option 6 was less frequently selected with Options 1 and 3 than Option 5, although it was more frequently selected than Option 5. Such a pattern would only be found by using the clustering algorithm. These results suggest that medical experts primarily adopted systemic transdermal absorbent preparations as a dosage form because they do not impose a burden on the digestive tract and their effects continue for many hours. Additionally, they were also chosen because diet does not have an impact on their efficacy.

We can regard the cluster of Options 1, 3, and 5 as a sign of concern about the burden. Figure 7 shows the number of respondents who selected each option by occupation. Medical experts selected Option 3 most frequently regardless of their profession, suggesting that the long-lasting effect is what they focused on. We found that more nurses selected Options 1 and 5 than pharmacists and doctors, who tended to select Options 2 and 6. This suggests that nurses focused more on the patient's burden than doctors and pharmacists.
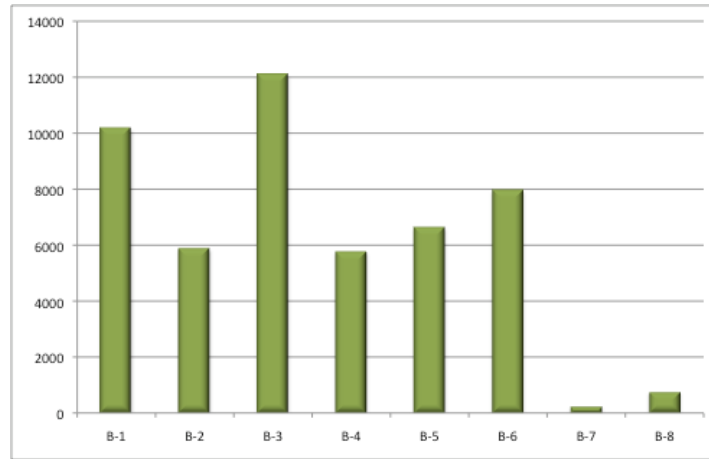
FIGURE 5: Bar Graph for Question B, Which Counts the Number of Respondents Selecting Each Option.
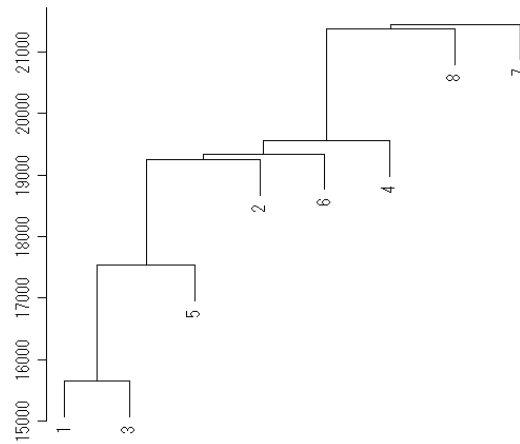

FIGURE 6: Dendrogram of the Reason for Selecting the Systemic Transdermal Absorbent Preparation (Question B).
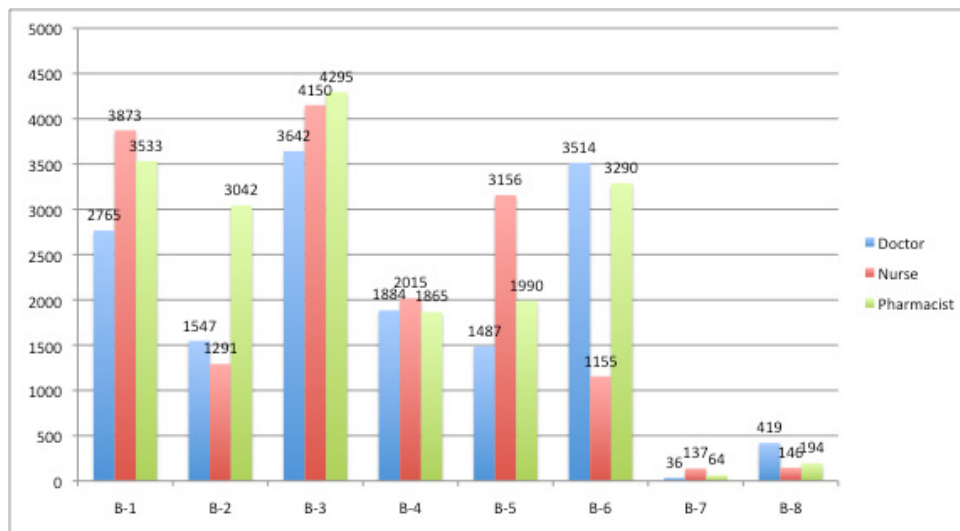

FIGURE 7: Number of Respondents Who Selected Each Option by Occupation (Question B).

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Question C asks about the design of the therapeutic classification mark and product name. Results are presented in Figures 8 and 9, which show that Options 1, 3, 5, and 7 were selected together. This can be interpreted as the design being valid for the prevention of medical accidents, having a high level of visibility, and being preferable. This suggests that medical experts had a favorable opinion of the mark and the product name label on the transdermal patch.
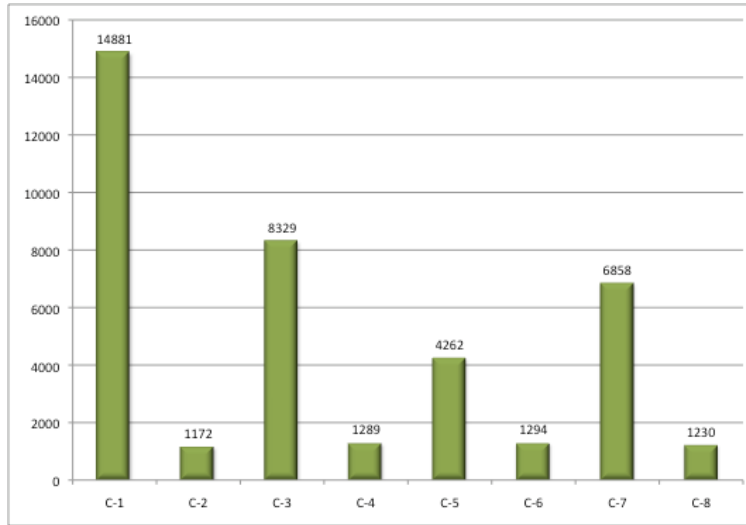

FIGURE 8: Bar Graph for Question C, Which Counts the Number of Respondents Selecting Each Option.
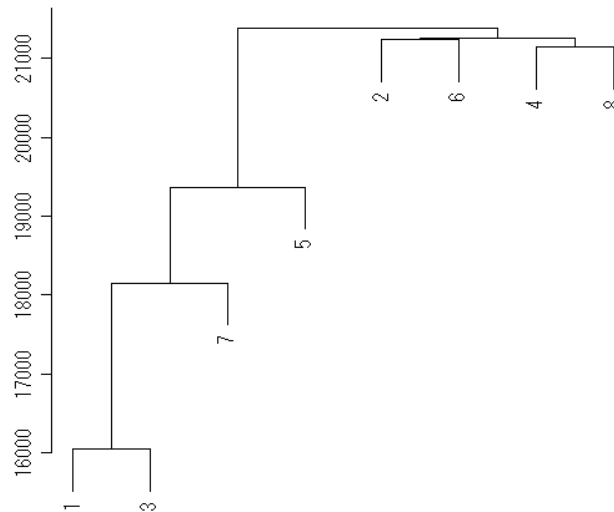

FIGURE 9: Dendrogram of Opinions Regarding the Design (Question C).

Figures 10 and 11 show results of Question D, which addresses preventive measures against medical accidents. These figures indicate that there is a cluster of Options 2, 4, and 6. This suggests that most medical professionals thought that the therapeutic classification mark and the product name label are necessary, should be integrated to for medicines that have the same efficacy, and should be widely recognized. These options represent a positive response to the use of the classification mark on patches. Options 1, 3, and 5 can be regarded as negative opinions on promotion of the therapeutic classification mark.

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Figure 12 shows the number of respondents who selected the options by occupation. Pharmacists and nurses tended to be more in favor of promoting the mark and label (Options 2, 4, and 6). More doctors than nurses and pharmacists answered that the display of the mark and label was sufficient, and that the mark should be unique to each company (Options 1 and 3). This suggests that doctors were not interested in disseminating the mark. Taking into account that nurses and pharmacists directly deal with the transdermal patch when it is administrated to a patient, the selection of options by nurses and pharmacists can be interpreted as reflective of opinions of patch users. It has been said that the accident mentioned in the Introduction could have been prevented if the people concerned had recognized what the patch was. Opinions to utilize the mark and the name label as a countermeasure are compatible with the lesson learned from the accident.
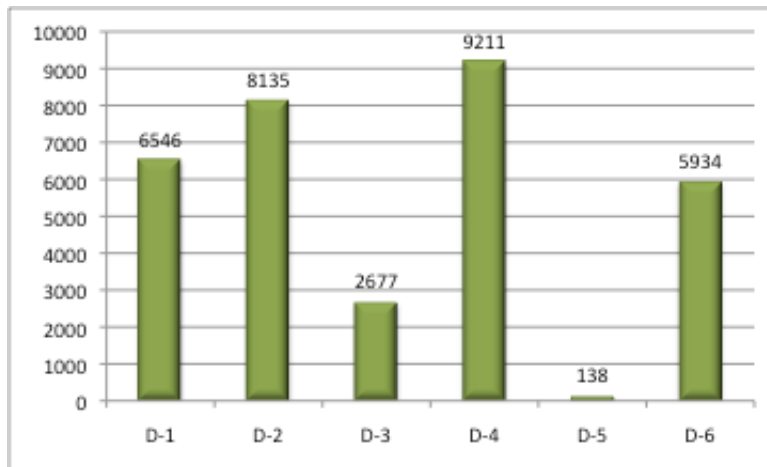

FIGURE 10: Bar Graph for Question D, Which Counts the Number of Respondents Selecting Each Option.
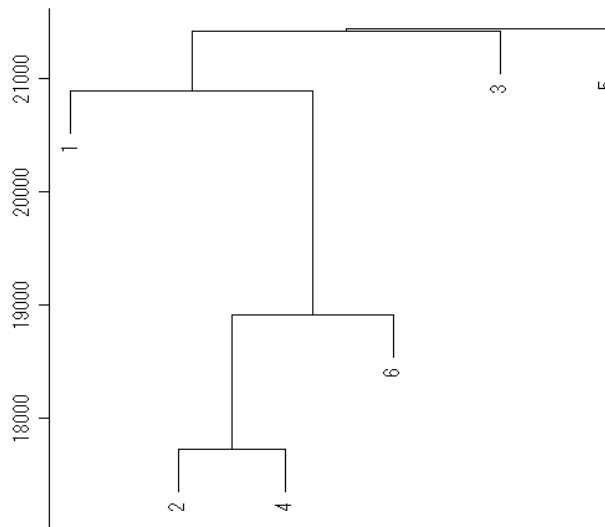

FIGURE 11: Dendrogram of Opinions on Preventive Measures against Medical Accidents Related to Systemic Transdermal Absorbent Preparations (Question D).
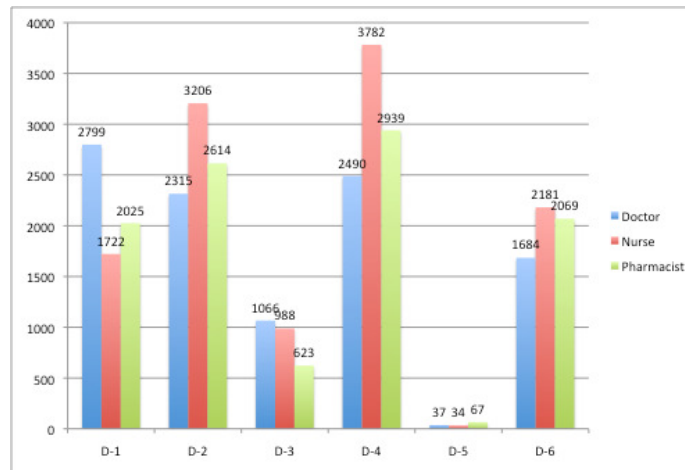
FIGURE 12: Number of Respondents Who Selected Each Option by Occupation (Question D).

4. CONSLUSION

In this paper, we analyzed questionnaire data to assess medical experts' opinions concerning the safety of using a transdermal patch printed with a therapeutic classification mark. Since questions in the questionnaire consisted of multiple-choice options, we employed not only a descriptive statistical method, but also a hierarchical clustering method with our pseudo-distance measure.

We found that many medical experts routinely deal with systemic transdermal absorbent preparations of cardiac, asthma, and cancer pain-relief medications. Medical experts selected transdermal patches as a dosage form primarily because of their long-lasting effects and the lack of burden imposed on the gastrointestinal tract. Many medical experts thought that the design of the transdermal patch is desirable from the perspective of medical accident prevention, and that the mark should be integrated for the same efficacy and be widely recognized. Although pharmacists and nurses thought that the therapeutic classification mark and product name label should be promoted, doctors were satisfied with the current situation. This also suggests that different attitudes regarding the therapeutic classification mark may be occupation-specific.

Based on the opinion of those who deal directly with medications, we conclude that medical experts consider it reasonable to utilize the systemic transdermal patches printed with a therapeutic classification mark with a unified design and product name label to help identify the medication as a countermeasure to accidents.

In the past studies of pictogram validity for medication safety [6, 7], the authors reported that pictograms are valuable in communicating their meanings but pointed out that their successes are limited without their contexts, e.g. appropriate text explanations. As for our results, though our target therapeutic classification mark accompanies no text explanation, medical experts judged the mark is valid. We can comprehend this if we regard the fact that the mark is printed on the transdermal patch as a context, namely, the heart mark printed on the patch is regarded as the body part affected by the medicine. If the designs of the marks for the medicines with the same efficacies are different, their contexts will be confusing for medicinal experts. This would be the reason why we obtained the answer that the design of a therapeutic classification mark should be united.

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