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Review

Importance of risk/benefit communication in patient care and pharmacy education: An expert opinion

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ABSTRACT

Appropriate risk/benefit communication about the medical treatment is necessary in ensuring the safety of patients. This facilitates patients' decision-making with healthcare professionals leading to optimal patient care. Risk communication is an essential component of risk analysis, as well as risk assessment and risk management. The provision of information about treatment and pharmaceutical products to patients in an appropriate fashion is necessary to perform risk communication. Potential goals of risk communication include "sharing information" and "changing beliefs and behavior". The purpose of this article is to discuss how to evaluate the usability of drug information leaflets scientifically as part of risk/benefit communication effectively and to recognize its importance in pharmacy education and adopt it.

As to the official drug information (written information) for patients, Drug Guides for Patients (DGPs) are provided in Japan whereas Package Leaflets (PLs) and Medication Guides are provided in the European Union (EU) and the United States (US), respectively. We conducted comparative verification of the characteristics of each of those leaflets. In terms of the usability of the written information, it is necessary to evaluate its readability, understandability, and accessibility. One of the useful methods to evaluate those factors is user testing involving patients or consumers. Here, I would like to emphasize the importance of risk/benefit communication in pharmacy education and practical exercises for the appropriate use of medicines in Japan.

Key words: risk and benefit communication, drug information for patients, decision-making, readability, understandability, accessibility, written information

1. Introduction

The discussion on the importance of risk and benefit communication for both health care professionals and patients has been ongoing as safety of drugs, including medical treatments, is uncertain (Avorn, 2009; Bahri et al., 2012; Urushihara et al., 2014; Yamamoto, 2018). In pharmacovigilance, risk communication has a major role with respect to the measures for drug safety; and its importance will be further recognized over time (Edwards, 1997). According to the World Health Organization Uppsala Monitoring Centre (WHO-UMC) glossary of pharmacovigilance terms, risk is defined as the probability of an outcome. The term "risk" normally, but not always, refers to a negative outcome. Contrary to harm, the concept of risk does not involve severity of an outcome (Lindquist, 2007).

It is through risk communication that stakeholders exchange information interactively regarding a certain risk. It has been a component of risk analysis as well as risk assessment and risk management in the field of food safety (Codex, 2005). Nowadays, the interactive process of information and opinion exchange between stakeholders is considered valuable for risk/benefit communication (Lindquist, 2007). It is the basic concept in the "shared decision making." Ideally, the relevant stakeholders, which means patients and healthcare professionals, should be involved from the start. The communication is aimed at offering essential information so that patients can make an independent decision about risks and benefits. Patients need to know the risks that can affect their health and safety; and they need to decide on a proper way to cope with those risks.

2. "Shared Decision-Making" and "Concordance"

Every patient expects, and has the right to receive, good quality drug information during medical treatment (American Hospital Association, 1973; American Hospital Association,

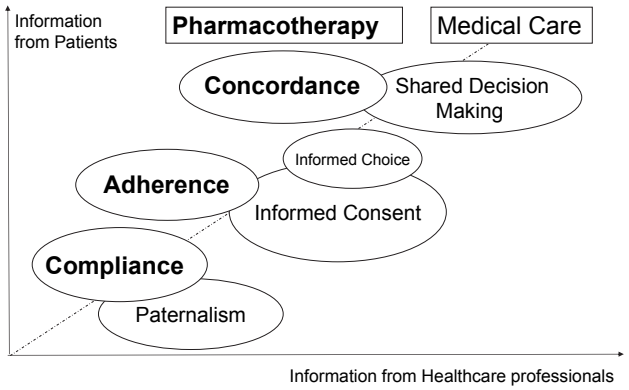

Fig. 1. Relationship of Compliance, Adherence, Concordance and Shared Decision Making.

2003; World Medical Association, 1981). The relationships between "Compliance", "Adherence", "Concordance" and "Shared Decision-Making" are shown in Figure 1. Historically, the relationship between patients and healthcare professionals has been paternalistic (Wear, 1983; Emanuel et al., 1992). Since now informed consent is required, and it is recognized that shared decision-making is necessary, significant change has come to be seen.

"Shared Decision-Making" and "Concordance" have a common point with risk communication in sharing the information and advice/opinions between experts and people. "Shared Decision-Making" is a collaborative process that allows patients and their healthcare professionals to make informed healthcare decisions together (Whitney, 2003; McNutt, 2004). This considers the available scientific evidence as well as the patient's values and preferences and healthcare professionals' expertise. "Compliance" has been used to describe the degree to which patients comply with the medical advice of their healthcare professionals regarding drug administration methods. However, patients' compliance with medical advice with respect to patients' decision making is becoming more frequent with time. (Haynes et al., 1979; Aronson, 2007). "Concordance" is the process of prescription and the use of drugs (pharmacotherapy) based on partnership agreement. In 1996, the concept of "Concordance," which is a subset of shared decision-making, was introduced by the UK-based Medicines Partnership program (Marinker et al., 1997).

The following issues are considered important in concordance;

- Patients need to have sufficient knowledge to maintain an effective partnership with healthcare professionals.
- Healthcare professionals also need to be prepared to maintain a good partnership with patients.
- Even during drug treatment, patients are involved in treatment together with healthcare professionals.
- Patients also receive support for taking medicine.

It is desirable that a model for therapeutic decision-making not only uses evidence but also acknowledges the importance of patient factors and clinical expertise of healthcare professionals.

The definition of Concordance has changed over time from one that focused on consultation process, in which healthcare professionals and patients agree on therapeutic decisions that incorporate their respective views, to a wider concept that extends from communication of prescription to patients' support in medicine taking. "Concordance" is sometimes used, incorrectly, as a synonym for adherence (Horn et al., 2005). Adherence is defined as the extent to which the patient's behavior matches agreed recommendations from the prescriber. Adherence develops the definition of compliance by emphasizing the need for agreement. As information from patients and healthcare professionals has accumulated over time, the importance of "Concordance" and "Shared decision-making" has been recognized now; and it is expected to lead to ideal pharmacotherapy and medical care. In any case, it is required that a doctor and a patient must form a mutually benefitting partnership and focus on the process of decision-making. Informed decisions made on the basis of reliable medical information are indispensable to patients. In addition, it is absolutely necessary to improve not only on compliance but also on the therapeutic effects of the medicine. Useful information enables patients to participate fully in concordant decision-making about medical prescriptions for them or recommendations to them by their healthcare professionals.

3. Drug Information for patients

Patients are the end users of drugs. In several countries, drug information leaflets are mostly provided to patients when drugs are prescribed to them.

In Japan, prescription drug information, so-called "Yakujo", are provided to patients at pharmacies. However, since a form and content of "Yakujo" are different in each pharmacy, Yakujo information was omitted from our comparative studies this time.

However why is the provision of drug information so important for patients? First of all, patients have the right to receive optimal medical treatment, and in order to ensure that, they need to know about the drugs they are taking. Second, it is important for healthcare professionals to share this essential information with patients in order to enable the patients to make the right decision. Finally, and most importantly, this sharing of information maximizes the benefits and minimizes the risk of medication. In other words, it is critical for risk minimization since it facilitates the early detection and prevention of the progression of a disease.

A comparison of the authorized drug information leaflets for patients in the EU, the US, and Japan is shown in Table 1. In Japan, Drug Guides for Patients (DGPs) that are endorsed by the Ministry of Health, Labor and Welfare (MHLW) are available (MHLW, 2005). In the UK and the EU, Patient Information Leaflets (PILs) and Package Leaflets (PLs) are

Table 1. Comparison of the official Drug Information Leaflets for Patients in Japan, EU/UK and US.

Regulatory Agency	JAPAN (MHLW)	EU (EMA), UK (MHRA)	US (FDA)
Name	Drug Guide for Patients (DIGs)	Package Leaflets (PLs), Patient Information Leaflets (PILs)	Medication Guides (MGs)
Goal	Risk Management Plan (RMP) To urge to detect serious adverse reactions	To support for decision-making	Risk Evaluation and Mitigation Strategies (REMS) To prevent serious adverse effects, To support for decision-making, To improve adherence
Readability	16–18 years old (Grades 11–12)	11 years old (Grade 5)	11 years old (Grade 5)
Range	Restricted, Designated by RMP	All medicines	Restricted, Designated by REMS
Provided mode	Web (PMDA) PMDA: http://www.pmda.go.jp/PmdaSearch/iyakuSearch/	Web (EMA, MHRA, eMC) EMA: https://www.ema.europa.eu/ MHRA: http://www.mhra.gov.uk/spc-pil/index.htm eMC: https://www.medicines.org.uk/emc Printed Materials, attached box	Web (FDA) https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=medguide.page Printed Materials
Duty of provide it to patients Obligation to offer to patients	not obligated	obligated	obligated (in general)
Adverse events	Serious Adverse Reactions only (Not required to describe occurrence frequency)	Serious side effects and Common side effects (listed by seriousness and then by frequency)	Serious side effects and Common side effects (Not required to describe occurrence frequency)
Table of contents	Not provided	Provided	Not provided
Reference	Ministry Health and Labour and Welfare, Notification relevant to Drug Guides for Patients. http://www.pmda.go.jp/safety/info-services/drugs/items-information/guide-for-patients/0003.html	European Commission, Enterprise and Industry Directorate- General, Guideline on the Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use. Revision 1, 2009. Brussels. https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-2/c/2009_01_12_readability_guideline_final_en.pdf	FDA, Guidance Medication Guides — Distribution Requirements and Inclusion in Risk Evaluation and Mitigation Strategies (REMS), November 2011. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM244570.pdf

MHLW: Ministry of Health, Labour and Welfare
EU: European Union
EMA: European Medicines Agency
MHRA: Medicines and Healthcare products Regulatory Agency
FDA: Food and Drug Administration
PMDA: Pharmaceuticals and Medical Devices Agency
eMC: electronic Medicines Compendium in UK

endorsed by Medicines and Healthcare Products Regulatory Agency (MHRA) and European Medicines Agency (EMA), respectively (MHRA, 2014; European Commission, 2016). In addition, Medication Guides (MGs) are endorsed by the Food and Drug Administration (FDA) in the United States (FDA, 2011). PILs, PLs and MGs have the same position as DPGs, targeted for patient-oriented pharmaceutical leaflets comparable to package inserts.

Compared with Leaflets in Europe and the United States, DGPs in Japan have readability set for a higher age. PILs/PLs and MGs are meant for 11-year old children while DGPs target youth between 16 and 18 years of age. Further, PILs and PLs are prepared for all drugs. However, DGPs and MGs are restricted. Also, the form of delivery and the distribution obligation are significantly different in DGPs, PILs/PLs and MGs. In Japan, DGPs are provided only on the web, whereas PILs/PLs are also available in printed form in the product box. There is an obligation to distribute PILs/PLs and MGs, but there is no such obligation for the distribution of DGPs.

Moreover, unfortunately, the awareness of DGPs in Japan is only about 7% (Yamamoto et al., 2018). In this study, we recruited the adult patients which received prescribed medicines within the past one year except the healthcare professionals using an Internet investigation panel (Macromill, Japan). We conducted with 1,095 people in 2016 as the first survey, and with 1,086 people in 2017 as the second one. The results showed that the awareness of DPGs was 7.5% and 6.7% respectively.

Since the purpose of the description of adverse drug reactions is “To urge to detect serious adverse reactions,” only serious adverse reactions are stated in DGPs. In PILs/PLs and MGs, both serious side and common side effects are described. Considering this, Japanese DGPs may need to verify their usability.

4. Evaluation of written information for patients

4.1. User testing

It is important for patients to understand written medical information and link it to appropriate actions. In order to provide drug information to patients, a framework is required to ensure the quality of the information. It is important for a patient to be able to find the essential information without any difficulties and understand the information provided. To consider patients' opinions and preferences while preparing the drug information for patients, patients must be directly involved in the process and it is necessary that their view-points are reflected in written information.

Through performing the user test on each drug, the suitability of the safety message on the leaflet can be verified, including how the information can be delivered as well as what kind of information and evidence are needed to ensure patient safety. In 2005, the user testing of PILs in the UK was made mandatory to ensure the quality and comprehensibility of the information provided to patients and consumers (MHRA, 2005). Accessibility to information, readability, and understandability are verified through testing that involves asking for a patient's opinion on the information provided. (European Commission, 2009).

This user testing also functions as a diagnostic test to improve the delivery of drug information. Such information includes pamphlets, Patient Leaflets as well as the information on the web. To increase the accuracy of the results obtained, it is important that the user test is conducted in circumstances that are as close as possible to an actual life event.

In order to understand how the test participants deal with information regarding their drugs for the treatment, it is necessary to consider and understand how these participants interpret the information. Before performing the user testing, a questionnaire should be prepared to determine whether or not these participants are able to decipher specific parts of the information (Sless et al., 2006). The number of questions for patients by an interviewer should be between 12 and 15 (European Commission, 2009). As its success criteria, 90% of test participants should be able to find the information requested on the package leaflet, of whom 90% should be able to demonstrate that they understand it (Sless et al., 2006).

Since ensuring the safety of patients is another aim of the user test, it is important to discuss and plan how the importance of safety messages can be incorporated into the questionnaire. According to Dr. Baruch Fischoff of Carnegie Mellon University, "if its message is not understood by the recipient, you should conclude that the responsibility lies with the informer and not with the recipient." Further, I think it is important to ensure that such safety-related information is provided to patients. (Fischhoff, 2011).

We need to involve consumers or patients to ensure the quality of readability, accessibility, and understandability of drug information for patients. This will enable us to make effective use of DGPs in Japan. Now, we would like to present the results of user testing.

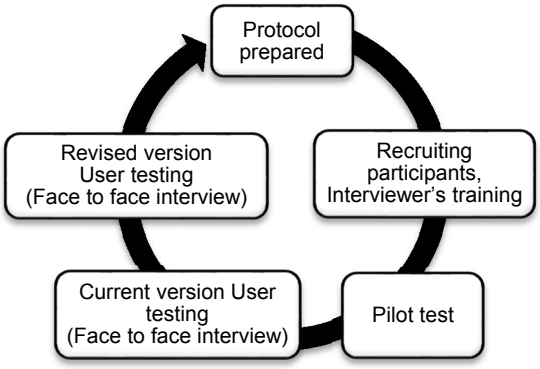

Fig. 2. Process for the user testing for drug information for patients.
Success criteria: the information requested within Drug Guides for Patients can be found by 90% of test participants, of whom 90% can show that they understand it.
Accessibility (Found): to find the answer to the question within 3 minutes.
Understandability (Understood): to rephrase the answer.

4.2. User testing in Japan

The proper and safe use of drugs depends on providing accurate drug information to patients. In Japan, patient leaflets called DGPs are officially available; however, their usability has never been verified.

This is the first attempt to improve DGPs via user testing in Japan (Yamamoto et al., 2017). Figure 2 shows the process of user testing. We compared the current DGPs and the revised DGPs for Mercazole® (generic name: Thiamazole) and Strattera® (generic name: Atomoxetine hydrochloride). Next, we conducted user testing through semi-structured interviews with participants to compare the two versions of DGPs. We divided the participants into two groups with similar distributions of sex, age and literacy level to test the two versions of Mercazole's DGPs. After completing user testing, the participants evaluated both DGPs in terms of the amount, readability, usefulness, and layout and appearance of information. Participants were also asked for their opinions on the DGPs. The revised versions of both DGPs were superior or equal to the current versions in terms of accessibility and understandability.

The revised versions of DGPs showed better score for readability and layout ($p < 0.01$) than did the current DGPs. User testing was effective in evaluating the usability of DGPs. In addition, the revised version had superior accessibility and understandability. Table 2 shows the accessibility and understandability of the DIGs of Mercazole.

Such user testing method can be used for Problem-Solving-Learning (PBL) in clinical pharmacy education. How to make the framework of user testing in PBL showed in Figure 3. In our case, P4 year students are targeted as

Table 2. Accessibility and understandability of the Mercazole Drug Guides for Patients.

Quastionnaire items	Current version (n=27)		Revised version (n=27)	
	Found	Understood	Found	Understood
1. Contraindication to liver disorders	88.9%	70.4%	96.3%	77.8%
2. Action for some cold-like symptoms	96.3%	92.6%	100.0%	96.3%
3. Indication	100.0%	63.0%	100.0%	85.2%
4. Storage	100.0%	96.3%	100.0%	100.0%
5. Clinical tests before treatments	81.5%	59.3%	92.6%	92.6%
6. Overdose	100.0%	92.6%	100.0%	100.0%
7. Serious side effects	88.9%	59.3%	100.0%	88.9%
8. Forget to take medicines	100.0%	92.6%	100.0%	100.0%
9. Clinical tests before treatments	96.6%	81.5%	96.3%	96.3%
10. Concomitant use of Warfarin	92.6%	77.8%	92.6%	85.2%
11. Contraindication to pregnancy	100.0%	96.3%	100.0%	96.3%
12. Dosage for children	100.0%	88.9%	100.0%	92.6%
13. Action for bleeding	100.0%	96.3%	100.0%	100.0%

Citation: Yamamoto M, 2017

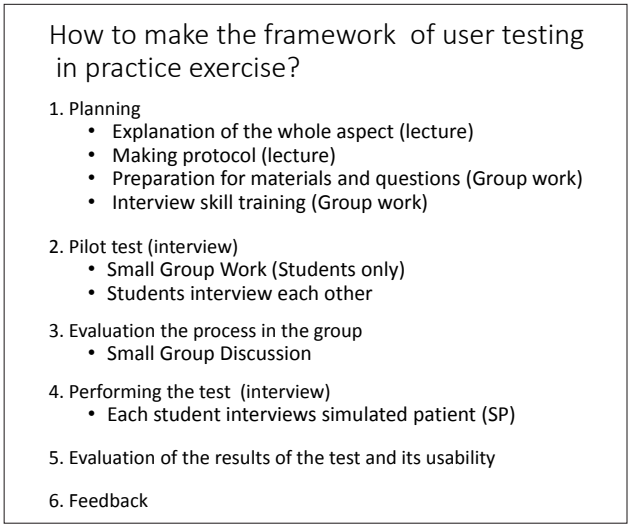

Fig. 3. The process of the user testing in PBL.

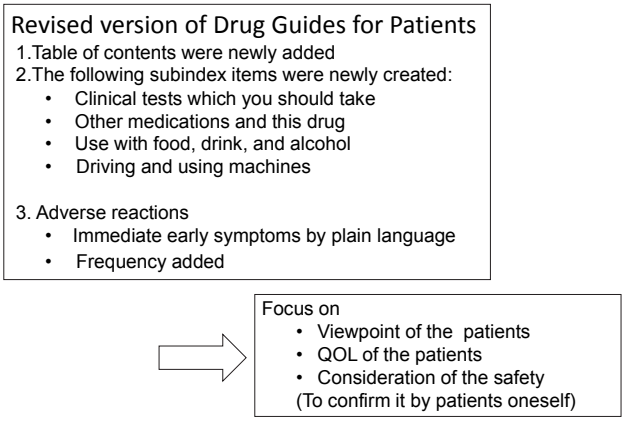

Fig. 4. Example of improvement in Drug Guides for Patients.

pre-pharmacy practice experiences. Through patient communication with patients or Simulated Patients (SP), we can assess patients' understanding of Patient Leaflets (written information) and the difficulties faced by patients. Based on their assessment, students can create a revised version considering the items showed in Figure 4 and check whether the quality of information was improved by user testing. These can be conducted in small group discussions or workshop-style sessions, and feedback can be exchanged between students or students and SPs. In order to evaluate SP's understandability and accessibility of the leaflets, the questionnaires for them should include questions on dosage, indication, overdose, and drug and drug interaction. Table 3 shows actual questions included in the questionnaire for Mercazole. The students should ask the questions randomly and not in the order in which they appear on the leaflets. Through the practice exercises, our students could learn how to evaluate the usability of leaflets in written information for patients and know what was the difficulties for patients. Moreover, they could understand how to improve them for the patients' understandability.

This can help them become better pharmacists since they can recognize that it is important to share information with patients, leading to concordance in medical treatment.

5. Discussion and Summary

Appropriate risk information should be provided to patients and consumers as well as healthcare professionals concurrently by regulatory agencies and pharmaceutical companies. In particular, healthcare professionals must share written information with patients, which can eventually lead to shared decision-making and concordance. What is

Table 3. The questionnaires of the Mercazole Drug Guides for Patients in user testing.

Q1.	Imagine that you had some sort of abnormality in your liver. Would you be able to take Mercazole?
Q2.	What would you do if you developed some cold-like symptoms while taking this medicine (e.g., "sore throat," "feeling sluggish in general")?
Q3.	What kind of treatment is Mercazole used for?
Q4.	Please tell me how to store this medicine.
Q5.	Do tests need to be performed before using Mercazole? If so, what kinds of tests?
Q6.	Let's say you took more Mercazole than the recommended dosage by mistake. Please mention one symptom that you think might occur in such a case.
Q7.	Are there any severe side effects that can develop within 2 months of starting this medication?
Q8.	You forgot to take a dose of Mercazole at some point. What should you do in this case?
Q9.	What kinds of tests will you undergo, and when?
Q10.	Imagine that you are already taking warfarin potassium for myocardial infarction. How should you approach taking Mercazole at this time?
Q11.	Imagine that you are pregnant. What kinds of things do you think the doctor will caution you about?
Q12.	Imagine that your 12-year-old child is taking Mercazole. At what dosage should his/her pediatric treatment begin?
Q13.	After you have been taking Mercazole continuously for a while, you notice bleeding from your gums when you brush your teeth, and this continues for about a week. What should you do in this case?

important for risk information has been summarized in the following three points:

1) Risk information should be made easily available and accessible to public through not only web sites but also printed materials.

2) In consideration of the literacy level of the patient, appropriate risk information should be provided.

3) Drug information for patients should be evaluated for readability, understandability, and accessibility by performing user testing.

For risk and benefit communication to consumers or patients, transparency, interactivity, and sharing of the evidence-based information are significant. With the progress of IT, wide range of drug information is easily available to people. However, since the size of the information content available is large, it is necessary to show them which information is appropriate for them. The drug information is a highly expertized area; hence it would be difficult for consumers or patients to understand the information precisely. Therefore, healthcare professionals' support for patients is indispensable. In order to use medicines effectively and safely, risk/benefit communication between stakeholders (pharmaceutical companies providing risk information, administration office responsible for them, healthcare professionals, and patients) will become increasingly important from now on.

According to our experience, it would be suggested the importance of risk/benefit communication in pharmacy education and practical exercises for the appropriate use of medicines. It should be incorporated into the curriculum of clinical pharmaceutical education. I believe that understanding the scientific basis of drug safety will become an important aspect of medical care for all healthcare professionals; and especially pharmacists will be able to make significant contribution in this regard.

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