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ORIGINAL RESEARCH

Thai Patients' Drug Safety Knowledge and Perceptions Relating to Different Forms of Written Medicine Information: A Comparative Study

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Purpose: The aim of the study was to evaluate the medication safety knowledge, quality of the written medicine information (WMI), and perceptions of taking the medicines in patients receiving package inserts (PIs) in comparison with patient information leaflets (PILs).

Methods: A cross-sectional, comparative study was conducted from December 2020 to May 2021 at two university hospitals in Thailand. Outpatients who visited the pharmacy departments and were prescribed one of the three medicines: atorvastatin, celecoxib, or metformin were randomly selected by a permuted block randomization. The medication safety knowledge was measured using a set of validated and closed questions. The quality of the WMI was measured by the Consumer Information Rating Form (CIRF). Satisfaction with information and perceptions of the benefits and risks of medications were rated by the participants using a visual analog scale (0 to 10).

Results: Of the 1150 invited patients, 750 completed the questionnaires (65.2%). A higher proportion of respondents with high level of medication safety knowledge was found in those reading the PILs than the PIs (44.5% and 20.8%, respectively). The type of leaflet received was a significant predictor of the high knowledge level ($p < 0.001$). The mean CIRF scores were significantly higher among those reading the PILs than the PIs ($p < 0.001$). Patients reading the PILs were also more satisfied with the information and had more positive perceptions of the benefits from taking medicines and intention to adhere than those reading the PIs. Patients' perceptions of risks after reading both leaflets were moderate (median score = 5.0), with the PIL group having slightly more concern about risks than the PI group.

Conclusion: The PILs showed superior effectiveness to the PIs in enhancing knowledge about medication safety, providing greater satisfaction with the information, and positive perceptions of benefit and intention to comply with the medications. PILs should be provided more frequently to patients receiving medicines than PIs.

Keywords: patient information leaflets, package inserts, medication safety knowledge, consumer testing, perceptions of benefits and risks

Introduction

Studies indicate that patients with various chronic diseases have suboptimal knowledge of prescribed medications and have a low level of awareness regarding medication safety including side effects and precautions.[1–3] Although information about indications and potential benefits of medicines is usually understood, patients are often less informed about their risks.[4,5] Educating patients about benefits and risks of medications could not only improve patients' knowledge

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about medicines and improve safe use, but may also help them balance benefit/risk perception.[6,7] Previous studies have found that knowledge about the safe use of medication positively affected attitudes and behavioural practices associated with medication.[8,9] A recent study also indicated that having adequate knowledge of chemotherapy treatment enhanced patients' self-care practice to manage side effects.[10]

Written medicine information (WMI) is one of the most widespread sources of material that people can easily access to improve their knowledge.[11] Pharmaceutical manufacturers are responsible for producing package inserts (PIs), which are generally available in medicine packages, aimed at health professionals. However, patients have difficulty reading and understanding the information in the PIs due to the language used, which is complex and full of medical terms, uses small font size and has an unattractive design.[9,12,13] Patient information leaflets (PILs) are designed specifically for patients to be user-friendly and have been required in many countries for a number of years.[14]

In Thailand, most of the WMI available is in the form of PIs.[15,16] To promote reliable, easily accessible, and up-to-date medicine information for the Thai public, the Thai Food and Drug Administration has set out strategies to develop patient information leaflets (PILs) and has promoted the manufacturers to voluntarily develop PILs.[17] PILs for chronic medications have been generated which cover important information including indications, how to use, precautions, and adverse effects of medicines, in a user-friendly format, divided into six sections.[18]

Studies of consumers' understanding about WMI commonly focus on the development of information for patients,[19,20] evaluation of medicine information,[21] and impacts of WMI on knowledge, attitudes, and practices.[9,22,23] In Thailand, a cross-sectional survey of orthopedic patients found that patients had a low level of knowledge and perceptions of the risks associated with non-steroidal anti-inflammatory drugs.[24] To our knowledge, three pre-post studies have been reported in Thailand, which found that patients' knowledge was improved after receiving PILs.[25–27] However, there are no studies which have compared the type of WMI that patients receive on either knowledge or perceptions. This study, therefore, aimed to evaluate the medication safety knowledge and perceptions of taking the medicines in patients receiving PIs in comparison with PILs, as well as gathering views on the quality of these forms of WMI.

Methods

Study Design and Settings

This study was a cross-sectional, comparative study conducted between December 2020 and May 2021, in outpatient clinics at two university hospitals in Northeastern Thailand: Srinagarind Hospital and Queen Sirikit Heart Center of the Northeast.

Participants and Sample Size

The study population included outpatients aged 18 years or over who visited the two study settings during the data collection period. All outpatients who were receiving any one of the three prescription medicines atorvastatin, celecoxib, or metformin were invited to join the study. These three medications are commonly prescribed for chronically ill patients. Although these medications had different side effects and specific precautions, this allowed for different medicine classes to be included in the evaluation. Both the PILs of these medicines supported by the Thai Food and Drug Administration (FDA) and the PIs supplied by the manufacturers were available to enable the comparison of the different forms of WMI. The potential participants were randomly allocated to receive either a PI or PIL for the medicine they were prescribed using permuted-block randomization. The participants were excluded if they had any problems with communication or eyesight problems.

The required sample size was calculated to enable investigation of the difference between the two proportions.[28] It was based on previous research showing that the number of participants who could comprehend the instructions in PIs was 69.6%,[29] and the average percentage of those who had good knowledge about medicines after reading PILs was 77.7,[25,30] with an alpha error at 0.05, a statistical power of 0.80 (beta = 0.02). Therefore, a total number of 750 patients were required to detect the difference in the proportions of respondents having good comprehension between reading PIs and PILs.

Study Instruments and Measurement

Written Medicine Information

The three PIs used in the study were those produced by the manufacturers (one PI from a local manufacturer and the others from the originators) which were included in the medicine packages. The PIs provided full information about drug names, active ingredients, pharmaceutical forms, indications, method of administration, special precautions, interactions with other medicines, adverse effects, overdose, pharmacodynamic and pharmacokinetic properties, preclinical safety data, and special precautions for storage.

The three PILs used in the study were supported and published by the Thai FDA.[18] These contained six essential topics of information on one A4-page: what is the medicine and what is it used for; precautions before using the medicine; how to take the medicine; things to do while using the medicines; possible side effects; and how to store the medicines. Headings and subheadings were used to help patients easily find and understand the information.

Questionnaire Development and Piloting

A structured questionnaire was developed consisting of four sections: (1) demographic questions; (2) medicine safety knowledge test consisting of eight multiple-choice questions covering contraindications, precautions, missed-dose management, serious and non-serious side effects, actions while taking the medicine, actions to avoid side effects/overdosage management, and medicine-specific information; (3) Consumer Information Rating Form (CIRF) in Thai version[31] to evaluate the quality of the medicine information. The CIRF covered questions including ease of the WMI to read, understand, locate information, remember and keep for future reference (5 items), likely future use of the WMI (3 items) and utility of the information (6 items), and design quality of the WMI (7 items); and (4) six questions adapted from a previous study covering satisfaction with information provided, perceptions of benefits and risks and intention to take the medicine, using a visual analog scale ranging from 0 (lowest) to 10 (highest).[6] Please see the complete questionnaire at supplemental material.

The questionnaire assessing patients' safety knowledge of the medicines and their perceptions of benefits and risks of taking the medicines was tested for content validity based on the index of item objective congruence (IOC) technique by three experts: one hospital pharmacist and two clinical pharmacists. The calculated IOC of the questionnaire was 0.875. A pilot study of 120 patients was performed to determine the reliability of the questionnaire. The internal consistency assessed by Kuder-Richardson 20 (KR-20) was 0.793 for the medicine safety knowledge questions. A group of 30 patients was asked to read and provide suggestions to ensure that the questionnaire was simple, easy to understand, and answer. A minor change was made after piloting and validation tests. For the CIRF, the validity and reliability of the CIRF had previously been established for use in Thai patients.[31]

Data Collection

Potential participants were invited to join the study while waiting for or after receiving their prescribed medicines at the hospital pharmacy department. Informed consent was verbally taken from each patient. A permuted block randomization (block size of four) was used to allocate participants into the study groups. The participants who agreed to join the study were given a sample of either the PI or the PIL, plus a self-administered questionnaire together with the aims of the study by the researcher. They were allowed sufficient time to read the PI/PIL thoroughly and complete the questionnaire. According to the pilot study, the average time spent reading the PIs was 13.4 ± 9.47 minutes and 5.9 ± 3.79 for the PILs. The questionnaire was returned directly to the researcher the same day after completion.

Data Analysis

The demographic variables between participants who read PIs and PILs were summarized using descriptive statistics and differences between groups assessed using Pearson's chi-square test. Knowledge about the safety of medications was calculated as the frequency of correct responses to each question. A correct response was scored as +1, a blank response or incorrect response were scored as 0. The number of correct responses was summed and categorized into two levels: poor to moderate knowledge level and high knowledge level. The criteria for high knowledge level were applied using previous studies regarding medicine knowledge assessment[25,26] and acceptance rate of user-testing for WMI (80% of

readers should find and comprehend the information).[19,32] Hence, the average number of high knowledge levels required at least 7 of 8 correct points. Significant variables associated with medicine safety knowledge levels found in univariate analyses were included in multiple logistic regression.

The scores for the quality of the WMI were summed within the four dimensions: (1) consumer comprehensibility measured by a 1–5 Likert scale, (2) future use of information measured by a 1–3 Likert scale, (3) consumer utility computed from the quantity of information, and (4) usefulness of information. The overall scores ranged from 1 to 4, and design quality was measured by 1–5 Likert scale.

Differences in participants' satisfaction, perceptions of benefits and risks of medications, and intention to adhere to medications, as well as consumers' rating of medicine information between PIs and PILs were compared using Mann Whitney-*U* test. Using Bonferroni adjustment, differences with p-values of $p < 0.0006$ were considered statistically significant. All valid questionnaires were analyzed using IBM SPSS for Windows version 23.0.

Ethical Approval

The study protocol was approved by the Khon Kaen University Ethics Committee for Human Research (HE611500) and conducted in accordance with the Declaration of Helsinki. All participants were explained the purpose of the study. Verbal informed consent was obtained from all participants before the study. The Khon Kaen University Ethics Committee approved verbal informed consent from study participants because all participants were anonymized from hospital identification number. All data were kept securely to protect participants' confidential information.

Results

Response Rate and Demographic Data

A total of 1150 patients were verbally invited by the researcher, of which 801 (69.6%) were willing to participate in the study. Recruitment continued until the required number of participants fully completing the questionnaire was achieved, giving an overall response rate of 65.2%. Around two-thirds of participants were aged 41–65 years, and most respondents had educational levels at a bachelor's degree or higher (n = 547, 72.9%). A majority of respondents had 1–2 underlying diseases (n = 488, 65.1%) and were taking more than 5 medications (n = 257, 34.3%). In addition, nearly two-thirds had never received any forms of written information about their medicines (n = 477, 63.6%). The characteristics of the patients allocated to receive the PI and PIL are presented in Table 1. A significant difference in age group between the two groups was found, the proportion of older respondents was slightly higher in the PIL group than the PI group ($p < 0.001$).

Comparison of Medication Safety Knowledge Received from PI and PIL

The range of correct responses achieved in respondents who received the PI was 43.7% to 73.9%, with over half failing to provide correct responses to three of the eight safety questions. The proportion of correct responses from respondents who received the PIL was 62.7–78.1%. The number of respondents who provided correct responses was significantly higher in the PIL group compared to the PI group for questions about precautions, missed-dose management, non-serious side effects, actions while taking the medicines, actions to avoid side effects/overdosage management, and medicine-specific information ($p < 0.001$) (Table 2). The proportion of patients expressing a high knowledge level (total score >7 points) for the PIL group was significantly higher than for the PI group (44.5% vs 20.8%, $p < 0.001$).

The type of WMI received was the factor with the greatest influence on achieving a high knowledge level for medication safety (adjusted odds ratio; adjOR 3.612, 95% CI 2.554–5.108). Females and patients educated to degree level were also more likely to achieve a high knowledge level (female: adjOR 1.524, 95% CI 1.096–2.119; degree: adj OR 1.863, 95% CI 1.260–2.754). However, patients 65 years or older were less likely to achieve a high knowledge level (adjOR 0.403, 95% CI 0.218–0.747) (Table 3).

Patients' Evaluation on Quality of the WMI

All aspects of the WMI assessed by the Thai CIRF were rated higher by respondents who received PILs compared to those who received PIs. Respondents reading the PILs rated them higher for comprehensibility compared to those who

Table 1 Demographic Data of Patients Divided by Types of WMI Received

Demographic Characteristics	Number of Patients (%)			p-value*
	Total (n = 750)	PI Group (n = 375)	PIL Group (n = 375)	
Gender				
• Male	349 (46.5)	161 (42.9)	188 (50.1)	0.048
• Female	401 (53.5)	214 (57.1)	187 (49.9)	
Age group				
• 18–40	95 (12.7)	75 (20.0)	20 (5.3)	**<0.001**
• 41–65	495 (66.0)	233 (62.1)	262 (69.9)	
• ≥ 66	160 (21.3)	67 (17.9)	93 (24.8)	
Educational level				
• < Bachelor's degree	203 (27.1)	103 (27.5)	100 (26.7)	0.805
• ≥ Bachelor's degree	547 (72.9)	272 (72.5)	275 (73.3)	
Occupations				
• Agriculture	92 (12.3)	39 (10.4)	53 (14.1)	0.014
• Civil servant	354 (47.2)	191 (50.9)	163 (43.5)	
• Employee, private employee	46 (6.1)	27 (7.2)	19 (5.1)	
• Own business	93 (12.4)	51 (13.6)	42 (11.2)	
• Unemployed/student/not specified[a]	165 (22.0)	67 (17.9)	98 (26.1)	
Income				
• ≤ 10,000 baht	162 (21.6)	87 (23.2)	75 (20.0)	0.474
• 10,001–30,000 baht	256 (34.1)	129 (34.4)	127 (33.9)	
• >30,000 baht	332 (44.3)	159 (42.4)	173 (46.1)	
Health insurance				
• Universal Coverage Scheme	75 (10.0)	37 (9.9)	38 (10.1)	0.103
• Social Security Scheme	49 (6.5)	30 (8.0)	19 (5.1)	
• Civil Servant Medical Benefit Scheme	585 (78.0)	282 (75.2)	303 (80.8)	
• Self-pay	41 (5.5)	26 (6.9)	15 (4.0)	
Underlying disease				
• No underlying disease	114 (15.2)	66 (17.6)	48 (12.8)	0.219
• 1–2	488 (65.1)	234 (62.4)	254 (67.7)	
• 3–4	126 (16.8)	62 (16.5)	64 (17.1)	
• ≥ 5	22 (2.9)	13 (3.5)	9 (2.4)	
Current medications				
• None	116 (15.5)	67 (17.9)	49 (13.1)	0.282
• 1–2	166 (22.1)	80 (21.3)	86 (22.9)	
• 3–4	211 (28.1)	99 (26.4)	112 (29.9)	
• ≥ 5	257 (34.3)	129 (34.4)	128 (34.1)	
History of receiving WMI prior to study				
• None	477 (63.6)	235 (62.7)	242 (64.5)	0.865
• Received only PIs	167 (22.3)	86 (22.9)	81 (21.6)	
• Received only PILs	106 (14.1)	54 (14.4)	52 (13.9)	

Notes: *Pearson Chi-Square test was used to determine differences between groups; $p < 0.05$ with Bonferroni correction ($p < 0.0006$). Bold numbers of p-value indicate statistical significance with Bonferroni correction ($p < 0.0006$). [a]Not specified (n = 5).

Abbreviations: WMI, written medicine information; PI, package insert; PIL, patient information leaflet.

read the PIs (total scores 20, interquartile range (IQR) 17–22 vs total scores 16, IQR 14–19, $p < 0.001$). Those reading the PILs also reported higher scores for using the information in future compared to those who read the PIs (total scores 14, IQR 12–15 vs total scores 12, IQR 11–14, $p < 0.001$). The information provided in the PIL was evaluated to be

Table 2 Comparison of Correct Responses to Safety Knowledge Questions Between Receiving Package Inserts and Patient Information Leaflets

Items of Safety Knowledge	Total (n = 750)	PI Group (n = 375)	PIL Group (n = 375)	p-value*
Q1. Contraindication for taking the medicine				
• Correct	512 (68.3)	277 (73.9)	235 (62.7)	0.001
• Incorrect	238 (31.7)	98 (26.1)	140 (37.3)	
Q2. Precautions before taking the medicine				
• Correct	397 (52.9)	160 (42.7)	237 (63.2)	**<0.001**
• Incorrect	353 (47.1)	215 (57.3)	138 (36.8)	
Q3. Missed-dose management				
• Correct	522 (69.6)	229 (61.1)	293 (78.1)	**<0.001**
• Incorrect	228 (30.4)	146 (38.9)	82 (21.9)	
Q4. Non-serious side effects				
• Correct	424 (56.5)	170 (45.3)	254 (67.7)	**<0.001**
• Incorrect	326 (43.5)	205 (54.7)	121 (32.3)	
Q5. Serious side effects				
• Correct	453 (60.4)	205 (54.7)	248 (66.1)	0.001
• Incorrect	297 (39.6)	170 (45.3)	127 (33.9)	
Q6. Actions while taking the medicine				
• Correct	492 (65.6)	211 (56.3)	281 (74.9)	**<0.001**
• Incorrect	258 (34.4)	164 (43.7)	94 (25.1)	
Q7. Actions to avoid side effects/Overdosage management[a]				
• Correct	492 (65.6)	206 (54.9)	286 (76.3)	**<0.001**
• Incorrect	258 (34.4)	169 (45.1)	89 (23.7)	
Q8. Medicine-specific information[b]				
• Correct	437 (58.3)	185 (49.3)	252 (67.2)	**<0.001**
• Incorrect	313 (41.7)	190 (50.7)	123 (32.8)	
Knowledge levels[c]				
• Poor to moderate level	505 (67.3)	297 (79.2)	208 (55.5)	**<0.001**
• High level	245 (32.7)	78 (20.8)	167 (44.5)	

Notes: *Pearson Chi-Square test was used to determine differences between groups, p<0.05 with Bonferroni correction (p<0.0006). [a]Actions to avoid side effects for celecoxib-PIL, and overdosage for atorvastatin and metformin-PIL. [b]Contraindication for celecoxib-PIL, dosage instruction for atorvastatin-PIL, and precaution for metformin-PIL. [c]Knowledge levels were categorized by low to moderate levels (< 7 points of 8), High level (≥ 7 points of 8). Bold values indicate significance at p<0.05 with Bonferroni correction (p<0.0006).

Abbreviations: PI, package insert; PIL, patient information leaflet.

significantly more useful than that in the PIs (total scores 22, IQR 19–24 vs total scores 19, IQR 17–22, p < 0.001). For the design aspects, the PILs were also rated as higher compared to the PIs most notably print size and line spacing (total scores 30, IQR 25–34 vs total scores 22, IQR 19–26, p < 0.001) (Table 4).

Satisfaction with Information and Patients' Perceptions After Reading PI and PIL

The median VAS score for satisfaction with information in the leaflets overall was 7.80 (IQR 6.10–9.30), with those receiving a PIL having higher scores than the PI group (p < 0.001). Only 60 (16.0%) of the participants reading the PIs gave the maximum score for satisfaction, while 91 (24.3%) of those reading the PILs gave the maximum score. The median scores for perceived benefits, greater perceived benefit over risk and intention to take their medicine were also slightly higher in the PIL group than in the PI group (p = 0.012, p = 0.008 and p = 0.009, respectively). In contrast, there was no statistical significance in perceived risks and severity of side effects between the two groups (Table 5).

Table 3 Multiple Logistic Regression Analysis of Factors Associated with Safety Knowledge About Medications

Factors	Number of Patients (%)		Adjusted Odds Ratio	Lower	Upper	p-value
	Low–Moderate Level (n = 505)	High Level (n = 245)				
Type of WMI						
• PI	297 (58.8)	78 (31.8)	1			
• PIL	208 (41.2)	167 (68.2)	3.612	2.554	5.108	**<0.001**
Gender						
• Male	250 (49.5)	99 (40.4)	1			
• Female	255 (50.5)	146 (59.6)	1.524	1.096	2.119	0.012
Age group						
• 18–40	64 (12.7)	31 (12.7)	1			
• 41–65	317 (62.7)	178 (72.6)	0.763	0.462	1.260	0.291
• >65	124 (24.6)	36 (14.7)	0.403	0.218	0.747	0.004
Educational level						
• < Bachelor's degree	157 (31.1)	46 (18.8)	1			
• ≥ Bachelor's degree	348 (68.9)	199 (81.2)	1.863	1.260	2.754	0.002

Notes: Adjusted for type of WMI, gender, age group, educational level, occupations, income per month, history of drug allergy, and history of receiving WMI prior to study. Bold values indicate significance at $p < 0.05$ with Bonferroni correction ($p < 0.0006$).
Abbreviations: WMI, written medicine information; PI, package insert; PIL, patient information leaflet.

Discussion

Our study demonstrated the impact of providing different forms of medicine leaflets on patients' knowledge of medicine safety and perceptions of benefit and risk, plus an evaluation of the quality of the leaflets. Patients reading PILs had higher knowledge scores compared to those reading PIs regarding precautions, side effects, actions for a missed dose, and overdosage and were also more satisfied with the information provided, more likely to take the medicine and to have a positive view of the medicine's benefits. PILs were rated more highly for all aspects of quality than PIs.

Previous studies in Asia have confirmed the benefit of medicine leaflets to improve patients' knowledge.[25,33] There is no definite cut-point for indicating good medicine safety knowledge. In this study, the correct response of 80% categorizing good and poor knowledge was adopted, based on standard criteria of user testing for evaluating PILs in most European countries and Thailand.[19,32,34] This level of acceptance has also been used in previous studies assessing the impact of medicine leaflets on patients' knowledge.[25,26]

An important aspect of medicine package leaflets is their comprehensibility, which is generally difficult to understand. Studies in many other countries have demonstrated that the readability level of PIs was above the recommended reading level.[35] A previous study in Pakistan showed that 24.1% to 39.8% of patients had problems in reading and understanding the PIs.[13] Another study also found that around 40% of patients has some difficulty in understanding the language and technical terms used in the PIs.[36]

A recent qualitative study in Thailand also found that PIs contained too much unnecessary information and complex medical language.[9] While research shows that simple, short, and clearly written information presented in a user-friendly format can provide a positive impact on medicine knowledge,[33] few studies have compared different forms of WMI on knowledge. One such comparative study in hypertensive patients showed that specially developed PILs were superior to standard drug monographs in relation to what to avoid during use of a medicine.[37] This study also found that the PILs were judged to be easier to read than standard WMI. Simple, shorter PILs incorporating pictograms can also result in higher knowledge scores than longer, more complex leaflets.[38]

Logistic regression analysis confirmed that the type of WMI received was the factor most strongly associated with knowledge of medicine safety, along with gender, age, and educational level. The latter findings are in line with other studies showing that increasing age is associated with lower knowledge, while higher educational level has a significantly

Table 4 Comparison of Consumer Rating Between Package Inserts and Patient Information Leaflets Using the Adapted CIRF

Items	PI Group (Median, Range) (n = 375)	PIL Group (Median, Range) (n = 375)	p-value*
Comprehensibility			
• Read	3 (2–4)	4 (4–5)	**<0.001**
• Understand	3 (3–4)	4 (4–5)	**<0.001**
• Remember	3 (3–4)	4 (3–4)	**<0.001**
• Locate	3 (2–4)	4 (3–4)	**<0.001**
• Keep for the future	4 (3–4)	4 (4–5)	**<0.001**
Total (min-max: 7–25)	16 (14–19)	20 (17–22)	**<0.001**
Future use			
• Read	4 (4–5)	5 (4–5)	**<0.001**
• Use	4 (4–5)	5 (4–5)	**<0.001**
• Keep	4 (3–5)	5 (4–5)	**<0.001**
Total (min-max: 3–15)	12 (11–14)	14 (12–15)	**<0.001**
Utility			
• Indication	3 (3–4)	4 (3–4)	**<0.001**
• Contraindication	3 (3–4)	4 (3–4)	**<0.001**
• Direction	3 (3–4)	4 (3–4)	**<0.001**
• Precautions	3 (3–4)	4 (3–4)	**<0.001**
• Side effects	3 (3–4)	4 (3–4)	**<0.001**
• Storage	3 (3–4)	4 (3–4)	**<0.001**
Total (min-max: 6–24)	19 (17–22)	22 (19–24)	**<0.001**
Design			
• Organization	4 (3–4)	4 (4–5)	**<0.001**
• Attractiveness	3 (2–4)	4 (3–5)	**<0.001**
• Print size	3 (2–4)	5 (4–5)	**<0.001**
• Tone	3 (3–4)	4 (3–5)	**<0.001**
• Helpfulness	4 (3–5)	5 (4–5)	**<0.001**
• Bias	4 (3–4)	4 (4–5)	**<0.001**
• Spacing	3 (2–4)	5 (4–5)	**<0.001**
Total (min-max: 7–35)	22 (19–26)	30 (25–34)	**<0.001**

Notes: *Mann Whitney-*U* test was used to determine differences between groups; $p < 0.05$ with Bonferroni correction ($p < 0.0006$).
Abbreviations: CIRF, consumer information rating form; PI, package insert; PIL, patient information leaflet.

Table 5 Comparison of Attitudes Towards the Information Provided in the WMI and Perception of Benefit and Risk from Taking the Medicines

Items	Overall (Median, Range) (n = 750)	PI Group (Median, Range) (n = 375)	PIL Group (Median, Range) (n = 375)	p-value*
1. Satisfaction with the information provided in WMI	7.80 (6.10–9.30)	7.10 (5.00–8.70)	8.30 (7.20–9.70)	**<0.001**
2. Benefit to health from taking the medicine	8.50 (7.00–10.00)	8.40 (5.00–8.70)	8.80 (7.50–10.00)	0.012
3. Risk to health from taking the medicine	5.00 (5.00–7.10)	5.00 (5.00–7.10)	5.00 (4.40–7.00)	0.222
4. Severity of side effects that would occur caused by taking the medicine	5.00 (3.60–7.23)	5.00 (3.70–7.20)	5.00 (3.40–7.30)	0.581
5. More benefit or more risk**	5.00 (2.48–6.80)	5.00 (2.15–6.20)	5.00 (2.80–7.15)	0.008
6. Intention to take the medicine	8.60 (7.00–10.00)	8.40 (6.30–10.00)	8.70 (7.40–10.00)	0.009

Notes: *Mann–Whitney *U*-test was used to determine differences between groups; **Higher scores indicate greater benefit. Bold values indicate significance at $p < 0.05$ with Bonferroni correction ($p < 0.0006$).
Abbreviations: WMI, written medicine information; PI, package insert; PIL, patient information leaflet.

positive effect on patient knowledge.[3,39] Female gender has also previously been associated with a higher knowledge of over-the-counter (OTC) medicines among Italian consumers.[40]

Our study showed that patients reading the PIs had a slightly higher perception of the risks of the medicines than those reading the PILs. The way in which side effects information is presented has been shown to affect how patients perceive risks.[41,42] A previous study in the UK found that presenting risk information in numerical frequency format (for example, 1 in 10 people) resulted in the highest degree of accuracy but a lower estimate of risk compared to either verbal format (for example "common") or a combination of both.[41] Presentation as combined verbal and numerical risk has also been shown to lead to risk overestimations when compared to numerical terms alone.[43] Another study in Australia found that most consumers misunderstood risk information presented as either percentages or frequencies, which could affect the benefit-risk appraisal of taking the medicines. In addition, many participants preferred leaflets to have no numerical description.[42] Not surprisingly, numeracy skills affect the ability to understand numerical descriptors and hence the benefits and risks of medications.[44] The PIs and PILs used in our study differed in the presentation of risk information. The Thai FDA has recommended a combination of verbal and frequency descriptions to classify the risks of side effects in PIs, while only verbal descriptors without numerical frequency were used in the PILs. Thus, it may be that this difference in risk descriptors might have affected the rating of risk perception in our patients. Further research is needed to assess the effect of using numerical descriptors for classifying side-effect risk on accuracy and risk perception in Thai populations.

In contrast, benefit perception differed between the two groups in our study, with those receiving PILs being more likely to perceive benefit from the medicine than those receiving PIs and also greater intention to take the medicine. Although our participants currently used the medicines, their intention might be changed to be more or less likely to take the medicines due to the information they received. The PILs did not contain any specific additional benefit information; therefore, possible reasons for this finding could be greater satisfaction with the information provided in the PIL or higher scores for understanding compared to PIs. Studies elsewhere have found that prescribed medicines were perceived to be low in risk but high in benefit[45] and that many patients taking chronic medicines had a sub-optimal understanding of the benefits and risks of their medicines.[46] Other studies have shown that a high level of knowledge is a strong predictor of positive effects in medication adherence.[47,48]

Implications for Practice and Policy

Providing safety information for medicines enables patients to understand potential risks and involve awareness of safe medication use. Our findings showed PILs were more effective in communicating safety information of the medicines and were more acceptable among patients. There is a clear need for the development of PILs, which have both appropriate content and are designed to be effective and provide useful medicine information for patients, rather than PIs. Routine provision of PILs with verbal counseling by healthcare professionals in Thailand should be encouraged. Directing patients to the FDA website is a simple option, which could enhance knowledge of commonly used medicines.

Strengths and Limitations

This is the first study comparing the impact of PIs and PILs on medication knowledge and perceptions of risks and benefits among patients in Thailand. It is also the first to incorporate a Thai version of the CIRF, enabling evaluation of the different forms of WMI. It was a real-life situation, in that participants were allowed to read the PIs or PILs as much as they wanted while completing the questionnaire. However, all participants completed the questionnaire by themselves, without any assistance from the researchers or healthcare professionals. Although we did not require participants in our study to take a health literacy test, most of them had at least a bachelor's degree, thus were of high educational level. Moreover, they were recruited from two teaching hospitals; hence, the results may not be generalizable beyond this population or to those with low literacy levels. This study did not include any evaluation of patients' knowledge and perceptions at baseline, prior to receiving the WMI. Nor did it include any follow-up to re-evaluate the level of safety knowledge acquired.

Conclusion

This study showed a higher positive impact of PILs on medicine safety knowledge in chronically ill patients compared to PIs. PILs also resulted in greater satisfaction, more positive perceptions of the benefits of taking the medicines and

intention to adhere. These could be related to the finding that all aspects of PILs were rated more highly than PIs. The results suggest a need to develop and distribute PILs with medicines, which are designed in a simple language and user-friendly format for patients. Consumer testing using the Thai version of the CIRF could be an effective method to improve the comprehensibility and overall quality of the WMI available in Thailand.

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Disclosure

The authors report no conflicts of interest in this work.

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