Written medicine information for patients and public: An international perspective

Pitchaya Nualdaisri

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DECLARATION

I certify that this work has not been accepted in substance for any degree, and is not concurrently being submitted for any degree other than that of Doctor of Philosophy being studied at the Universities of Greenwich and Kent. I also declare that this work is the result of my own investigations, except where the thesis identifies work undertaken jointly with others. In these cases, I have made clear exactly what was accomplished by others and what I have contributed myself, and have not plagiarised the work of others.

Pitchaya Nualdaisri

Dr. Sarah Corlett

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ABSTRACT

There are numerous sources of medicine information, including written medicine information (WMI), verbal information, health-related websites, and others. Patient information leaflets (PILs) are increasingly required in many countries. The aim of this thesis was to identify the scope of studies on medicine information, to identify problems in providing WMI to patients and the general public, and to examine the needs of the general public regarding WMI and other sources of medicine information.

Mixed methods were used in this Thesis. Scoping review and study appraisal were firstly conducted to identify the scope and quality of published research concerning WMI conducted in Asia, Africa and the UK. Regulations on WMI provision from four countries on four continents were examined. The quality, in terms of their content and design, of available Ibuprofen leaflets in the UK (n=18) and Thailand (n=18) were examined. Two surveys were conducted with 652 participants in the UK (n=300) and Thailand (n=352), as well as 15 online face-to-face in-depth interviews in the UK.

In comparison to the UK, Asia and Africa had fewer studies on WMI. Some trends were identified; studies were concentrated in specific countries and research groups. The topics were varied including of source of patient's medicine information, impact of WMI on patient's knowledge and behaviour, and the development and use of pictograms. Studies focussed on factors affecting reading and usefulness of PILs, content, design and format, and regulatory aspects on PILs. The quality of the studies was varied. The majority of randomised controlled trial (RCTs) and qualitative studies adhered to their respective standards whereas the quality of some of the non-RCT and cross sectional surveys were questionable.

In terms of the regulating WMI provision, the key important aspects of medication information were covered in all regulations. The content, details included and layout, were mostly appropriate although some aspects differed between countries. The Ibuprofen leaflets from the UK were generally consistent in terms of information provided and format. However, the information was assessed as difficult to understand. In respect of Thai Ibuprofen leaflets, greater variability was observed in both the information provided and the leaflet appearance. The majority of the leaflets collected provided information for healthcare professionals not patients or the public as provision of a PIL in Thailand is advisory, but not a legal requirement. The Thai leaflets had a wide range of content, text design and format. The evaluation showed that the Thai leaflets were not appropriate for patients or the public.

In the UK, the major source of medicine information was WMI, while verbal information was the common source in Thailand. The PILs were read at the first time of being given medicines. The side effect information was the most frequent reading. The existing leaflets still did not meet patients' needs regarding the information provided, and design. Participants in both countries preferred receiving information both verbally and in writing. In terms of WMI, the most preferred way among the UK participants was a leaflet, whereas, because of lacking experience in reading PILs, The Thai participants preferred information on the medicine container. Tailoring information for individual needs were a suggestion from the participants.

There should be a requirement for PILs to be compulsory by law to be made available to the public in Thailand with all medicines. Regulation revision, guideline updates, and end-user comprehension and satisfaction surveys are all required on a regular basis to ensure PILs adhere to local guidelines, are appropriate for patients/the public, and are continuously improved.

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ABBREVIATIONS AND ACRONYMS

A/BPO	0.1%/benzoyl peroxide 2.5% gel (A/BPO)
ACE	Angiotensin-converting enzyme
ADR	Adverse Drug Reactions
Anti-TNF	Anti-tumour necrosis factor
ARV	Antiretroviral therapy
ASEAN	Association of Southeast Asian Nations
AXIS	Appraisal tool for Cross Sectional Studies
BALD	Baker Able Leaflet Design
BNF	British National Form
CASP	Critical Appraisal Skills Programme
CBER	Centre for Biologics Evaluation and Research
C-CMI	Customized CMI
CDER	Centre for Drug Evaluation and Research
CEBM	Centre for Evidence-Based Medicine
CMI	Consumer Medication Information
DDI	Drug-Drug Interaction
DMARDs	Disease-modifying anti-rheumatic drugs
DOACs	Direct oral anticoagulants
EAC	East African Community
EC	European Commission
EMA	European Medicines Agency
FDA	Food and Drug Administration
FDR	Flesch–Dayani readability
FKGL	Flesch-Kincaid Grade Level
FRE	Flesch Reading Ease
GFS	Gunning-Fog Score
GI	Gastrointestinal
GP	General Practitioners
HD	Haemodialysis
HIV-AIDS	Human immunodeficiency virus infection and acquired immunodeficiency syndrome
HIV-ASES	HIV Treatment Adherence Self-Efficacy Scale
HRQoL	health-related quality of life

IFDA	Iran Food and Drug Administration
IMD	Index of Multiple Deprivation
MAH	Marketing Authorisation Holder
MHRA	Medicines and Healthcare products Regulatory Agency
MINORS	Methodological Index for Non-Randomised Studies
MOH	Ministry of Health
MoPH	Minister of Public Health
NHS	National health service
NNTs	numbers needed to treat
NSAIDs	nonsteroidal anti-inflammatory drugs
OECD	Economic Co-operation and Development
OTC	over-the-counter
PILs	Patient Information leaflets
PIPS	Public Involvement in Pharmacy Studies
PIs	Package inserts
PPIs	patient package inserts
QRD	Quality Review of Documents
RCT	Randomised Controlled Trial
SEM	supplementary patient education material
SIMS	satisfaction with information about medicines
SMOG	Simplified Measure of Gobbledygook
SmPC	Summary of Product Characteristics
T2DM	Type 2 diabetes mellitus
TGA	The Therapeutic Goods Administration
ThaiFDA	Thai Food and Drug Administration
TKP	Ten Key Principles
TRC4Thai	Text Readability Checker for Thai Documents programme
TTM	Thai traditional medicine
UK	United Kingdom
US	United States
USKCC8	United States Keystone Consensus Criterion 8
USP	US Pharmacopeia
WMI	Written Medicine Information

DISSEMINATION

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Chapter 1 Introduction

Patients are able to access their healthcare product information easily. They increasingly anticipate being able to make decisions about their health based on available evidence.[1] In healthcare sciences, the aim of patient safety is to achieve a trustworthy system of healthcare delivery by utilising various healthcare disciplines. It decreases the unwanted impact of and maximizes recovery from, adverse events associated with delivery of healthcare interventions.[2]

The safety of patients is recognised as a fundamental principle in the practice of health care. Patient safety is a discipline in health care which aims to prevent and minimise the risk, errors and harm in patients during health care provision.[3] Clear policies, leadership capabilities, data to improve safety, qualified health professionals, and the effective involvement of patients in their care are all needed to ensure successful application of patient safety strategies.[3]

The patient safety improvement strategy should take account of the perspective of patients. The perspective of patients in receiving good quality care includes gaining access to care, responsiveness and empathy, good communication, clear provision of information, adequate treatment, improvement of the condition of health, and, in particular, safety and freedom from medical harm.[4] The patient's role in enhancing patient safety is to involve them as a major agent; to take their opinions and wishes into account. The patients should have an active role in their care.[4] An approach to establishing the effective involvement of patients' care to enhancing patient safety, and involving patients to be a part of their care is providing quality and clear medicine information to the patients.[4]

1.1 Understanding patients' medicine information needs

Patient-centred care (PCC) is a concept of patient involvement in decision making in order to create a partnership between health care professionals (HCPs) and patients to share power and responsibilities.[5] PCC can improve communication, patient involvement, the patient-health care provider relationship, and treatment adherence, according to several studies.[5] Understanding the patients' needs and use of medicines information and their views and perceptions on various information sources is essential for understanding behaviours regarding the use, misuse, and abuse of the medications, and in facilitating PCC.[6] To establish PCC, patients must be empowered by providing them with information that is easy to understand and meets their information needs. Those patients who have received clear and reasonable recommendations and advice about their medicine information are more likely to follow through with it.[5]

With regards to medicine information needs, patients' needs reflect their desire for receiving more information, in order to better care for themselves, through either verbal or non-verbal mechanisms.[7] There is a knowledge gap of information between health care provider and patients. Enhanced awareness regarding the needs and information-seeking behaviour of patients would help health care professionals to customize health information to meet patients' expectations in an effective manner.[5] This could support the patients' decision making, optimise their use of a particular medicine and lead to improved quality of patient care.[1,7]

It is therefore vital to provide patients with up-to-date and pertinent information to enable them to make informed choices about the health options available to them. For example, patients could develop a stronger sense of self-care with regard to the prevention and management of diseases and treatment-related behaviours if they were able to easily access appropriate and relevant health information.[8] Providing patients with information is vital to facilitate their understanding of the likely benefits and risks of treatment and to encourage appropriate use of medicines.[1,9] The quality of information provided can be measured in terms of it achieving certain standard criteria or meeting the information user's needs. Satisfying patients' information needs involves providing information in a timely and concise manner that is tailored to their actual needs.[6]

1.2 Sources of information on medicines for patients

At present, society is overwhelmed with information. Many different sources of information on health and medicines are available. Patients increasingly expect to be able to access high quality medical information.[1] However, information is neither always easy to access for patients, nor reliable.[1] There is no guarantee of quality of medicine information.

A wide range of medicine information sources for patients are available, including doctors and pharmacists, patient information leaflets (PILs), drug regulatory authorities, and pharmaceutical companies. Newspapers, magazines, and books, as well as radio and television (TV) are additional sources of medicine information.[10] For many people, the Internet is their go-to source.[6] Overall, the majority of medicine information consist of two main types: verbal medicine information, and written medicine information (WMI).

1.2.1 Verbal medicine information

Verbal information in this context means the medicine information is from HCPs such as doctors, pharmacists, and nurses. Most patients rate receiving the information from a HPC as their highest priority. Relationships between patients and HCPs, which can facilitate adherence to the particular treatment can be developed most effectively with verbal information. This can be a

channel for a face-to-face communication, and two-way exchange of views, which is at the heart of the partnership between HCPs and patients.[7]

It appears that verbal information is a default source which patients expect to receive. This is standard practice and a duty of HCPs when providing care service or medicines to the patients. The essential task of health workers is also to provide a reliable source of information for medicines.

Verbal advice is most usually related to a consultation with a medical specialist on prescription medicines; however, time limitation is a major obstacle to information provision. Provision of medicine information between the patient and HCP can also be limited or even not available for medicines bought over the counter. There's a huge amount of information about medicines which may be important, such that people have trouble absorbing and remembering it.[7] Verbal information therefore cannot be relied upon as the sole source of information. Other sources of medicine information might be needed. Therefore, in order to encourage safe medicine use, written information will become increasingly important.[1]

1.2.2 Written medicine information

WMI is important as supportive information. The majority of WMI for patients includes PILs and information on the Internet. The information on the Internet might be provided from health care organisations, charity bodies, or pharmaceutical companies. The Internet carries an enormous amount of information about medicines and healthcare, although the usefulness of such information is questioned in terms of its trustworthiness.[10]

For many people in highly developed countries, the primary source of information about their medicine is PILs. The PILs provide the essential and basic information about certain medicines which patients need to know, and enable them to use medicines safely.[1] The PILs is the major type of WMI on which this thesis will focus.

1.3 Patient information leaflets

Medicines are the most widely used health care intervention world-wide. PILs –easy to access data– are one tool for enhancing patients' safe use of medicines. PILs are leaflets containing easy to understand facts about medicines to give to the patients. Providing patients with suitable information is vital to encourage their appropriate use of medicines and an understanding of the likely benefits and risks of their treatment.[9]

Since 1977, patient information on medicines has been controlled in the United Kingdom. The leaflets which were introduced had to be included in every pack of medicines with certain legal requirements.[1] In the 1970s and 1980s, patients were given leaflets for inhaled medicines and other medications that required instructions for use by patients self-medicating outside the supervision of HCP.[1,11] In 1992 the European Commission issued a Directive on the labelling of medicinal products for human use and on package leaflets. The fundamental goal of the labelling and the requirements for PILs was to provide patients with complete and understandable information so that medicines may be administered safely and efficiently. By 1999, all medicines launched onto the market had authorised patient information. The Medicines Control Agency (forerunner of the Medicines and Healthcare Regulatory Agency; MHRA) published a guideline document on interpretation of the regulatory position to help manufacturers fulfil the new standards for PILs. The European Commission drew on this guideline to generate guidance. As a result, all of the European Union's Medicines Directives have been consolidated into one.[1]

PILs are tools which can facilitate communication between HCPs and patients to educate patients about their medicine, and to enhance patient safety.[1] The PIL is a source of medicine information which is usually a piece of folded paper packed into a medicine container. Each PIL is unique to a certain medicine. It relates to a fixed number of strengths, and brand-name and its contents and quality are the responsibility of the market authorisation holder for that medicine. The information contained in the PIL is derived from the pharmacology data which is written in the Summary of Product Characteristics (SmPC) for that product.[1,12] This is also a legally required document.[1] The PILs may contain varied word counts; however, they are not longer than the SmPC. In some countries, PILs are required to be written on one page. The content and information contained, and layout and design are the vital attributes to be considered.[13]

The PILs, unlike package inserts (PIs) which are designed for HCPs, are specifically written for patients. The content and information contained in a PIL must be easy to comprehend because patients may have a lower level of health literacy compared with HCPs.[14] Information about the medicine, including the therapeutic indications, dose and the usual instructions for use, a description of side effects, and storage conditions, must be set out in a particular order and written in terms that the patient could understand. The format of the information- language, words, font and size, line space, and quality of paper have to be set out in a particular order, so that this can attract patients to read the document and navigate through it.[1]

Generally, the information contained in PILs consists of medicine name, indication, dosage, contraindications, precautions, use in pregnancy and lactation, administration, drug interactions, possible side effects, storage, name and address of manufacturer / marketing authorization holder, and the date of revision of the leaflet. However, the topics are written using different

descriptions, using lay language. For example "Contraindications", will be written as "What you need to know before you take X", and "indication" as " What X is and what it is used for". This is so that lay people could understand it easily.[15]

The content of the PILs is set to be standard for the majority of the general public who are likely to use the medicine. This means that the information is general, it is not adapted to be suited to some specific condition. However, information about dose difference in certain age groups, and some certain conditions e.g. pregnancy or breast feeding are covered in PILs.[16]

In addition to what needs to be written, how the information is written on the PIL is also important. For example, information about the benefits and risks of the medicine should be weighted to facilitate understanding, and the possibility of side effects should be written in numbers or text.[17–22]

As far as patient satisfaction is concerned, people expect a good quality of information about their medicines, whether prescribed or over the counter (OTC).[1] Patients' attitudes, opinions and knowledge in all stages of leaflet development should be taken into account. All those involved in PIL preparation must aim to produce usable PILs designed to meet the patient's needs and support the safe and appropriate use of medicines.[1]

In order to achieve the best possible content and presentation, patients' preferences for PILs should be investigated. How information in PILs is provided, and updated so that it meets the needs of patients in the changing environment with increasing levels of technology should be explored.[1]

Unlike other sources of information, PILs are highly regulated. All PILs are required to be reviewed and approved by a country's authorised regulatory body before the medicine is issued to patients.[1] Generally, basic information is a regulatory requirement, but the quality of the information is variable depending on the regulations and context of countries and drug companies.

User-testing is a performance based, flexible development method which identifies barriers to readability and understanding and use of the data presented in a PIL, and indicates problem areas which should be amended. It should be used as part of a leaflet development process.[23] All PILs in the EU must be subjected to user-testing, but this process is less common in other countries.

The PILs are becoming increasingly required in many countries including in developing countries, such as Thailand and other Association of Southeast Asian Nations (ASEAN) and African countries.[24,25] In Thailand, guidelines for leaflet development for drug research and innovation

have been introduced in Thailand since 2013,[26,27] with an updated guideline version (minor change) published in 2019.[28] Even though, there is the guideline stating that a Thai PIL should be provided with medicines, this is still optional and they are voluntarily produced and supplied by pharmaceutical companies. Hence there is a very limited number of PILs available.[25]

Recently, there is a working group who are encouraging the Thai Food and Drug Administration (Thai FDA) to establish the provision of written information to patients (PILs) in Thailand as standard practice. This working group was formed from university bodies. This guidance is in a transitional period during which Thai FDA have tried to encourage the drug companies to provide PILs for the prescription medicines. In this period, the research evidence from published studies is needed to support the development of policies and organizational facilities. Furthermore, comparing research and guideline between developed and developing countries must be undertaken because the evidence obtained can help authorities in developing countries to adopt the strengths, and avoid the weaknesses found in other countries. Finally, these can shorten the timelines in establishing the regulation.

In the initial stage of PILs regulation in Thailand and other areas of interest such as Asia and Africa, research studies could play an important role to support these issues. A critical evaluation and comparison regarding WMI between the UK, where medicine information systems are well established, and all the various medicine leaflets in Thailand where the system is developing, could therefore be useful to both countries in terms of bench-marking, and future improvement in PILs development, and policy establishment.

1.4 Aim of the present thesis

The study aims to identify the scope of current studies related to medicine information, especially PILs, and identify problems in providing WMI to patients and the general public. Additionally, the study aims to identify the needs of the general public in the UK and Thailand regarding WMI and other source of medicine information.

1.4.1 Objectives

1. To review all studies on the provision of medicine information for patients in Asia and Africa in comparison to studies in the UK through a scoping review.
2. To assess the quality of intervention studies and surveys identified in the scoping review
3. To examine the guidelines on PILs in the EU, the United States, Australia, and Thailand.
4. To evaluate the quality of a sample of UK PILs and Thai PIs of Ibuprofen provided in the UK and Thailand.

5. To identify medicine information sources used, views on different sources of and perceived needs for medicine information among the general public with experience of using medicines in a region of England.
6. To identify medicine information sources used, views on different sources of and perceived needs for medicine information among the general public with experience of using medicines in Songkhla Thailand.
7. To compare the sources of medicine information used, views on different sources and perceived medicine information needs among the general public between the UK and Thailand.
8. To explore in depth views of the general public in England on PILs and how they use them.

1.5 Structure of this thesis

This thesis describes a mixed-methods research study examining WMI for patients and the public. A scoping review of the literature, study appraisal, and several empirical studies were conducted. The guidelines from several countries regarding the provision of WMI and the availability of WMI were reviewed and evaluated. In addition, the needs of the general public regarding WMI and other sources of medicine information were examined.

Chapter Two provides an overview of the methodologies and data collection methods used in this thesis.

Chapters Three and Four present a scoping review of the literature, and associated study appraisal. The review was to scope and appraise the quality of published research concerning PILs conducted in Asia, Africa and the UK, between 2004-2017.
Chapter Five presents an examination and comparison of the guidelines on PILs in the EU, the United States, Australia, and Thailand.

Chapter Six presents an evaluation of the layout and design, readability, and regulatory compliance of a sample of UK PILs and Thai PIs for Ibuprofen provided from pharmacy in the UK and Thailand.

Chapters Seven, Eight, and Nine present a cross-sectional survey study. Chapter Seven and Eight describe the development, piloting and distribution of a questionnaire to examine medicine information sources used, views on different sources of and perceived needs for medicine information among the general public in the UK and Thailand, respectively. Then, the results from these two countries were compared, and are presented in Chapter Nine.

Chapter Ten presents the results from conducting a qualitative study in the UK to explore the views of the public on what information about their medicines they want or need, how they use PILs, how they feel or react to the information within a demonstrated PIL.

The final chapter of this thesis, Chapter Eleven summarises the results from earlier chapters and includes a discussion of the strengths, limitations, implications for pharmacy practice, and research and policy from this study, plus priorities for future research and conclusion.

Chapter 2 Methodology

2.1 Introduction

The thesis falls under the umbrella of pharmacy practice research and aimed to explore WMI in terms of studies related to its regulations and provision, quality of available PILs and PIs, public's views on PILs and other source of medicine information. There was an important study which has informed research into WMI. It was a systematic review published in 2007. Most of the studies identified were conducted in highly developed countries. There were only two published studies included which were from either Asia or Africa. To update what is already known and has been published focused in Africa, Asia, compared to the UK, a new scoping review of the literature conducted in these geographical areas was, therefore, undertaken. Despite much research into PILs in the UK, and a small study in Thailand, little work has focused on the content and format of WMI in these countries and the leaflets which were available in the UK and Thailand public have not been evaluated, comprehensively. There was also relatively little research on the general public's needs for medicine information either in the UK or Thailand. In terms of novelty, this thesis will investigate these knowledge gaps.

The thesis aimed to explore WMI in terms of studies related to, its regulations and provision, quality of available PILs and PIs, general public views on PILs and other source of medicine information. The scope of related studies and current problems of WMI were also investigated. To explore and fill the knowledge gaps, different methods were needed and therefore, this thesis has adopted a mixed methods approach. This chapter presents the introduction to the research methodology, and methods of data collection used in this thesis. Detailed descriptions of the methods used for each study are described in the relevant chapter.

2.2 Methodology

2.2.1 Pharmacy practice research

Pharmacy practice research is a type of health services research.[29] The International Pharmaceutical Federation has defined pharmacy practice research as a discipline that studies the clinical, behavioural, economic and humanist implications of pharmacy practice, and changes in practice and implementation into routine practices of innovations and new services.[30] Internationally, the term "pharmacy practice research" is also known as Social and Administrative pharmacy, or Social pharmacy.[31] Pharmacy practice research is a tool to develop effective

services, transferring and achieving the long-term implementation and sustainability in routine practices.[29]

The thesis aims to identify the scope of and address problems in pharmacy practice services in providing WMI to patients and the general public. In addition, the needs of the general public regarding WMI and other source of medicine information are examined. The findings are beneficial to the process of developing and improving pharmacy services, as well as policy formulation.

2.2.2 Mixed methods research

Mixed methods research is now a recognised research paradigm in the health services and pharmacy practice research fields. Mixed methods research can be viewed as a distinct category of multiple methods researches. Multiple methods research is an overarching term which refers to all of the various combinations of research methods involving more than one data collection procedure. This can include combinations of exclusively qualitative and quantitative approaches. In order to achieve all objectives, mixed methods which included qualitative and quantitative were used in this thesis.

Mixed-methods were used to provide greater insight into the general publics' experiences, views and attitudes towards medicine information. This approach enabled the combined strengths of qualitative and quantitative methodologies, which answer different research questions, to be integrated. In this study quantitative and then qualitative approaches were used sequentially enabling divergencies or inconsistencies in the findings between the two approaches to be explored providing a more in depth understanding of the subject area.[32]

However, some scholars have argued that because qualitative and quantitative methods are based on incompatible assumptions, they cannot be meaningfully combined in a single framework.[33] By their nature, the qualitative and quantitative methods shouldn't be compared directly; they should be merged by combining their strengths in a complementary way.[33] Using mixed methods in a single study is challenging for a single researcher as it requires them to have proficiency in both methodological approaches, including both the collection of data and its analysis. If there are problems interpreting conflicting results, the researcher must take more effort and work. The mixed-method research is also more costly and time-consuming and therefore requires greater research resources.[32]

2.3 Method

As aforementioned, within this thesis, mixed methods were used to examine WMI for patients and public. The scope and provision of WMI to patients and the general public was explored. Guidelines in providing WMI and available WMI were reviewed and evaluated. In addition, the needs of the general public regarding WMI and other sources of medicine information were examined.

2.3.1 Scoping review

Scoping review is one applicable approach to literature review. This type of review provides a preliminary assessment of the potential size and scope of available research literature.[34] The scoping review aimed to determine the nature and scope of research evidence in this field. This type of review is designed to use as both a methodology for assessing emerging evidence and as the first step in research development. This main distinguishing feature is that it provides an overview of a broad topic. As a kind of review, scoping reviews share several characteristics with systematic reviews; beginning with a primary question, being systematic, transparent, and replicable. However, instead of focusing on providing answers to a more particular question, a scoping review allows for a more general question and exploration of the related literature. It also primarily focuses on a review process rather than a quality assessment process. A scoping review, has less depth but a broader conceptual view compared to a systematic review.[35]

A scoping review is also more adaptable than a traditional systematic review or meta-analysis. It can account for a wide range of relevant literature and studies using various methodologies, which a traditional review cannot do.[35] Theoretical and narrative reviews, grey literature, as well as both qualitative and quantitative research can be eligible to be included within the review. When the studies related to a research area are vast and complex, a scoping review is an appropriate alternative. The results of a scoping review are usually summarised narratively with little or no statistical data. It can be considered as a highly informed starting point for additional investigations in order to understand and make contributions to research, education, practice, and policy.[35]

Current studies regarding WMI in terms of clinical impact, patient's view, and usability are broad and utilise a range of methods. Hence, a scoping review is a suitable methodological technique to explore the scope of this research evidence. As a prelude to carrying out empirical studies in Thailand and England, it was considered essential to scope the literature in these countries. However, given the paucity of literature generally in low to middle income countries, it was considered appropriate to extend the review to all of Asia and Africa. Chapter3 presents a scoping

review of the literature regarding medicine information leaflets in Asia, Africa and the United Kingdom. The study was registered with PROSPERO: registration number CRD42019127001.

2.3.2 Systematic review; Study appraisal

A systematic review is a study which aims to identify, appraise and synthesize research evidence in a systematic manner often adhering to the guidelines on the conduct of a review provided by the Cochrane Collaboration.[36] It is transparent about its methods in order to make it easier for others to replicate the process. Systematic reviews employ explicit, systematic methods that are chosen with the goal of minimising bias in order to produce more reliable findings that can be used to inform decision making.[37]

In comparison, there are several differences between the systematic review and the scoping review. While, a scoping review concerns a much broader range of topics in comparison with a systematic review, systematic reviews are intended to summarize the literature to address a specific question. The systematic review is thought of as a method for combining the findings of several studies that address the same research subject.[34,35]

Study appraisal is a critical component of systematic review. The appraisal aims to understand the validity of the studies, to discover reasons for differences in study results and to provide information to judge the applicability of the systematic review to clinical practice.[38] Internal and external validity are essential components of study quality. The term "internal validity" refers to the reduction of method error or bias in a study. External validity refers to the generalizability of a trial's findings to other populations.[39]

A systematic literature search was carried out for the scoping review. All studies included were categorised by methodology. There were some studies utilising standard methods with similar objectives, which meant that their quality could be assessed using specific tools, notably intervention studies and surveys. Chapter 4 describes the appraisal of these studies with particular tools.

2.3.3 Cross-sectional surveys

Cross-sectional survey is an observational study design. The survey is a method of gathering people’s opinion on a particular topic, such as their perception or reported use of health services. Many cross-sectional studies are done using questionnaires. The key message of this kind of study is the interesting outcomes are measured in a specific point in time. The participants or subjects are selected based on the inclusion and exclusion criteria set for the study. The selection process or sampling protocol is a vital component of this type of study.[40]

Within this thesis, three cross-sectional surveys were conducted. In Chapter Six, a survey of available PILs in the UK and PIs in Thailand is described. These documents were conveniently collected at one point in time. Then, the appropriateness of layout and design, readability, and regulatory compliance were investigated, using standard methods where available and a novel method for the Thai leaflet readability assessment. No similar study has been reported.

Chapters Seven and Eight also describe a cross-sectional survey study, designed to seek the views of the general public in both England and Thailand on the sources of medical information used, as well as public perceptions and opinions of different sources of medicine information. Face-to-face interviews, rather than postal or other methods, was used in order to achieve a representative sample of the general public, who had recent experience of medicine use. Quota sampling was used in both countries to ensure a representative sample as far as possible. Face-to-face recruitment was used in order to conduct the interviews, while facilitating participants to use an online version of the questionnaire, and to indicate their preferred response to each question, or provide a verbal response. The questionnaire was developed specifically for the study to enable comparisons between countries, described in Chapter Nine, therefore is a novel instrument.

2.3.4 Face to face interview

In-depth, face-to-face interviews are an excellent method to use to deeply explore the respondent's feelings and perspectives on a subject with open-ended questions. As a result, there is a wealth of background information that can be used to shape further questions about the topic. In-depth interviews are distinguished by open-ended questions, a semi-structured format, recording of responses, and an attempt to understand and interpret.[41] Face-to-face interviews are structured interviews conducted by trained interviewers who follow a standardised interview protocol and record the responses of participants.[42] Depending on the individual participants, the interviewer may rephrase the questions and how they are asked.[43]

In Chapter Ten, online- face to face in-depth interviews were conducted to explore the views of the public in England on what information about their medicines they want or need, how they use PILs, how they feel or react to the information within the PIL and how they believe the emotions triggered may influence their subsequent behaviour. A topic guide was specifically developed for this interview, based on the results of the UK survey described in Chapter seven, to enable an exploration of these findings. Due to social distancing requirements enforced during the coronavirus pandemic, online in-depth face-to-face interviews with participants in the UK were conducted instead of meeting in person.

2.4 Ethics approvals

In this Thesis, all studies in which humans were involved were considered for ensuring the safety, confidentiality, and informed consent of any participants. Substantial protocols which outlined research processes, questionnaire, informed consent, and declaring ethical issues were provided to the Medway School of Pharmacy (MSoP) ethics committee. The studies in Chapter 7 (appendix 7) and Chapter 10 (appendix 13) were approved by MSoP ethics committee. With regards to the survey in Thailand (Chapter 8, appendix 8), all similar documents which were translated into the Thai language were submitted to, and then approved by Prince of Songkla University (Thailand) Ethics Committee (document number: PSU 161/1047). The studies which were involved with documents analysis did not require ethical approval.

Chapter 3 Medicine information leaflets in Asia, Africa and the United Kingdom: A scoping Review of the literature

3.1 Introduction

An important study which has informed research into written medicines information, such as PILs, is a systematic review published in 2007.[44] This summarised the results of available well-designed studies and provided a high level of evidence on the effectiveness of PILs. It sought to determine the role and value of written information in improving patients' knowledge and understanding of treatment and health outcomes. This revealed that people had different attitudes to many aspects. Most people do not take into account the written information they receive with medicines. They considered these used complex language and poor visual presentation. Most studies found that the information did not increase patients' knowledge. In contrast, patients acknowledged their preference for tailored written information which was designed for their individual use. Patients required information to enable them to share their decision about taking a medicine. Some patients did not want written information instead of information from their prescriber. Some health professionals thought that leaflets for patients should be plain and easy to understand. It demonstrated that there is still a gap between currently provided leaflets and information which patients expect to receive.[44]

Therefore, there is a challenge for the development and provision of flexible leaflets. This review also pinpointed that future research should identify and fulfil the best options to meet patients' needs, improve the regulations, and finally strengthen the patient safety system.

A key point of interest in relation to this review is that most research identified was conducted in developed countries. After the authors applied their exclusion criteria, only two published studies included were from either Asia or Africa.

To establish what is already known and has been published, a review of the literature conducted in the area of interest must be undertaken. In the initial stage of PILs regulation in Thailand and other areas of interest such as Asia and Africa, research studies could play an important role to support these issues. Therefore, a review of the literature carried out in Asia, Africa in comparison to work conducted in the UK, where PILs have been in widespread use for a long time, is of value. It is also of use to compare regulation of PILs between regions, in order to make this review of greater value to the policymaker.

The research question posed for the scoping review is “what is the scope and quality of published research concerning PILs conducted in Asia, Africa and the UK, between 2004-2017?”

3.2 Aim and Objective

To review all studies on the provision of medicine information for patients in Asia and Africa in comparison to studies in the UK through a scoping review.

3.3 Methodology

3.3.1 Search Strategy

An initial search was carried out in selected health-related databases with potential keywords. To achieve comprehensive searching, these initial searches used a mixture of related keywords which were developed by research team discussion. The key term “patient information leaflet” was used initially to start the search. Further searches for common words such as ‘medicines’, ‘patient’ and ‘information’ were made for finding more groups of keywords particularly in health databases, and the results of these pilot searches were reviewed to find more relevant keywords.

Key terms relating to “information and leaflet” were connected, using the Boolean operators AND, and OR, with terms relating to medicines, such as medicine, drugs, prescriptions, labelling, or labeling. Other words which were found from preliminary searches, such as “package inserts”, consumer, and patients’ sheet, illustrated, were combined and used. To thoroughly search, the asterisk symbol was used looking for all matches containing the prefix.
Finally, the relevant key terms and subject headings selected included: Medic* information, Drug information, Drug labelling, Illustrated medic* information, Medic*package leaflets, Medic* information leaflets, Package inserts, Package Leaflet, Patient information leaflet, Written medic* information, Consumer drug leaflet, Patient information sheet.

To ensure the most appropriate databases were utilised searches using one simple strategy “drug information” AND “patient” was applied to a number of different databases in two ways, both titles only and all fields. Screening the first 50 hits from each result ensured selection of most relevant databases. These were Medline, CINAHL, Web of Science, Scopus. Once the databases were selected, running the full search strategy in each of these was conducted. For each database, the number of hits from each database search was recorded and the number excluded from the initial screening. An example of a searching strategy is shown in Box 3-1. The full searching strategies are given in Appendix 1.

Box 3-1 Searching strategy

1. “Medic* information”
2. “Medic* information” AND Patient
3. “Drug information” AND Patient
4. “Drug labelling” AND Patient
5. “Illustrated medic* information”
6. “Illustrated medic* information” AND Patient
7. “Medic*package Leaflet”
8. “Medic*package Leaflet” AND Patient
9. “Medic* Information leaflets”
10. “Medic* Information leaflets” AND Patient
11. “Package inserts”
12. “Package inserts” AND Patient
13. “Package inserts” AND Medic*
14. “Package Leaflet”
15. “Package Leaflet” AND Patient
16. “Package Leaflet” AND Medic*
17. “Patient information leaflet”
18. “Patient information leaflet” AND Medic*
19. “Patient information leaflet” AND Patient
20. “Written medic* information”
21. “Written medic* information” AND Patient
22. “Consumer drug leaflet”
23. “Consumer drug leaflet” AND Patient
24. “Patient information sheet” AND Patient

Inclusion/exclusion criteria: To limit the number of the papers, and keep this research up to date, searching was strictly limited from 2004 to 2021. In line with the main purpose of the review, studies were included if they were conducted only in Asian, African countries, and the United Kingdom. Furthermore, the study should contain information on medicines for patients; therefore: articles were excluded if they: were information for health activities, behavioural changes, drug information for health professional, protocol for study, letter to the editor or not an empirical study. The articles written in a language other than English were not included, however those with an English abstract were included.

Potential keywords together with the identified databases were combined, and when there was any possibility the study might be relevant, the free full-texts, and those available through the universities of Kent and Greenwich were downloaded.

The reference lists of the selected papers and forward citations were searched for additional relevant publications. Citation searching was applied to the references cited in those papers that were identified by searching electronic databases. Then, reference searching for all of the selected papers was conducted to obtain more relevant papers. All of the papers which met the inclusion criteria were reviewed.

The obtained papers were systematically filed. The team agreed that papers be divided into four folders with separate lists for each of the four groups of full-texts: Asia, Africa, UK and papers relevant to general background. To create a database, the article titles were recorded and combined in a single sheet on the Excel database called “master list”. After merging the results from the different search engines, duplicate publications were removed by a reference management programme. This was followed by screening each title independently for inclusion by two members of the team, then discussing by the full team (PN, SC, JK) to reach agreement on whether to include each article or not, and recording reasons for exclusion at this point. At the end of this process, all reviewers had agreed on which papers were to be included or excluded from the review.

3.3.2 Data extraction

All obtained articles were scrutinized by screening their abstracts for scoping the main study aim. Before starting extraction, the purpose of each of them was identified, so that they could be evaluated using the same method. The papers could be separated into three groups along with their main focus or objectives: (i) on the leaflet, (ii) on the patient, and (iii) on the source of drug information. Focusing on the leaflet, it was identified that these kinds of papers described studies on design, accessibility, availability, readability and content of the leaflets. Studies in patients were carried out on patient views, attitudes, knowledge and adherence: the main criterion for inclusion in this group was patient involvement. The last group was studies whose main purpose was to find patients’ source of drug information, where the PIL was one of the main sources.

General data were extracted from all relevant articles in term of the researchers’ data, year, study objectives, type of medicines, study site, study design, outcome measurement, statistics, and key study findings. For studies on leaflets, their specific focus: design, accessibility, availability, readability and contents were noted. Demographic data, sampling frame and sample size, study design, test method, inclusion and exclusion criteria were specially recorded on studies with

patients. Demographic data, sampling frame and sample size, study design, survey method, inclusion and exclusion criteria were extracted from studies which aimed to find the source of drug information for patients.

The reviewer recorded the main findings stated in each paper. For qualitative studies, their main results were recorded, the same as for quantitative studies.

3.3.3 Study appraisal

After data extraction, the team discussed the results. After screening all papers, the consensus was that all of papers could be firstly classified in terms of their quality by their focal point: content, content plus design, and patient-related issues. Basically, it was agreed that all studies involving patients were likely to be of greater importance than other types. A categorisation was developed iteratively to enable classification. (Table 3-1) This had three main sub-types of study: 1 which were studies involving patients, 2, which included studies looking at the content plus design of PILs/PIs, and 3 studies which looked at content only. Within the subgroups, the studies were qualified further by their methodology.

Three researchers independently categorised all obtained papers. Then, the team meeting was conducted for matching the category result. Where there were disagreements in category between the team, sharing opinion and discussion was the way for finding consensus.

Table 3-1 Categorisation for studies involving assessment of patient information leaflets.

Study Focus	Quality	Category
Content	**Descriptive** – what the PIL includes only and/ or comparison to the literature or best evidence	3B
	Comparison – content of PIL vs. regulatory requirements	3A
Content plus Design – including language and/or format	Descriptive or evaluated using **in-house** scheme	2C
	Evaluation utilising **validated criteria** e.g. Flesch- Kincaid.	2B
	Formal user-testing for comprehension using internationally accepted method – **Cross sectional or before/ after surveys**	2A
	Formal user-testing for comprehension using internationally accepted method – **RCTs**[a]	2A*
Patient views/ attitudes +/or impact of PIL on patient behaviour – e.g. adherence – an 'intervention study'	Quantitative studies - descriptive	1C
	Qualitative studies – in-depth analysis)	1B
	Quantitative using tools to measure effect of using PIL (before/ after; cohort; **non-randomised studies**)	1A
	Quantitative using **tools** to measure effect of using PIL (**randomised studies**)	1A*

[a] RCT = Randomised Control Trial

3.4 Results

3.4.1 Summary of studies identified

A total of 893 articles were identified: 691 of these were excluded because they were either not conducted in the target countries or not specific to medicine information. There were 29, 102 and 53 from Africa, Asia and the UK, respectively. The ratio between the number of papers published per number of countries in their continent (or the UK) was 0.63, 2.17, and 53in Africa, Asia and the UK, respectively. The number of studies in each Category is shown in Figure 3-1. List of the originator countries and the number of studies in each country are shown in Table 3-2 and Figure 3-2.

Figure 3-1 Flow diagram showing the number of obtained studies

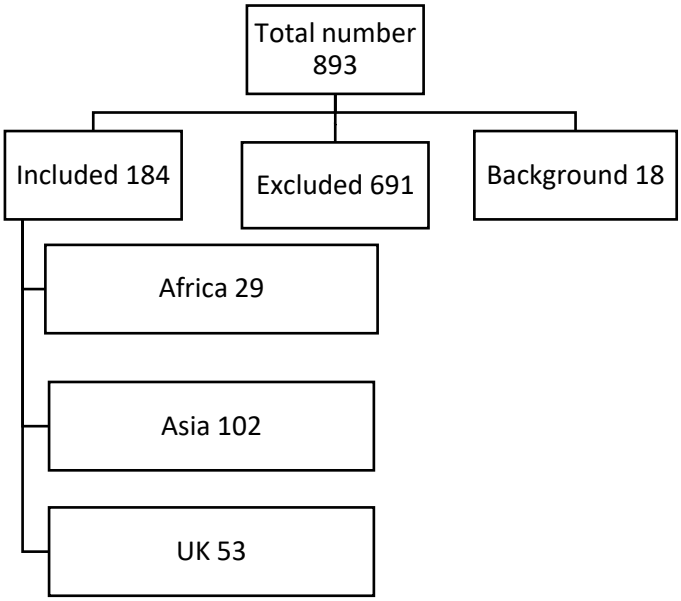


Table 3-2 The list of the originator countries and the number of studies in each country

The UK		Asia		Africa	
Country	Publication	Country	Publication	Country	Publication
The UK	53	Armenia	1	Cameroon	1
		Bangladesh	1	East Africa	1
		China	2	Egypt	1
		Emirate of Abu Dhabi	2	Ethiopia	1
		Hong Kong	2	Ghana	5
		India	23	Nigeria	6
		Indonesia	1	South Africa	12
		Iran	6	Sudan	1
		Israel	1	Tanzania	1
		Japan	8		
		Korea	5		
		Kuwait	2		
		Malaysia	2		
		Pakistan	4		
		Palestine	7		
		Qatar	4		
		Saudi Arabia	10		
		Singapore	4		
		Sri Lanka	2		
		Taiwan	3		
		Thailand	8		
		Turkey	1		
		United Arab Emirates	2		
		Multi-Country	1		

Figure 3-2 Map showing the number of studies in each country

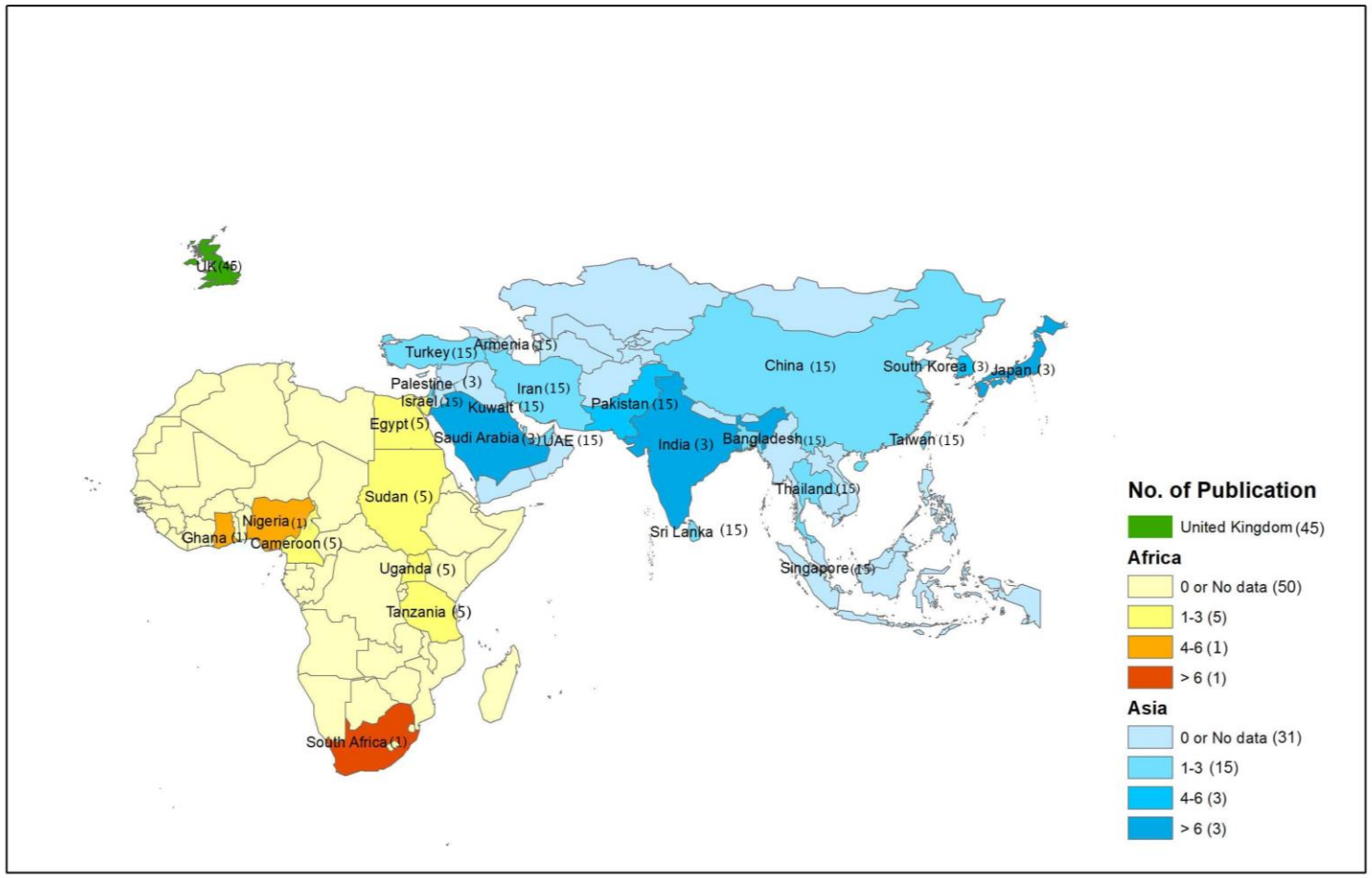


Figure 3-3 The number of studies in Africa, Asia, and the UK from 1996 – 2021.

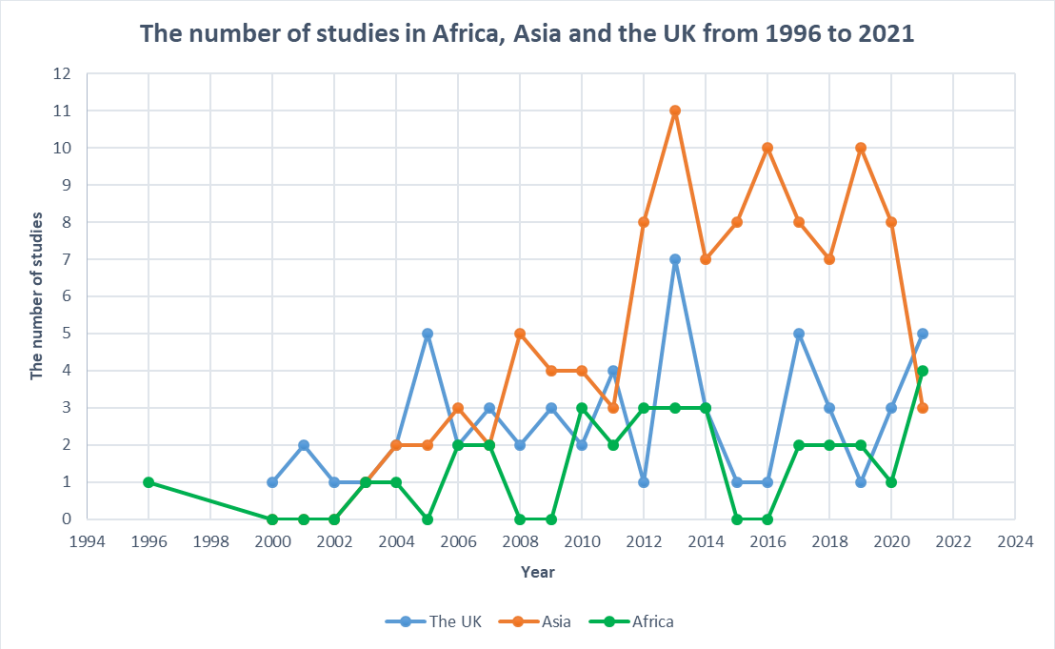


Figure 3-3 shows the fluctuation in the number of studies in Africa, Asia and the UK between 1996 and 2017. In Africa, the earliest study was found in 1996. The number of articles have fluctuated over the period. The trend was not consistent and numbers low, with the maximum number of the studies being three. In contrast, there was a steady increase in number of research papers over the period in Asia. The number of articles reached a peak with 11 and 10 papers in 2013 and 2016, respectively. In the UK, the tendency is increasing over the duration. However, there was also a slight fall in the number of papers in 2012 and again between 2015 and 2016, the overall trend has been an upward one.

Overall, In Africa, 11 studies focused on the impact of PILs on patients' behaviour and six involved some form of user-testing. In contrast, a large proportion of studies in Asia assessed only the content of PILs, 26 were patient surveys relating to sources of medicine information and relatively few (12) assessed the impact of PILs. Almost all studies in the UK either assessed impact of PILs on patients' understanding of information, or involved user-testing.

3.4.2 Study design

The research interest could be divided into three main groups. Group (i) studies on PILs/PIs mainly evaluated the content, by collecting a wide variety of PILs and comparing them with either domestic or international regulations, literature or best evidence. Some studies also evaluated readability utilising validated criteria e.g. Flesch-Kincaid, Simple Measure of Gobbledygook (SMOG). In other studies, PILs were re-designed with new content such as pictograms, headline sections or benefit information, often followed by user-testing.

Group (ii) studies involving patients were conducted to test the impact of PILs in term of change in knowledge as well as assessing patients' attitudes, acceptability, perceptions and behaviour. These studies used several methodologies including randomised controlled study, before-after method and cross-sectional surveys.

With regard to sources of medicine information, most group (iii) studies used quantitative cross-sectional surveys to identify different sources used by patients to obtain medicine-related information, with PILs being one of these. A few articles in this group were qualitative studies.

By using the categorisation system devised, all of the papers were categorised into 10 classes. Most of the studies in Asia were categorised in groups 1 and 3, whereas the studies in the UK were mostly in group 1. In Africa, the number of research studies was distributed across all groups in small numbers. The number of studies of each category is shown in Table 3-3. Studies with each class were then reviewed together to produce a narrative description.

Table 3-3 Categorisation of studies across Africa, Asia and the UK

Type	**Class**	**Africa**	**Asia**	**UK**	**Total**
Patient views/ attitudes	1A*	5	7	5	17
+/or impact of PIL on	1A	2	5	0	7
patient behaviour – e.g.	1B	2	1	8	11
adherence – an 'intervention study'	1C	7	27	16	50
Content plus Design –	2A*	1	1	2	4
including language	2A	3	3	4	10
and/or format	2B	2	4	7	13
	2C	3	10	6	19
Content	3A	1	28	4	33
	3B	3	16	1	20
Total		29	102	53	184

3.4.3 Description of studies by category

3.4.3.1 Category 1A* studies

Category 1A* was defined as quantitative studies using tools to measure effects of using PILs. They must be randomised studies conducted to assess patient views, attitudes or impact of PIL on patient behaviour – e.g. adherence assessed within an 'intervention study'. Ten articles were categorised in this category of which three originated from each of Africa and the UK and four from Asia. Table 3-4 Summary of studies in Category 1A* shows the summary of studies in Category 1A*

Table 3-4 Summary of studies in Category 1A*

Continent	Country	Number	Summary
Africa	South Africa	5	Assessing the impact of medicines information in HIV/AIDS patients.[45–49]
Asia	Kuwait	2	Assessing patients' opinion on written instruction, PIL comparing with verbal information.[50,51]
	Qatar	3	Developing pictogram and evaluating comprehension of them.[52] Assessing impact of customized CMI (C-CMI) on health-related quality of life (HRQoL). [53] Evaluating impact of Consumer Medicine Information (CMI) on medication adherence and glycaemic control [54]
	Thailand	1	Assessing impact of patient education on medication adherence in patients with rheumatoid arthritis (RA). [55]
	Turkey	1	Evaluation of effect of written or verbal information on asthma knowledge.[56]
UK	UK	5	Evaluating written information for patients undergoing anaesthesia, patients with rheumatoid arthritis, patients with acne, and side effect information[57–61]

In Africa, there were five studies which assessed the impact of medicines information in Human immunodeficiency virus infection and acquired immunodeficiency syndrome (HIV/AIDS) patients. One assessed the impact of medicines information on adherence to chronic co-trimoxazole therapy in low-literate HIV/AIDS patients. Adherence with the co-trimoxazole tablets was assessed using two measures; self-report adherence and tablet count.[45] Another study investigated the influence of a simple pre-tested patient information leaflet (PIL) containing both text and illustrations on HIV- and antiretroviral drugs (ARVs)ARV-related knowledge and on self-

efficacy over six months in a limited literacy African population.[46] A 22-question knowledge test evaluated three knowledge areas: ARV side effects, additional ARV information and HIV/AIDS information. Self-efficacy was assessed using a slightly modified version of the HIV Treatment Adherence Self-Efficacy Scale (HIV-ASES). Another evaluated the effect of distributing a patient information leaflet (PIL) on knowledge acquisition and recall. Participants were questioned about their current medicine practices and their perceptions and expectations of their medicine in order to assess if these practices, perceptions and expectations had any influence on the extent of their medicine knowledge.[47] A randomised controlled study was aimed to access the impact of using simple text combined with pictograms to present side effect information. As with earlier studies, the study was carried out in limited literacy HIV patients taking ARVs. Providing simple written information with pictograms significantly enhances the knowledge of the side-effects in rural South African patients with limited literacy .[48] Another RCT study was carried out to assess the effect of pictograms on reporting adverse drug reactions (ADRs) of ARVs in Northwest Ethiopia. In native HIV-positive patients with limited literacy, using pictorial representation has resulted in small improvements in identification of several medicines but only of one ADR.[49] These studies all found improved adherence to therapy, medicines knowledge, and self-efficacy.

In Asia, all seven of the studies involved interventions in addition to PILs. One study in Kuwait assessed depressed patients' opinion toward receiving written or specialised verbal pharmacists' instructions using a survey and also determined the effect of these two interventions on patients' medication knowledge. This survey was based closely upon a questionnaire which had previously been validated for use in depressed patients in the United Kingdom, however the method of knowledge assessment was designed in-house specifically for the study.[50] A second Kuwaiti study in depression by the same authors assessed the effectiveness of a PIL with or without pharmacist counselling on patterns of antidepressant medication knowledge, using the same instrument, and adherence. Both studies found increased knowledge with both the PIL and counselling, the latter also showed increased adherence, measured using self-report and pill counts.[51] In Qatar, there were three research studies conducted. The study authors developed pictograms illustrating selected medicine label instructions and evaluated comprehension of the pictograms or conventional text supported with verbal instructions in foreign workers with low literacy skills. They found that pictograms alone were poorly understood, but when combined with verbal instructions, were superior to text plus verbal instructions.[52] A randomized controlled intervention study was aimed to assess the impact of customized CMI (C-CMI) on health-related quality of life (HRQoL) among type 2 diabetes mellitus (T2DM) patients. There was a difference between groups in the HRQoL utility value at 6 months. The intervention group compared with the control group had significantly greater EQ-VAS at 6 months.[53] Another RCT study aimed to

evaluate the impact of Consumer Medicine Information (CMI) on medication adherence and glycaemic control among patients with type 2 diabetes. The results showed that T2DM patients who examined CMI additional to usual care had improved their adherence score. The intervention CMI resulted in better glycaemic control, but this did not reach statistical significance.[54]

In Thailand, a study aimed to assess the impact of patient education on medication adherence in patients with rheumatoid arthritis (RA). The multi-component intervention group received 30-minute directed counselling and a disease information pamphlet, which contained some medicine information. The single intervention group received only a disease information pamphlet. The study found that patient education significantly improved adherence in both groups. There were no differences between single education intervention and multi-component education intervention in improving medication adherence.[55]

In Turkey, one study was carried out to assess the effect of asthma education, provided as written or verbal information or a combination, on asthma knowledge using a questionnaire developed in-house, adherence, correct inhaler uses and morbidity as assessed by hospital admission in asthmatic patients. The study found improvements in knowledge and correct inhaler use, in the combined group but no effect on adherence and admissions.[56]

In the UK, there were a variety of studies assessing varying aspects of information provision. One study investigated anxiety in patients undergoing anaesthesia, and found that more patients who received a standard leaflet plus the manufacturers' patient information leaflets felt that they had received too much information, compared to the standard leaflet alone, but anxiety levels did not differ between groups.[57] One study assessed the feasibility of giving patients with written material for rheumatoid arthritis information in groups as opposed to individually, using adherence and satisfaction as outcome measures. It was found that providing counselling to groups of patients was feasible, with important time savings while maintaining high levels of patient satisfaction. Moreover, there was no differences in adherence depending on the method of delivery.[58] Another study evaluated the effect of supplementary patient education material in the form of video, information cards and on-line on adherence and satisfaction in patients with acne. The intervention achieved better results in both adherence and satisfaction compared to PIL and verbal instruction.[59] One RCT study was also conducted in the UK investigated whether changes from using standard side effect risk information to positive wording of side effect information in a PIL for a hypothetical medicine would reduce symptom reporting. Participants read either PIL, then took the tablet (a placebo) and reported any symptoms. The participants were less likely to attribute nocebo-induced side effects to the tablet because of the positive words.[60] Another RCT study was also conducted in the UK aimed at accessing a secondary analysis of a RCT to investigate predictors that influenced expectations of side effects which were or were not warned

of in the PIL for a hypothetical medicine. Majority of participants expected side-effects that were warned about in the PIL, and only a minority expected side effects that were not warned about. Beliefs about medicines, anxiety and health worries were some of the factors which influenced expectations.[61]

3.4.3.2 Category 1A studies

This category included studies measuring patient views or attitudes and, or impact of PILs on patient behaviour such as adherence. These were 'intervention' studies which used before/after, cohort or non-randomised designs. Table 3-5 shows the summary of studies in category 1A.

Table 3-5 Summary of studies in Category 1A

Continent	Country	Number	Summary
Africa	South Africa	2	Comparing the accuracy of the interpretation of medicine use instructions[62,63]
Asia	India	3	Measuring impact of information in leaflet form to improve patients' knowledge, understanding and behaviour.[64–66]
	Indonesia	1	Analysing the efficacy of counselling for the adherence of Tuberculosis (TB) drugs.[67]
	Thailand	1	Evaluating effectiveness of a brochure on patients' knowledge in preventing recurrent drug allergy.[68]

For non-randomised controlled trials, there were two studies conducted in South Africa. One study compared the accuracy of the interpretation of medicine use instructions from two different information of oral rehydration (OR) dry-mixture sachet labels between the text only label and text with pictograms. The results found that text and pictograms could help the patients understand medicine instructions.[62]

Another study aimed at developing and evaluating the findings of a tailor-made, simplified MDI leaflet for asthma patients with limited skills in literacy. Pictograms were developed involving patients; then a pre-post design educational intervention study was conducted. The tailored pictograms significantly increased the correct MDI technique for patients with low literacy. The pictograms were appreciated by the patients and seen as more preferable than the manufacturer leaflets.[63]

The objectives of the five Asian studies found were to measure the impact of information in leaflet form to improve patients' knowledge, understanding and behaviour. To be specific, in India, two

papers developed PILs on hypertension and diabetes mellitus, ensuring readability using the standard formulas Flesch Reading Ease (FRE), Flesch-Kincaid Grade Level (FKGL), plus assessment of the layout and design of the leaflet assessed according to the Baker Able Leaflet Design (BALD) method. Then, the effectiveness of the PIL after implementation on patients' knowledge was assessed. In-house questionnaires were developed to test knowledge of either hypertension or diabetes, including medicines, initially in English and then translated into local languages. Both studies found an improvement in knowledge after provision of the PIL.[64,65]

A further Indian study measured the impact of PILs on patients' knowledge about the correct use of medicines and adherence, using a non-randomised parallel group design. A multidisciplinary team prepared PILs in Hindi and English for a range of commonly dispensed medicines, then patients in the intervention group received PILs, while control patients received only standard verbal information. Pharmacists and one medical doctor were adequately trained on how to conduct patient interviews to assess knowledge and adherence, scored using pre-designed and pre-tested in-house questionnaire, together with pill counts. Leaflets were found to improve both knowledge and adherence.[66]

In Indonesia, a study was aimed at analysing the efficacy of counselling for the adherence of TB drugs with and without leaflets compared to usual care. Pre-post-test design was used. The study found that both counselling alone and counselling with a leaflet impacted on patients' adherence compare to usual care.[67]

In Thailand, a before/after study using two non-contemporaneous groups evaluated the effectiveness of a brochure alone or with pharmacist counselling on patients' knowledge, understanding and behaviour in preventing recurrent drug allergy. Both groups showed improvement, which was higher in those counselled by a pharmacist.[68]

3.4.3.3 Category 1B studies

These studies all sought patient views, or attitudes and behaviour, using qualitative methods. All used a semi-structured topic guide for either interviews with individual patients or focus groups. Two qualitative studies were identified from African countries and one from Asia, the rest being carried out in the UK. Table 3-6 shows the summary of studies in Group 1B

Table 3-6 Summary of studies in Category 1B

Continent	Country	Number	Summary
Africa	Ethiopia	1	Assessing readability, and patients' perception and understanding of medicine information materials[69]
	South Africa	1	Investigating medicine information-seeking behaviour and information needs in patients with limited literacy.[70]
Asia	Thailand	1	Examining patients' experiences and information needs, and their views on PILs[71]
UK	UK	8	Identifying patients' beliefs and preferences depending on their medicines and diseases.[21,72–78]

A mixed methods study was conducted to assess the readability, and patients' perception and understanding of medicine information materials provided in an Ethiopian hospital. Quantitative and qualitative approaches were used. The FRE and FKGL tools were used to evaluate readability of provided leaflets. A structured interview was also carried out. The results have shown that information materials in the hospital had poor readability. Most patients preferred information via both written and verbal forms while physicians and pharmacists were the most preferable sources of information.[69]

In South Africa, a study investigated medicine information-seeking behaviour and information needs in patients with limited literacy. The result revealed that there was poor awareness of information sources, a lack of health-related knowledge and that stigma contributed to a lack of information-seeking practice. Patients neither asked questions nor were encouraged to ask questions. All expressed an unmet need for information and a desire for receiving illustrated written medicines-related information. The main sources of information were health-care professionals, followed by family and friends.[70]

In Thailand, a qualitative study was carried out to examine patients' experiences and information needs, and their views on PILs. Patients perceived that PILs are useful and were satisfied with the information provided. However, they were considered as additional material to verbal information provided by health professionals.[71]

In the UK, eight studies were identified which focused on exploring patients' beliefs and preferences. There were five studies involving specific types of medicines; clopidogrel[72] , anti-tumour necrosis factor (anti-TNF)[73] , simvastatin[21] , over-the-counter (OTC) medicines[74] , and cardiovascular medicine[75] in particular the angiotensin-converting enzyme (ACE) inhibitor

ramipril. These studies mainly explored peoples' desire for medicine information, sources used, the acceptability and comprehensibility of the medicines information, including format. One study had a focus on beliefs, opinions and preferences for benefit information in medicine leaflets and examining peoples' understanding and reaction to learning about treatment benefits. Several studies involved people in Australia as well as the UK.

For over-the-counter (OTC) medicines, similar studies were conducted among Australian and UK consumers. Consumers infrequently sought spoken information and reported that pharmacy staff provided minimal spoken information for OTC medicines. Leaflets were not always received or wanted, and had a less salient role as an information source for repeat OTC purchases. Consumers tended not to read OTC labels or leaflets. Product familiarity led to consumers tending not to seek information on labels or leaflets. When labels were consulted, directions for use were commonly read. However, OTC medicine information in general was infrequently revisited.[74]

A study explored experiences of receiving information in patients receiving Anti-tumour necrosis factor (anti-TNF) This population had few concerns about side effects as potential symptom control was viewed as more important.[73]

Another of the two-country studies explored views on individually tailored medicine information. Participants welcomed the concept of tailored information, preferring information tailored to their condition, age and gender, but also desired verbal information with a healthcare professional.[75] The third sought views on the inclusion and possible format of benefit information in leaflets using Clopidogrel as the example.[72] In general, benefit information was viewed positively; however: participants were shocked by the numerical data presented and most found numbers needed to treat (NNTs) difficult to interpret. The format of benefit information presentation was also explored in a UK study using simvastatin as the example. This study suggested that patients preferred textual as opposed to numerical benefit information. Significant barriers to the acceptance of numerical benefit information included difficulty in understanding the numbers. Patients overestimated the benefits of statins and again expressed surprise at the numerical information.[21]

Two studies examined the patient perspective of medicines information and sources in people with asthma[78] , and people with cancer.[77] In the study in asthma, most participants of the focus groups described primary care health professionals as their main source of information. Individualised information was strongly valued, so medicine leaflets were generally seen as less helpful than face-to-face advice, and they were often thrown away. Some negative views were expressed about PILs. For example, their prime purpose was to cover manufacturers if anything went wrong, or to sell products. Some also felt strongly that patients with long experience should

be involved in the development of medicine information leaflets. The study in cancer involved 15 participants and found that all used the media both to increase knowledge and facilitate decision-making, although they recognised variation in the quality of the material. In addition, most participants used the Internet as it was a trustworthy source. Moreover, the information provided by their health professionals was too technical.

Finally, one study explored the acceptability and comprehensibility of the 'Medicines in Scotland: What's the right treatment for you?' factsheet designed for the general public. An interview schedule was developed to explore the acceptability and comprehensibility of the factsheet. The study found that the factsheet was generally perceived as helpful and comprehensive. It was highlighted that reading the leaflet may generate new knowledge and may have a positive impact on behaviour.[76]

3.4.3.4 Category 1C studies

In group 1C, the studies involving patients explored patient views or attitudes and behaviour towards medicine information using questionnaire-based surveys. There were 50 papers in this group, 27 studies originated in Asia, 16 in the UK and seven in Africa. Table 3-7 shows the summary of studies in Category 1C.

Table 3-7 Summary of studies in Category 1C

Continent	Country	Number	Summary
Africa	Ghana	4	Investigating the factors associated with reading PIL, and ophthalmic patients' view on PILs[79,80] Evaluating source of medicines and medicine information of persons living with hypertension and diabetes[81,82]
	Egypt	1	Identifying patients' drug information sources[83]
	Nigeria	2	Identifying patients' drug information sources[84] Conducting to assess the usefulness of PIs by both pharmacy customers for information and by pharmacists. [85]
Asia	Palestine	2	Finding on the extent of reading PILs, termed patient package inserts (PPIs), by consumers and possible factors. Investigating the attitude to PPIs[86,87]
	India	3	Assessing the awareness and attitude towards package inserts, degree of awareness regarding information, and knowledge.[88–90]
	Saudi Arabia	5	Determining public opinion in Saudi Arabia regarding the technical drug package insert. Determining the effect of providing different formats about side effect information (verbal versus numerical) to acne patients[20] Evaluating the percentage of, and experience with, online Arabic drug information by Arabic-speaking adults in Saudi Arabia.[91,92] Assessing public knowledge about medicine information, safety, and adverse drug reaction (ADR) reporting[93] Exploring on understanding of prescription drug labels, and to examine the factors influencing patients' understanding of prescription labels. [94]
	Pakistan	2	Investigating the knowledge and attitude of outpatients regarding pharmaceutical package inserts, and patients' needs and common sources of medicine information.[95,96]
	Armenia	1	Patients' needs and common sources of medicine information[97]
	Thailand	3	Patients' needs and common sources of medicine information[98] Survey on patients' use of PIs or PILs, and expectations and needs for patient information leaflets and related factors[99] Exploring practices, needs and expectations of Thai general public about written and electronic medicine information. [100]
	Singapore	2	patients' needs and common sources of medicine information [10] Explore patients' drug information needs and concerns, and the potential non-adherence rate. [101]

Continent	Country	Number	Summary
	Iran	2	Investigating patient attitudes toward package inserts and their accessibility. [102] Identified sources used by patients to obtain drug-related information[103]
	Sri Lanka	1	Assessing regarding information knowledge.[104]
	South Korea	2	examined whether medication-related information processing in the general public explained association between health literacy and quality of life. Investigated how consumers perceived package inserts[105,106]
	Israel	1	Exploring how patient information leaflets influence patient anxiety and adherence.[107]
	Malaysia	1	Evaluating the self-reported interpretation of medicine labelling and associated factors and to evaluate the sources of medicine information among the general public[108]
	China	1	Investigating the medicine information literacy of pregnant Chinese women. [109]
	Taiwan	1	Evaluating use and comprehensibility of information labels on OTC packages from consumers' perspectives[110]
UK		16	Evaluating impact of PILs on patients' opinions, attitude, and satisfaction, evaluated patients' information choice, and information needed, determine how patients use PILs.[22,111–125]

In Africa, there were four studies from Ghana, one each from Egypt and Nigeria. In Ghana, one study investigated the factors associated with reading the PILs among hospital out-patients. Only a third was advised to read the leaflet, but this sub-group were more likely to have done so and to discuss any problems with health professionals than those who were not given this advice.[80] The second study sought views on a PIL in a population of ophthalmic patients. Views were reasonably positive but 27% did not know why the PIL was provided and only 23% read the PIL. The PIL appeared to have not much influence on patient knowledge due to low readability and comprehensibility. This study also reviewed the readability of PILs for ophthalmic preparations.[79] The third survey was conducted to evaluate the source of medicines and medicine information of persons living with hypertension and diabetes. In the rural communities, sources of medicines and medicine information were health centre, hospital and over the counter medicine shop, while, in the urban communities, sources of medicines were hospital, and pharmacy. Participants' source of medicine and medicine information was influenced by both predisposing and enabling factors defined by Andersen's behavioural model.[81]The fourth random cross-sectional survey was conducted in various hospitals and pharmacies. The majority of respondents were provided with, and read PILs leaflets on their medicines. However, many people of those reading PILs leaflets reported being influenced by them to stop their medication.[82]

In Egypt, one study identified patients' perceived drug knowledge, need for more information and drug information sources, and how they varied by patient characteristics, particularly education level. More than 30% of the patients only read PILs selectively but 69% reported that they needed more information. It concluded that there is a need for healthcare professionals to evaluate patient comprehension and need for drug information, especially for patients with less schooling. Healthcare providers should also consider other information sources that a patient is using.[83,84]

In contrast, the study in Nigeria, found that 90% of patients claimed to read the leaflet they received with medicines, identifying the areas of greatest interest as dosage, indications, side effects and safety precautions, but also that some areas were not easy to understand, including pharmacology, chemistry and interactions.[84] In Southwest Nigeria, a cross-sectional self-administered questionnaire-based study was conducted to assess the usefulness of PIs by both pharmacy customers for information and by pharmacists. The utility of the PI was judged to be moderate by both pharmacists and pharmacy customers. The customers relied more on information provided by health care professionals than PIs. The pharmacists rarely referred to PIs during counselling.[85]

In Asia, the main objectives of the 18 studies can be divided into four groups. First, there were studies undertaken to assess the patients' attitude, or degree of awareness, level of trust to information provide regarding information in drug package inserts. Second, the studies focused on patients' needs and common sources of medicine information. The third group focused on patients' knowledge and the fourth sub-group were miscellaneous studies from different sources.

Within the first sub-group, there were two studies conducted in Palestine. One of them obtained data on the extent of reading PILs by consumers and possible factors affecting this, plus attitudes of both the Palestinian public and healthcare professionals towards the PPIs, as well as reviewing a random sample of PPIs for the availability of different information. They found that 45% of consumers always read the PPIs, and the public preferred an Arabic version, whereas health professionals preferred English versions.[86] Another study by the same authors investigated the attitude of the Palestinian public to PPIs that supported these findings. This study found that 52% read the PPI but felt it raised fears and concerns.[87]

There were two studies conducted in India, one assessed the awareness and attitude towards package inserts amongst a rural population. The questionnaire focusing on expectations and preferences of patients regarding package inserts was distributed to the patients who were either prescribed medication or those coming to the pharmacy for self-medication. The majority said that they "never" read the package inserts.[88] The other study assessed the degree of awareness

regarding information in drug package inserts at a tertiary care centre in western India among both doctors and patients. The study showed that 20% of doctors rarely read package inserts and 30% of patients did not read them, due to difficulties in comprehension.[89]

A similar, but much larger study examined public opinion in Saudi Arabia regarding the technical drug package insert (PIs) as a source of information, and to assess the need for potential changes to the existing format in favour of a more patient-oriented package insert. There were 88% of respondents who read the PI, with 47% viewing both indications and adverse drug effects as the principal sections of interest. Negative views on the format were expressed, with a desire for simple Arabic information, supplemented by illustrations to enhance comprehension.[91]

In Pakistan, one study investigated the knowledge and attitude of outpatients regarding package inserts in Karachi. Although the majority said they understood the insert, 24% of respondents faced problems in reading and 30% in understanding them, preferring again to read in their own language.[96] A survey study conducted in Iran aimed to investigate patient attitudes toward package inserts and their accessibility. The majority of patients reported that they read the PIs and considered them useful. The level of education was the only factor related to reading the PIs. The study found that medicines were generally dispensed with the PI. Side effect was the preferred information to read, but reading the PIs could raise participants' experience of fear.[102]

In the second group of studies, patients' needs and common sources of medicine information were identified. There were studies published from Armenia, Pakistan, Thailand, Singapore, and Iran. In Pakistan, a study of information sources found that 24% obtained written information and a further 5% both verbal and written, the rest receiving only verbal information. Almost all information was given by physicians (91%) 67% read information leaflets, but most of them had some difficulty in understanding language, technical terms, and reading the small font.[95] In Armenia, the study identified specific topics of medicines information which patients expect to receive, and evaluated the level of trust with regard to the information provided. Receiving medicines information from the staff of community pharmacies was judged important for patients, and the majority of them trusted the information received. The information viewed as most important was indications (91%), dosage and method of administration (91%), duration of treatment (86%), expiry date (86%), adverse reactions (85%) and contraindications (85%). While 71.5% read package inserts, only 36.7% fully understood the information they contain.[97]

In Thailand, one study determined sources of information about NSAIDs used by out-patients, factors related to receipt of information and patient attitudes towards receiving safety information. Patients received medicines information mostly from healthcare professionals, but safety information was limited. Type of NSAIDs, regularity of NSAID use and age affected receipt

of safety information about NSAIDs.[98] Patients' use of PIs or PILs, and expectations and needs for patient information leaflets and related factors was also surveyed. Most of the respondents received PIs and the majority reported they sometimes read them. Most participants had not known about PILs. After reading the patient information leaflets, respondents scored their needs and expected knowledge gains from PILs. Those who had previous experience of PIs expressed greater need for PILs than those with no experience.[99]

Another survey aimed to explore practices, needs and expectations of Thai general public about written and electronic medicine information. This study also found that the majority of participants received PIs and only a minority had received PILs. Level of education and income were related to receiving PILs and electronic information. Participants expected the usefulness of PILs would be high. However, they preferred verbal information from health professionals. Indication, drug name and precautions were the most frequently read information. They had positive overall attitudes towards PILs. Electronic information on medicine was seen as desirable and should be developed as optional source of medicine information.[100]

In Singapore, one study identified patients' needs for information about adverse effects (73%), dosing (55%), and indications (54%). Physicians (83%) and pharmacists (58%) were reported to be the most commonly used sources of information for prescribed medicines, but pharmacists and relatives or friends (41%) were the commonest sources for non-prescription medicines. It was perceived difficult to find reliable information on the Internet.[10] Another aimed to explore patients' drug information needs and concerns, and the potential non-adherence rate. The majority of the participants informed that they were provided with medicine information for the new chronic medication. This information consisted of indications, side effects and dose. They preferred verbal advice and written information. The participants were concerned about side effects, long-term safety and drug interactions.[101]

In Iran, the study identified sources used by patients to obtain drug-related information including the proportion of patients who study the PIL. Only 46% of patients in this study received information about dose and frequency, with only 6% receiving adequate drug information from their physician or pharmacist. Thus the majority often relied on friends and family as information sources and only 15% read PILs, mostly those with higher education levels.[103]

Six studies assessed knowledge. A study in India which found that 61.5% never read leaflets and that only 13% always did so, also assessed knowledge through an in-house instrument. The majority of respondents had no knowledge of interactions of medicines with other drugs and foods.[90]

In Saudi Arabia, a cross sectional study was conducted to assess public knowledge about medicine information, safety, and adverse drug reaction (ADR) reporting. There was a high score for medicine knowledge and a tendency to report ADRs, but an insufficient knowledge score regarding medication safety was poor.[93] This study also determined how often participants read PILs. Most respondents indicated that they always or sometimes read it and the majority was interested in reading the whole PIL, Others were interested in specific sections. Another study in Saudi Arabia was carried out to explore the current understanding of prescription drug labels, and to examine the factors influencing patients' understanding of prescription labels. The study found that there was a prevalence of poor understanding of the medicine labels among the participants. Age, level of education, income affected the degree of misunderstanding. Duration of treatment, and storage were commonly misunderstood topics.[94]

A study in Sri Lanka also found low knowledge among cardiac patients and found that education level was a key factor affecting knowledge, along with perceived severity of illness and receipt of information from a doctor.[104]

In Malaysia, a survey based study was undertaken to evaluate the self-reported interpretation of medicine labelling and associated factors and to evaluate the sources of medicine information among the general public. Most of the participants reported that they have adequate medicine information provided on medicine labels. They also read their medicine's label for the directions of usage, and dosage instruction. Some participants did not read the active ingredient label and safety information on their medicines. The factors which predicted reading of medicine labels were gender, ethnicity and level of education.[108]

In China, a study aimed to investigate the medicine information literacy of pregnant Chinese women. The participants had sufficient medicine information literacy in terms of medicine information needs, medicine -taking behaviour, medicine information source awareness, medicine information quality discrimination and medicine information sources. Significant differences were found related to education level, location of residence, occupation, household income, age, weeks of gestation and medication history.[109]

The last sub-group encompassed diverse studies, exploring a range of factors influencing use of information.

In Saudi Arabia, one study determined the effect of providing different formats about side effect information (verbal versus numerical) to acne patients that were newly prescribed Roaccutane®. The study found that patients overestimated the probability of occurrence of side effects in general and that verbal format was associated with higher estimation than the numerical

format.[20] A second study determined the percentage of, and experience with, online Arabic drug information by Arabic-speaking adults in Saudi Arabia. It found that there was a high proportion of Arabic speaking people in Saudi Arabia using and consulting Arabic drug information websites; 88% stated that they used Arabic websites to answer drug-related questions with queries about adverse effects being the most common (68%) and ease of use being the most common reason for using this source. Respondents easily found (65%) and understood (49%) information.[92]

There were two studies conducted in South Korea. The first involved the general adult population and examined whether medication related information processing, defined as reading of OTC drug labels, understanding prescription instructions, and information seeking, and medication adherence account for the association between health literacy and quality of life, and whether these associations may be moderated by age. Higher health literacy was associated with more thorough reading of drug labels, which was in turn associated with better perceived medication adherence.[105]

The other study investigated how consumers perceived package inserts by asking undergraduate students to rank 12 items of information according to their importance, indicate items they did not understand and additional material they felt should be included. The three most important items were efficacy and effects, warnings, and directions and doses. Difficulties in comprehension related to the language used, while many of the items desired were in fact already listed, but not found, suggesting poor layout of the inserts.[106]

The study in Israel explored how PILs influence patient anxiety and adherence. The PIL was read by 51.5%. Higher educational level and using a chronic medication were associated with reading the leaflet. In 34.9%, an increase in anxiety was reported after reading the leaflet. Among those who read the leaflet, 9.7% had decreased adherence. Patients who stated that reading the leaflet caused anxiety were more likely to reduce their use of the medication.[107]

A cross-sectional study in Taiwan was conducted to evaluate use and comprehensibility of information labels on OTC packages from consumers' perspectives. Participants informed that they read instruction labels before use regarding indications, drug names, and dosage and administration. However, only a minority of participants understood how to take the medicines correctly. Age, gender, and level of education influenced reading the package label information before purchasing or use the medicines.[110]

In the UK, there were three main types of survey studies. Firstly, there were six studies evaluating receipt of and opinions, attitudes, and satisfaction with PILs. A wide variety of methods were used such as short interview, telephone survey, online survey, or survey in the hospitals. The target

populations included both patients and healthy people. One study explored the satisfaction of cardiac in-patients regarding the information they received about their medicines. The survey found that patients were satisfied with information about the indication and usage of medicines. However, they were unsatisfied with information about potential problems with their medicines.[122] A survey in 2005 involving 152 patients recruited through community pharmacies, who were using 321 medicines found that for 16% of medicines no PIL was provided, and also that 47% of patients read their PIL, with the side-effects section being most commonly read.[125] A later survey in 2007 with 456 patients found that 97% were aware of the PIL, overall 35% had read at least some of the PIL, but it was higher (71%) for first-time users, and 87% of repeat users had read the leaflet at some time in the past. Again the side-effects section was most commonly read. In addition, 15% of patients had taken action as a result of reading the PIL.[120] A further large survey which recruited 1218 patients from hospitals reported in two papers[113,123] found that 44% patients were informed fully about their medicines by a hospital doctor, nurse or pharmacist, but 22.5% had received no information or could not recall any. Fewer than 20% had received written medicines information in hospital. The results showed that people read PILs for finding medicine side effects information, but 19% never read the PIL, and 6.5% only do so if something unexpected happens. Over half of those experiencing a suspected side effect had read the PIL. Reading the PIL helped most of them to decide that they had experienced a side effect. Educational level, general knowledge of medicines risks and number of regular medicines increased the likelihood of reporting experiencing an ADR. Instruments designed to measure the need for and satisfaction with information about medicines were used in two studies. One study using the Desire for Medicine Information Scale found that the diagnosis and disease have a significant bearing on patients' desire for medicine information. It recommended that healthcare professionals view patients as individuals when providing information that meets their needs.[124] A specific study in 221 patients with chronic kidney disease on phosphate binding medicines who completed the Satisfaction with Information about Medicines Scale (SIMS) showed a large proportion were dissatisfied with the information they received about side effects and interactions.[112]

Several studies explored the use of information to enable people to make decisions about using medicines. A study in which 30 patients were interviewed about patient choice of antipsychotic found that half of them had received no information and most felt they had no choice in the antipsychotic prescribed.[111] A second study in which a decision aid was developed to help patients who used antipsychotics in selecting a drug found that 90% considered the information leaflet improved their knowledge, 70% that it would improve the trust between them and their doctors, and 47% stated they were more likely to take their medicine after reading the leaflet.[119] Two studies involving fictitious scenarios assessed the suitability of a PIL to help people decide on choice of drug. The first was in 30 undergraduate students, excluding those studying medicine,

who were asked to rank their willingness to take one of five medicines for the treatment of an imagined diagnosis of hypertension and suggested information contained in PILs has the potential to influence attitude to antihypertensive selection.[118] The second found that a PIL provided sufficient information to enable men to self-assess their suitability for sildenafil.

Other studies explored the presentation of side effects and benefit information in PILs.[114] One study showed that numeracy in presentation format was correlated with greater accuracy of side effect risk estimates. In addition, numeracy was positively related to the perceived influence of the information on the decision to take the medicine and was negatively related to ratings of satisfaction with the information.[22] A later large study of the general public showed that the use of verbal descriptors to communicate side-effect risk in PILs could lead to high side-effect expectations. There were 52% and 45% of participants who considered that the EU descriptors of "very common" and "common" for specific side effects meant they were "very likely" or "likely" to happen to them, respectively.[121]

Benefit information is not routinely provided in PILs, as it is not required by EU regulations, however two studies explored the potential for including it. The first assessed providing no, one or two items of benefit information in a PIL in the general public. It found that any benefit information resulted in greater satisfaction with the helpfulness of the information, perceived effectiveness and appropriateness of the medicine, benefit and risk to health, and intention to comply with treatment.[115] The second involved three experiments around a fictitious scenario about being prescribed an antibiotic. The study found that information about benefits alone enhanced judgement, but did not influence the intention to adhere to treatment. Experiment 2 compared the relative effectiveness of two different forms of the benefit statement, and found that both were effective in improving judgements, with again no effect on intention to adhere. Experiment 3 also included side effect information and the combination received high rating and also increased intention to adhere.[116] A further study aimed to explore inpatients' satisfaction towards information about medicines provided during staying an in-patient hospital stay. Satisfaction scores for the information 'action and usage' subscale of SIMS were higher than for the 'potential problems' subscale of SIMS. Age, educational level and ethnicity were related to satisfaction towards information about medicines.[117]

3.4.3.5 Category 2A* studies

In group 2A*, the studies conducted were formal user-testing adopting an internationally accepted method; the RCT. There were only three such studies. Table 3-8 shows the summary of studies in Category 2A*

Table 3-8 Summary of studies in Category 2A*

Continent	Country	Number	Summary
Asia	Hong Kong	1	Accessing the comprehensive understanding of text label for medication information[126]
	Singapore	1	Accessing bilingual text and pictograms. [127]
UK		2	Evaluation of European Medicines Agency (EMA) recommendations on providing information on side-effect risk, and the interpretation of, and preferences for, numerical information. [128,129]

In Asia, one study accessed understanding of medication information in 50 Hong Kong Chinese older people. Participants were divided into two groups; the control group received only text labels, and the experimental group received text labels plus supplementary pharmaceutical pictograms. Then asked their understanding of the medication information. As with the African study, the pharmaceutical pictograms significantly improved the comprehension of medication information for elderly people ($p<0.05$).[126]

Another study in this category was found, from Singapore, where a study was conducted to access bilingual text and pictograms. Elderly participants were randomised into four prescription medicine labels: English-text; English-text-and-pictograms; Bilingual-text; and Bilingual-text-and-pictograms. Their correct interpretation and understanding was evaluated. The study found that, in order to substantially increase the understanding, adding bilingual text with or without the pictogram could improve elderly Singaporeans' understanding.[127]

In the UK, there were two studies conducted in this area. Firstly, the European Medicines Agency (EMA) recommendations on providing information on side-effect risk were evaluated. Four different formats of information about 10 side-effects of paclitaxel with random allocation were provided to participants recruited via the website "CancerHelpUK". Information was provided as numerical frequency or combined verbal terms and numerical bands. The results showed that the combined verbal and numerical risk expressions resulted in higher estimates of side-effects.[128] Secondly, a similar study evaluated the interpretation of, and preferences for, numerical

information on four side effects of tamoxifen in three different formats. It used a controlled design, with participants allocated at random to receive one of the three formats. Their interpretation and preferences were recorded. Findings showed that the three formats were not different in the interpretation, however, the combined format (frequency and percentage) was preferred.[129]

3.4.3.6 Category 2A studies

This Category was similar to the studies in group 2A*, in that the studies involved formal user-testing using internationally accepted methods, but were conducted using non-randomised methods, such as cross sectional or before/ after surveys. Table 3-9 shows the summary of studies in Category 2A.

Table 3-9 Summary of studies in Category 2A

Continent	Country	Number	Summary
Africa	South Africa	2	Accessing readability and understanding of a PIL and pictograms in HIV/AIDS patients.[130,131]
	Tanzania	1	Accessing a simple text and pictograms for a commonly used antiretroviral therapy (ART) regimen.[132]
Asia	Japan	1	User testing to improve drug guide for Patients[133]
	India	1	User testing of pictogram PILs for haemodialysis (HD) patients.[134]
	Thailand	1	Developing the Thai PILs for selected NSAIDs, then subjected the PILs to multiple rounds of user-testing by the general public. [135]
UK		4	Investigating using a headline section in PILs by a cross-sectional user-testing. [136] Evaluating the effect of a headline section on a PIL. Tested two different presentations of text, with and without features by user testing.[137,138] Evaluating the use of OTC diclofenac in Australia and in the UK. [139]

In Africa, there were three studies of this type, all involving antiretroviral therapy (ART). The first study described the development of a PIL with pictograms and minimal text, which was tested in 39 low-literate HIV/AIDS patients who had not used ART. These patients understood most of

information in the leaflet. Half of participants accepted that the leaflet was easy to read. However, the study suggested that the verbal counselling was still needed for HIV patients.[130] The PIL developed was further tested in two studies, one in South Africa and one in Tanzania. The South African study accessed the readability and understanding of the PILs for the first-line ARV (antiretroviral) regimen available in the South African public health sector in either English or isiXhosa. The 60 participants were asked to read the PIL and were then asked a series of questions to assess its comprehension and acceptability. The understanding rate was high.[131] The Tanzanian study evaluated a PIL readability and acceptability in 60 Tanzanian nationals in either English or Kiswhaili. Again understanding of the PIL was very high. The instructions illustrated by pictograms were correctly understood by all participants. Educational level and self-reported ease of reading the PIL were significantly associated with comprehension.[132]

In Asia, there were three studies. A user testing study was conducted in Japan to test revised versions of two examples of the Drug Guide for Patients (which are similar to PILs, but are not required to be subjected to user-testing). Participants evaluated their understanding of the information it contained, as well as readability, usefulness of information, and layout and appearance. The revised PILs were better in terms of accessibility and understandability.[133] In India, one study also developed PILs with pictograms, and tested them in 81 patients undergoing haemodialysis. As with the African studies, the PIL was offered in either English or a local language (Kannada). This quasi-experimental study assessed knowledge prior to and after receiving the PIL and found that overall knowledge mean scores were significantly improved.[134]

In Thailand, a study was carried out to develop the Thai PILs for selected NSAIDs, then subjected the PILs to multiple rounds of user-testing by the general public. Then, patient knowledge was assessed using a pre-post design. The study found that knowledge score increased significantly after providing the PILs. Level of education influenced the knowledge score. This study showed that user-testing of PILs was feasible in Thailand to enable the development of acceptable and desirable PILs.[135]

In the UK, one small study investigated using a headline section in PILs by user-testing in 20 people. The results showed the headline section was used just over one-third of the time to find information in the text.[136] In contrast, another study which evaluated the effect of a headline section on a PIL in 80 participants found that there were no differences in how well participants could find and understand the information in the leaflets. However, the participants were still positive about the headline section.[138] Another study focused on good design methods. It tested two different presentations of text for a fictitious drug, with and without good design features by user testing in ten individuals. The result showed that good design enabled information to be found quicker and users obtained more correct answers, as it helped readers in searching for key

information.[137] The final study assigned to the UK evaluated the use of OTC diclofenac in Australia and in the UK. The study explored consumers' perspectives on their design, content, usability, and potential improvements. Some of the important information accompanying diclofenac products has not been effectively communicated. The label and leaflet could be improved in terms of increased font size, bolding/highlighting, and use of colour.[139]

3.4.3.7 Category 2B studies

The studies in Category 2B aimed to evaluate the content of PILs utilising validated criteria. There are a number of published methods of doing this, which include the Simplified Measure of Gobbledygook (SMOG), Flesch Reading Index (FRE) and Flesch-Kincaid Grade Level (FKGL). Some studies already described used these measures in the development of new or revised PILs, which they then subjected to evaluation in patients. One other study from Ghana, described in a previous section[79] , included assessment of PILs using a validated method, along with a survey of patient opinions, concluding that poor readability contributed to lack of use. The remaining studies described in this section only assessed existing PILs, produced by manufacturers. Table 3-10 shows the summary of studies in Category 2B.

Table 3-10 Summary of studies in Category 2B

Continent	Country	Number	Summary
Africa	Nigeria	2	Evaluating the readability and basic elements of PILs for malaria medicine and chronic disease.[140,141]
Asia	India	2	Evaluating consumer' perception on PILs of obesity and lipid lowering drugs, and evaluating the design, content and readability of PILs for topical preparations of drugs.[142,143]
	Qatar	1	Evaluating the readability and comprehensibility of 45 PILs for type 2 diabetes mellitus medication.[144]
	Iran	1	Evaluating the readability and understand ability of PIs. [145]
UK		7	Evaluating PILs for several medicines.[146–152]

In Africa, two studies were conducted in Nigeria. One study evaluated the readability and basic elements of 45 PILs for malaria medicine using the SMOG. The results showed that for 75%, the SMOG readability score was equal to a tertiary level of education. It also found that generally, PILs were glossy, contained symbols and pictograms with font type size < 8, and were written in both English and local languages.[140] Another study assessed the readability using Flesch scores

and content validity of 60 PILs for chronic diseases. The study reported that the readability scores for both indigenous and imported products were low, but local PILs had lower readability scores. The foreign leaflets were also better in terms of content validity.[141]

In Asia, there were three studies. One Indian study evaluated the design, content and readability of leaflets for 60 topical preparations of drugs by using FRE formula. The results showed that most of the PILs were very difficult to read, with only 2% achieving a standard readability score. Contents and design also needed further improvement.[142] The other Indian study evaluated consumer' perception on PILs for obesity and lipid lowering drugs by using the standard method named Baker Able Leaflet Design (BALD). The study showed that 54% of the PILs were rated as 'standard or poor' in layout and design.[143] In Qatar, one study evaluated the readability and comprehensibility of 45 PILs for type 2 diabetes mellitus medication by using the FRE score for readability, FKGL, Gunning-Fog Index, and SMOG Grading for estimating school grade levels. Only 2% PILs achieved acceptable readability scores and 20% were only written in English so could not be read by most people in the country. All of them were rated as suitable for 11th grade, which is above the recommended level of readability for health-related materials.[144]

In Iran, a study was carried out to evaluate the readability and understand ability of PIs. The readability of 158 PPIs of 33 drugs was calculated by using the Flesch–Dayani readability (FDR) tool adjusted for the Persian language. The average number of the words and syllables was counted, graded the readability score. The study found that the average FDR readability score for all the 33 drugs was classed as difficult to read. Minority of PIs were suitable for the 5th–9th grade. A high number of the PIs in Iran had low readability level and were not suitable for some people.[145]

In the UK, there were seven studies in this area. First, PILs for all UK licensed osteoporosis medications and calcium/vitamin D supplements were evaluated by using FKGL and the SMOG formula. The results found that none of the PILs complied with the maximum recommended 6th grade level.[146] Second, the suitability of the content of 48 PILs for older adults was assessed in terms of the relevance of the information provided. The layout and readability were also checked by using the relevant regulatory guidelines, and the Gunning Fog Index, respectively. Only one of the PILs contained information on pharmacokinetic changes in older patients and only 15% listed side effects common in older people, whereas others provided only nonspecific warnings to the older population. Text font sizes of the PILs were generally too small. The readability score was poor in 63%, indicating leaflets were too difficult to understand.[147] In the third study, readability of information about disease modifying anti-rheumatic drugs (DMARDs) was tested by using the SMOG. The results showed that the level of information provided was too high, given that 1 in 6 people in the UK have low literacy levels.[149] Another study assessed readability of 42 PILs for UK

antidepressants using FRE and FKGL, as well as the suitability of the information provided for depressed patients, considering words as being positive, negative or neutral. Although the readability scores were acceptable, side effects information was difficult to read and 24% failed to mention problems with stopping these drugs abruptly. Overall, there was a preponderance of negative rather than positive or neutral words.[148]

Two further studies included UK materials, but also material from other countries. In one of these, 157 samples of PILs for 10 prescriptions and three over-the-counter medicines from six English-speaking countries were compared using the United States Keystone Consensus Criterion 8 (USKCC8) and the Ten Key Principles (TKP) of Consumer Medicine Information. Their readability was measured using FKGL and Gunning Fog Index tests. The results showed that compliance with USKCC8 and TKP varied greatly between countries, with the UK leaflets having the lowest compliance. Overall readability grades were above the recommended range.[151] Another study evaluated the quality of online antidepressant drug information on 14 English and eight Finnish Web sites. Both Web sites in the two countries had similar aesthetics, content coverage, and content correctness scores. English Web sites were more interactive. Adverse drug reactions were covered on 21 of 22 Web sites. The DISCERN score (a tool for assessing quality of health information found on the Internet) was significantly correlated with content coverage.[150] Finally, a study was conducted to access the readability of Patient Leaflets of licensed meningococcal vaccines in the UK and US. Five sources of meningococcal vaccine information were examined, including UK SmPC and PILs and manufacturers' websites. Readability was evaluated by using 10 readability metrics, including the Flesch Reading Ease and the Flesch-Kincaid Grade level. The UK PILs had the greatest readability scores. Pharmaceutical company websites had statistically poorer readability.[152]

3.4.3.8 Category 2C studies

The studies in group 2C aimed to describe or evaluate PILs but did not use standard measures of readability. Authors of these studies have developed in-house schemes, which differ across the studies. There was a total of 19 studies in this group, three in Africa, ten in Asia and six in the UK. Table 3-11 shows the summary of studies in Category 2C.

Table 3-11 Summary of studies in Category 2C

Continent	Country	Number	Summary
Africa	South Africa	2	Evaluating visual aids for ARV side effects. Examining comprehensive understanding of pictograms and 23 corresponding locally developed images.[153,154]
	Cameroon	1	Investigating factors associated with patient's prescription using patterns and explores patients' preferences.[155]
Asia	Taiwan	2	Describing characteristics of electronic medication-related information (e-MRI) provided by hospital, and comparing preference and comprehension of pictographs for medicine use instructions between low-literacy patients and medical staff.[156,157]
	Palestine	1	Evaluating and comparing local and imported PILs of 15 anti-infective medicine.[158]
	Hong Kong	1	Testing guessing performance of participants with pharmaceutical pictograms and sign features.[159]
	Saudi Arabia	3	Examining the information relevant for the safe and appropriate use in package inserts (PIs). Examining recognition and comprehension the various information items in over-the-counter (OTC) medications package leaflets in patients. Assessing readability of two types of WMIs in Arabic language.[160–162]
	United Arab Emirates	1	Comparing ability of pharmacy and non-pharmacy students to comprehend pharmaceutical pictograms.[163]
	India	1	Identifying awareness and deficiency in drug label by using questions prepared for medical personnel.[164]
	Korea	1	Exploring the readability and comprehensibility of the information contained on two package inserts [165]
UK		6	Evaluating the content, presentation, accuracy and completeness of non-steroidal anti-inflammatory drugs in websites. Test understanding ability in adults in comparing between 2 sets of pictograms for instructions or warnings Estimating understanding of the verbal risk descriptors recommended for use in PILs by the European Commission (EC). Investigating the effectiveness of presenting medicine side effect risk information in different forms.[17–19,166,167] Exploring information design on information communication, methods of warning design, and investigate perception of students on OTC codeine[168]

The three studies in Africa all concerned pictograms. The first study set out to examine comprehensive understanding of 23 internationally available pictograms and 23 corresponding locally-developed images in 304 low-literate respondents from eight different South African

language groups. Locally-made images achieved more successful correct interpretations than those obtained from international pictograms, but educational level had a significant influence on interpretation, while there were no significant differences between the African language groups, suggesting that the same images could be used for multiple groups.[154] This research group , then went on to design pictograms for side effects from ARV drugs and to evaluate them in 40 low-literate South African Xhosa participants in South Africa. Some which reflected familiar body experiences (e.g. vomiting) gained more understanding than those showing abstract elements (e.g. fever). This study suggested that visual images should consider an audience's literacy skills and culture, requiring an iterative process of development. These pictograms were subsequently used in some of the studies already described in Section 3.4.3.6 (Group 2A).[153] The third study , in Cameroon, investigated patients' preferences for different ways of presenting prescriptions (pictograms, text, symbols and Latin abbreviations) and the factors associated with patient's preferences by interviewing 204 patients. Most patients (90%) understood symbols especially patients with low levels of education, and fewest (27%) Latin abbreviations. However patients mostly preferred pictograms (40%) and written prescriptions (31%).[155]

Several of the studies in Asia also concerned pictograms. One study in Taiwan compared preferences and comprehension of three different pictograms for each of four dosage instructions (e.g. bedtime, with meals) between low-literacy patients and medical staff. There were significant differences in preferences between these groups in preference and comprehension, suggesting patients need to be involved in pictogram development. Older patients had lower comprehension of the medicine instruction pictograms.[157] In Hong Kong, a study tested the ability of participants to guess the meaning and assess five features (familiarity, concreteness, complexity, meaningfulness, semantic distance) of 25 pharmaceutical pictograms. Occupation, age and education level significantly affected guessing performance. For sign features, semantic distance (the closeness of the relationship between what is depicted on a sign and what it is intended to represent) was the best predictor of guess ability score, followed by simplicity, concreteness, meaningfulness and familiarity.[159] In the United Arab Emirates, a study compared the ability of pharmacy and non-pharmacy students to comprehend 28 internationally available pharmaceutical pictograms. Most students in both groups agreed that pictograms should be included in medicine leaflets and they were helpful for all patients, however few of the pictograms reached the standard required by the American National Standards Institute of 85% correct interpretation, even in students.[163]

Several studies assessed the content of PILs or other sources of medicine information. In Taiwan, one study compared the characteristics of electronic medication-related information (e-MRI) concerning digoxin provided by hospital websites including transparency, referencing and

navigation, as well as drug-related content. The characteristics varied among the hospitals, but content differed little, not all providing information about side effects, contraindications, interactions or precautions.[156]

In Palestine, one study evaluated and compared 36 local and 15 imported PILs of 15 anti-infective medicine in terms of the number of words used in eight main headings and the presence or absence of certain information regarding nine statements. Warnings, dosage and administration, the presence of the nine informative statements, and side effects were more often presented in locally manufactured products than imported products. However, locally manufactured products did not show inactive ingredients, clinical pharmacology or date of last revision, but all of them provided information on the use of the drug during pregnancy and lactation and on the duration of therapy. However, in general they provided less information than the imported medicines.[158]

In Saudi Arabia, one study examined the information relevant for the safe and appropriate use in PIs supplied with 37 prescriptions and 23 over-the-counter (OTC) medications. Unclear dosage instructions, lack of measures to be taken, inappropriate presentation of side effects, lack of serious side effects management was found.[160] Another study examined recognition and comprehension of the various information items in OTC medication package leaflets in patients. The participants had some difficulty recognizing and comprehending certain information items in PILs.[161] The last study in this country was to assess the readability of two types of WMIs in Arabic language based on vocabulary use and sentence structure using a panel of experts and consumers. Two different types of materials, including the online text from King Abdullah Bin Abdulaziz Arabic Health Encyclopaedia and medication leaflets submitted by the manufacturers to the Saudi Food and Drug Authority were evaluated. The results found that the majority of the vocabulary and sentence structure was considered easy to read by both experts and consumers. The precautions and side effects sections were identified as difficult or intermediate vocabulary and sentence structure.[162] In India, a study was conducted to obtain views of doctors, nurses and patients on PIs supplied with medicines, but did not assess content directly. Over 80% of all groups agreed that PIs give relevant information, more doctors and nurses thought that PIs did not give all negative points about medicines, while more doctors than nurses or patients thought font size was too small.[164]In Korea, one study explored the readability and comprehensibility of the information contained on two package inserts (acetaminophen and cold remedy containing acetaminophen) among 51 first year undergraduate students. Most participants correctly replied to the questions relating to some words, name, disease, indication, dosage, duplication, use in pregnancy and contraindications. Less than half answered correctly in use in children, and in side effects.[165]

Only one of the five studies conducted in the UK concerned pictograms. This study tested adults' understanding of two different sets of ten pictograms for instructions or warnings (from the US and South Africa), and also tested the effects of pictogram size and repeat presentation in older adults. The pictograms for the ten different instructions and warnings showed great variation in understanding from 7.5 to 90%, but with small differences between the US and South African versions. In older adults, larger pictograms and repeat presentation improved understanding.[167]

Another study appraised the content, presentation, accuracy and completeness of information on websites for two non-steroidal anti-inflammatory drugs compared with official patient leaflets. Each site was scored for presence, accuracy of each point of information included in official leaflets, and quality of presentation. The results showed that there were a small number of inaccuracies related to dose, with potentially dangerous consequences. The websites scored well overall for quality of presentation, but contained only about half of the relevant information.[166]

Three studies explored understanding of risk information in PILs. The first study conducted two experiments by, first, asking participants to imagine that they had to take a chemotherapy drug, then estimating the risks of two side-effects occurring. Second, participants were asked to estimate the risk for three different side-effects occurring with the painkiller ibuprofen. The results showed that verbal descriptions led to significant over-estimations of side-effects. Being given information as frequencies resulted in more accurate estimates than being given percentage information.[17] The second study also offered side effect information in different forms. Participants were randomly allocated to one of the three formats for representing risk information, also were asked to estimate the risks of four side effects occurring, and complete Likert scales relating to their satisfaction with the information. The results indicated that absolute frequency format achieved greater accuracy in estimating the side effects with more participants also being satisfied.[18] A more recent large study estimated understanding of the verbal risk descriptors recommended for use in PILs by the European Commission (e.g. common, rare) and alternative verbal risk descriptors (likely or unlikely, high or low chance) in the context of mild and severe side effects by using an online survey. Overall results showed that the risks conveyed by the EC recommended verbal risk descriptors led to risks being greatly overestimated. In general, mild side effects were more likely to be overestimated than severe side effects. The authors concluded that the verbal risk descriptors currently used in PILs were ineffective and misleading.[19] More recently a study was conducted to explore information design on information communication, methods of warning design, and investigate perception of students on OTC codeine. PILs for codeine-containing analgesics included warning terms relating to potential for addiction, but those for cough medicines generally did not. Heat maps generated from an eye-tracking experiment were also used together with the total time spent in reading PILs to answer

questions about addictive potential. Online surveys were used to collect user perceptions, most were not familiar with codeine and not aware of its addiction potential. Information design significantly affected how user processes information and researchers suggested that an addition warning should be located prominently within the possible side effects section of the PIL.[168]

3.4.3.9 Category 3A studies

The studies in Category 3A were designed to compare the content of PILs with regulatory requirements. There were 22 studies in this category from Asia. Most of studies (12) were conducted in India. Few studies (5) came from Japan. The five remaining were from Singapore, Palestine, Emirate of Abu Dhabi, Thailand and Saudi Arabia. There were no studies from Africa and only three from the UK. Table 3-12 shows the summary of studies in Category 3A.

Table 3-12 Summary of studies in Category 3A

Continent	Country	Number	Summary
Africa	East African	1	Examining extent to which PIs of medicines circulating on the markets of the East African Community (EAC) Partner States. [169]
Asia 22	India	13	Investigating the completeness of the available PILs in general.[170–182]
	Japan	5	Comparing in-house PILs with imported PILs.[183–187]
	Singapore	1	Evaluating the completeness of PILs content.[188]
	Palestine	1	Assessing and comparing the PILs of antihypertensive agents locally produced in Palestine and their imported brand.[189]
	Emirate of Abu Dhabi	1	Investigating the safe and appropriate use information in PILs for prescription medicines.[190]
	Thailand	1	Evaluating content and availability of Thai information leaflets for different nonsteroidal anti-inflammatory drugs (NSAIDs). [191]
	Saudi Arabia	1	Evaluating usefulness and scientific accuracy using the Keystone Criteria for Arabic PILs of celecoxib, paroxetine, and lamotrigine. [192]
	Malaysia	1	Examining how adherence of medicine safety information[193]
	Iran	2	Examining conformity of 92 PIs related to 22 best-selling neurological and psychiatric drugs with the health communications standards of Iran's FDA (IFDA). [194] Evaluating completeness of PIs supplied with the 100 top-selling medicines against the criteria required by the IFDA, and critical comments of clinical and industrial pharmacists. [195]
	Sri Lanka	1	Examining completeness, and compatibility of, essential information of selected PIs against the British National Formulary and/or Australian Medicines Handbook, [196]
	Republic of Korea	1	Examining discrepancies in the label information for direct oral anticoagulants[197]
UK		4	Examining method used to describe adverse effects, methods used to define risk of side effects frequency terms or numbers, and the use of the risk format. Evaluating quality of PILs for atenolol, glyburide (Glibenclamide), atorvastatin, and Nitroglycerin (glyceryl trinitrate) in the United States, United Kingdom, and Australia. [198–200] Examining differences in the languages use in prescribing information and patient information for new vaccines between the United States (US) and European Union (EU, including SmPCs and PILs in the UK). [201]

In Africa, a study was conducted to examine the extent to which PIs of medicines circulating on the markets of the East African Community (EAC) Partner States. The PIs were evaluated as the degree complying with the harmonised guidelines and the national guides. Majority of the medicines' PIs highly followed the guidelines. The information included the description and composition of the medicine, indications, dosage and methods of administration, warnings and precautions, contraindications and storage conditions. However, some details relating to disposal, container package description, excipients used, clinical pharmacology of the medicines, and overdose warnings were less compliant. Notably, the leaflets made by European based manufacturers had greater conformity when comparing with those based in Asia and EAC Partner States.[169]

In India, thirteen studies were included, which assessed the content of package inserts (PIs). PIs are the primary source of drug information for the physician, the pharmacist and the patient in India. Six studies investigated the completeness of the available information in PIs in general. The findings indicated that many required considerable improvement. Clinical information was not well presented and was often incomplete, not containing all the sections as required by the Indian Drugs and Cosmetic regulation. Authors advocated the need for greater standardization of PIs, especially with size, shape, font size, references, effect on ability to drive machines, updated information, and provision of full information, as well as making them mandatory with all medicines.[171–173,175,176,182] For specific medicines, a study was undertaken to assess the presentation and completeness of clinical information provided in available 130 PIs for anti-diabetic, antihypertensive and hypolipidemic drugs analysed based on criteria mentioned in Schedule D of Drug and Cosmetic act 1945. The results indicated that PIs were inadequate in many aspects. The information relevant to the safe and effective use of medication was not presented.[170] A second study compared the PIs for acarabose, metformin, glimperide, glicazide, glibenclamide and pioglitazone of the Indian company with the innovator companies. Discrepancies were found in undesirable effects section, contraindication, special warnings and precautions for use and interaction with other drugs. Indian companies did not have any mechanism/process for development of package inserts with important sections on safety of these drugs missing with several discrepancies.[177] There were four studies which compared generic PIs and original brand SmPCs in narcotic pain, cardiac, CNS, and anaesthetic medications in India. The results found that standard labelling guidelines were not adhered to, and the details were not always updated. There were discrepancies in many sections.[178–181] An observational study aimed to evaluate the information adequacy and accuracy of PIs collected from various retail pharmacies. compared to a checklist extracted from regulation guidelines. As with many other studies from India, the results found that some important information was absent from many PIs or judged inadequate.[174]

In Japan, five studies were undertaken, which compared the content of 'drug labels', another term for package inserts (PIs), which are equivalent to the Summary of Product Characteristics (SmPC) in the EU, across countries. Patient information leaflets are not a requirement in Japan. First, a study investigated the difference in adverse drug reactions (ADRs) information in 44 oncological drug labels between United States (US) and Japan. The study concluded that the substantial differences observed were due to differences in regulatory considerations and historical factors in both local and global contexts.[184] Second, a study assessed differences in pharmacogenomics biomarkers in 118 drug labels from the US, the United Kingdom (UK) and Japan. Substantial differences in the pharmacogenomics information between three countries were found.[187] Third, a study compared the regulations concerning statements in the information on drug metabolizing enzymes between Japan, the US and the UK. Of 306 drugs, 100 included such a statement, most frequently for hypnotics and sedatives, and anxiolytics.[186] Fourth, one study compared differences in safety information on 189 new molecular entities approved in the USA, the UK, and Japan. There was less patient safety information on Japanese drug labels than on UK or US labels, but other differences in safety information among these countries depended on outcome measures and therapeutic areas.[185] The last study analysed interactions involving glucuronoconjugates with three drugs (zidovudine, valproic acid and lamotrigine), and examined how the literature information is reflected in the relevant PIs in Japan, UK and USA. The results showed that the information, including quantitative data, was not always properly provided in the relevant PIs in Japan, UK or USA.[183]

In Singapore, the study aimed to evaluate the completeness of 21 PILs content. The branded PILs of statins, macrolides, protease inhibitors and selected drugs of narrow therapeutic index were scrutinized in comparison to the criteria for PILs from the Food and Drug Administration (FDA) labelling recommendation guidance document. Completeness was evaluated by a scoring system. The study found that the completeness varied extensively among and within drug classes.[188]

In Palestine, the study assessed and compared the PILs of 35 antihypertensive agents locally produced in Palestine and imported equivalent brand. A scoring system was used. The study found that the imported PILs were superior to local PILs in terms of quality and quantity of information provided such as brand name, active ingredients, indications, directions for use, adverse drug reactions, drug–drug interactions, pregnancy and lactation considerations, and storage.[189]

In Emirate of Abu Dhabi, a study investigated information for supporting the safe and appropriate use in 67 PILs for prescription medicines. The same as in other studies, the result showed that there were many deficiencies of information provided with regard to the Ministry of Health (MOH) requirements. In contrast however, the study found that some of the prescribing

information could be defined as a PI intended for healthcare professionals, others for patients, and others a combination of the two.[190]

In Thailand, the study evaluated the content and availability of 76 Thai information leaflets for ten different nonsteroidal anti-inflammatory drugs (NSAIDs), using a checklist derived from multiple sources. The results showed that no leaflet covered all topics in the checklist, and that local product leaflets provided less information than originator products. No leaflet included all the warnings required by Thai regulations.[191]

In Saudi Arabia, one study evaluated the usefulness and scientific accuracy using the Keystone Criteria for Arabic PILs of celecoxib, paroxetine, and lamotrigine. Overall, the results showed that the Arabic leaflets failed to meet the definition of useful scientifically accurate information, containing 24% and 20% of the essential information respectively.[192]

In Malaysia, a study aimed to examine how adherence of medicine safety information was provided on 133 randomly sampled OTC product labels and PILs to the Malaysian and international regulatory guidelines. The results found that some of OTC medicines did not provide the PILs at all. The majority of PILs complied with all the regulations. Advice on missed doses, advice on consulting a doctor/pharmacist for further information and disposal instructions were generally missed. The compulsory statement about adverse drug reaction reporting was absent from all the PILs. The minority of the PILs contained a revision date. As has been found elsewhere, locally manufactured products were slightly less adherent than the imported products.[193]

A study in Iran aimed to examine the conformity of 92 PIs related to 22 best-selling neurological and psychiatric drugs with the health communications standards of Iran's FDA (IFDA). The results found that the content provided with the PIs was insufficient in various aspects. The warnings and precautions were more adherent than other aspects.[194] Another study in Iran evaluated the completeness of PIs supplied with the 100 top-selling medicines against the criteria required by the IFDA, and critical comments of clinical and industrial pharmacists. The study found that some of medicines did not provide PIs. None of the PIs adhered to all the criteria required by the IFDA. Medicine name, description, and adverse reaction were written in all PIs. The majority of PIs included information about patient counselling information, warnings, precautions, pregnancy/lactation, and storage conditions.[195]

In Sri Lanka, a study which aimed to examine the completeness, and compatibility of, essential information of selected PIs against the British National Formulary and/or Australian Medicines Handbook, found that the minority of the PIs reviewed did not include at least one aspect of the

essential information required by the regulations. Pharmacokinetic data, duration of treatment, overdose, and special dosage information were frequently absent.[196]

In the Republic of Korea, a study aimed to examine discrepancies in the label information for direct oral anticoagulants (DOACs) (dabigatran, rivaroxaban, apixaban, and edoxaban) approved in the US, Europe, Korea, and Japan and review the causes of those discrepancies, focusing on regulatory practices. The study found that while labelling information was written by the same global pivotal clinical data across all four regions, it varied in line with regulatory judgements regarding the risk/benefit balance. These were based on their own requirements, rules, regulatory decision perspectives and the experience with regulatory approval, as well as review of the scientific data.[197]

In the UK, there were three studies in this group, two of which looked at information about side effects in PILs. One study examined the method used to describe adverse effects, and the format of this information the leaflets which supplied with the 50 most frequently prescribed drugs in England. This found that a wide range of methods was used to describe adverse effects, and 40% of the leaflets did not provide any frequency information about side effects, while in those that did different formats were found, such as recommended EU terms, verbal descriptors, numerical indication, or long lists of adverse effects.[198] The second study used similar methods, repeating the evaluation, but including leaflets for the 50 most frequently dispensed medicines and the 50 most recently licensed medicines. In particular the study evaluated whether the risk format recommended by the European Medicines Agency (EMA) in PILs was used. Most of PILs (66%) used the recommended format with no differences between branded and generic medicine, with all 50 recently licensed medicines using this format. PILs from the 2012 sample were much more likely than those from the 2006 sample to include risk description and to use a consistent method.[200] The third study evaluated the quality of PILs for atenolol, glyburide (glibenclamide), atorvastatin, and nitroglycerin (glyceryl trinitrate) in the United States, United Kingdom and Australia. The study indicated that quality of leaflet varied among the three countries with leaflets from Australia meeting 90% of criteria, UK 81% and the USA 68%. However there was more consistency within each country, because of the differing regulatory context.[199] A further study examined the differences in the language use in prescribing information and patient information for new vaccines between the United States (US) and European Union (EU, including SmPCs and PILs in the UK. There was little harmonisation between prescribing information and PILs showed even less harmonisation between both regions, despite the same information being available to the regulatory authorities.[201]

3.4.3.10 Category 3B studies

Studies in this group were descriptive, covering either what the PIL includes only and/ or comparison of the content to the literature or best evidence, not to regulatory guidelines, or studies seeking opinions of health professionals on the desirable content of PILs. No studies of this type were conducted in the UK. Table 3-13 shows the summary of studies in Category 3B.

Table 3-13 Summary of studies in Category 3B

	Country	Number	Summary
Africa	Ghana	1	Investigating various linguistic realizations and functions of hedges in PILs.[202]
	Sudan	1	Assessing knowledge, attitude, and practice of Sudanese doctors toward written medication information in the PILs.[203]
	Nigeria	1	Evaluating opinions of community pharmacists on the usefulness and reliability of PILs.[204]
Asia	China	3	Analysing descriptions of 'precautions for application' in package inserts via text mining methods. Review drug information for the elderly in package inserts of national essential drugs. Investigating distribution of lexical errors in Chinese-English.[205–207]
	Japan	2	Design and create new PILs for oral diabetes drugs with simpler and easier to understand and use concise wording and illustrations. Investigating problem of the descriptions in PILs for renal impairment.[208,209]
	Pakistan	2	Evaluating errors and incomplete information in inserts with marketed medicines Evaluating information written on PILs of products in local market[210,211]
	Korea	1	Comparing PILs on cardiovascular drugs regarding pregnancy information.[212]
	Palestine	3	Evaluating perception of health professionals and industry personnel towards the appropriate use of oral drops[213] Evaluating leaflets, aimed at patients and healthcare providers, of local produced NSAIDs against imported products, using 31 statements obtained from the literature. [214] Comparing PIs of local and imported anti-diabetic agents against 31 criteria. [215]
	Saudi Arabia	1	Assessing quality of written prescribing leaflets for generic drugs and imported drugs in various countries of the Middle East[216]
	Bangladesh	1	Determining extent and nature of information on drug-drug interaction information in PILs.[217]
	Iran	2	Examining safe and use information in PIL[218] Examining regulations regarding PILs, with a focus on the lay-friendliness of the content. [219]
	Muticountry	1	Evaluating the effective and safe use of insulin glargine across 17 countries.[220]
UK		1	Accessing the characteristics, clinical information, and storage instructions contained in package inserts from medicine-induced abortions provided in low- and middle-income countries, including some in Africa and Asia. [221]

In Africa, three studies were conducted. In Ghana, one study investigated the various linguistic realizations and functions of hedges in 50 PILs. It was found that drug companies frequently used certain lexico-grammatical hedging devices (words such as 'may', 'might') to improve their claims.[202] In Sudan, one study was to assess the knowledge, attitude, and practice of Sudanese doctors toward written medication information in PIs, and its usefulness for both doctors and patients. The results showed that most of the 400 doctors regularly read PIs. However, only a minority of doctors advised their patients to read the PI, because they believed that PIs might be difficult to understand.[203] The last one evaluated the opinions of 61 community pharmacists on the usefulness and reliability of PIs by using a questionnaire survey. Community pharmacists in south-western Nigeria believed that a modified PI could be a useful and reliable source of drug information helpful in achieving therapeutic success, but the large majority thought changes were needed to the PI to achieve this.[204]

There were sixteen studies conducted in Asia. Three studies were conducted in China, two of which were related to the actual language of the information. First, one study analysed the descriptions of 'precautions for application' in PIs via text mining methods. They analysed by using Chinese language. The results suggested that the precautionary statement should contain information such as the actions described in the statement, the flag to express an order or interdiction, the subject to be ordered, and the timing.[205] The second study carried out investigated the distribution of lexical errors in Chinese-English translation of PILs and explored the underlying causes and propose some translation strategies for correction and reduction of lexical errors in PILs. This study showed a number of errors in PILs including 54 substance errors, 446 text errors and 76 discourse errors. Authors proposed ways of improving translation from English to Chinese to minimise such errors.[207] The other Chinese study reviewed drug information for the elderly in PIs of national essential drugs. The researchers found that there was lack of medication information for the elderly in domestic drug PIs, and some drug descriptions were not clear.[206]

Two studies were conducted in Japan, one study described the design and creation of new PILs for oral diabetes drugs with simpler and easier to understand language and concise wording and illustrations, but provided no evaluation of these.[208] Another one investigated the problem of the descriptions in PIs for renal impairment by extracting data from 337 prescription drugs from the website of the Pharmaceuticals and Medical Devices Agency. The study concluded that PIs did not included sufficient information on "renal function" for medical workers.[209]

There were two studies conducted in Pakistan. One evaluated the errors and incomplete information in PIs provided with marketed medicines. The study found both major errors such as incompleteness of information of indications, adverse drug effects, drug mechanism, dosage

errors, drug-drug and drug-food interactions, precautions and warning, pharmacokinetic profile and pregnancy and lactation, and minor errors including of omission of structural formula, molecular formula, molecular weight, chemical names, laboratory tests, clinical trials data, font size, paper quality, and failure to use the national language (Urdu).[210] Another one evaluated information written on PIs of products in the local market. The results showed that most of PIs achieved met the 20 criteria developed from the literature. However, there was a lack of information in some, including directions for use, duration of use and drug interactions.[211]

In Korea, one study, aimed to compare PIs on cardiovascular drugs regarding information concerning pregnancy for their similarities between Korea, USA, UK, and Japan. The results found that Japanese labels had the largest proportion of 'contraindicated' level, followed by Korea, the UK and the US.[212]

In Palestine, one study evaluated the perceptions of health professionals and industry personnel towards the appropriate use of oral drops by using cross-sectional self-administered questionnaire, and reviewed PILs with regard to presence of proper instructions for use and storage. Instructions for storage and proper use were not available in package inserts of many oral drop products. The results found that drug companies did not perform the recommended tests for dose uniformity and calibration. Instructions for storage and proper use were not available in PILs of many oral drop products.[213] A further study already described in Section 3.4.3.6 (Category 2A) was also reported from Palestine, which reviewed the content of PILs for a range of medicines and found many important sections were missing.[86] A study in Palestine which evaluated 35 information leaflets, aimed at patients and healthcare providers, of local produced NSAIDs against imported products, using 31 statements obtained from the literature. The majority missed some information. Again, local products provided less information than products imported.[214]

Another similar study in Palestine compared 18 PIs of local and imported anti-diabetic agents against 31 criteria. This study also found that the PIs of imported products scored better than local PIs. However, none met the whole criteria. Most of the local PIs lacked information about dosage, instructions regarding effects on ability to drive or possibility of tablet splitting, and possibility of tablet crushing.[215]In Saudi Arabia, one study assessed the quality of 37 PILs for generic drugs manufactured in various countries of the Middle East and imported branded drugs, using the British National Formulary as a standard. The study found substantial disagreement in information between generic package inserts versus both the British National Formulary (BNF) and PILs of the branded products.[216]

In Bangladesh, one study was conducted to determine the extent and nature of information on drug-drug interaction (DDI) information in 150 PIs for 10 commonly used drugs. The DDI information was not presented properly including no information (56%), no rate of occurrence or morbidity of DDIs, no mechanisms, and not specifying a DDI as clinically significant.[217]

In Iran, one study examined information on safe use in PILs of 104 PIs of 34 psychiatric drugs manufactured by 29 Iranian pharmaceutical companies against criteria compiled from the literature. Overall, the study concluded that there was lack of sufficient information in PILs regarding their safe and appropriate use.[222] Another study examined the regulations regarding PILs, with a focus on the lay-friendliness of the content. There was a limitation of legislation relevant to the production and assessment of lay-friendly PILs, even though this is a requirement. Documents or guidelines concerning about lay-friendliness of PIL were not issued by the Food and Drug Administration of the Islamic Republic of Iran.[219] One further multi-country study evaluated the information for the effective and safe use of insulin glargine in drug labels across 17 countries: Abu Dhabi (United Arab Emirates), Argentina, Brazil, Canada, China, Germany, Israel, Italy, Japan, Mexico, Russia, Saudi Arabia, South Korea, Spain, Turkey, UK, and the USA. The study compared content in term of label characteristics governed by a local regulatory authority (11) versus countries where labels were administered by a regional body (3 – EU) or adopted from another locale (3). The study showed variation between countries in the content, which may lead to inconsistency in quality of care for diabetic patients. For example, five did not describe actions in case of hypoglycaemia.[220]

In the UK, a study aimed to access the characteristics, clinical information, and storage instructions contained in package inserts from medicine-induced abortions provided in low- and middle-income countries, including some in Africa and Asia. The 41 PIs for mifepristone, misoprostol, and combined mifepristone-misoprostol (combipack) products from 20 countries were collected. Indications, storage, side effects, and contraindications, and revision date were extracted. Date of last revision ranged from 1991 to 2016. The storage instructions information was inadequate, and details relating to gestational age limits and regimens was frequently outdated.[221]

3.6 Discussion

3.6.1 General summary of studies

From the scoping review of 141 studies, there is literature on medicine information sources including PILs undertaken in Africa and Asia, but it is limited in term of both volume and scope. Many more studies have been carried out in the UK than in countries in Asia and Africa. This is

possibly because of the regulation of medicine information in the UK, which has been established since 1977. Therefore, many studies have been conducted to support and to improve the provision.[1] In Asia and Africa, however, the regulation is still developing. Awakening interest in PILs studies has occurred within the last decade. For example, in Thailand, PILs regulation was launched in 2013, although it still does not cover all medicines.[27] Since then only three studies have been established in Thailand, suggesting that the partial introduction of regulations has resulted in some albeit limited interest in the topic.

There were some trends found in the literature, for example, studies were concentrated in some countries (e.g. India) and others were carried out by specific research groups (e.g. Dowse, Knapp/Raynor). In Asia, most of studies were conducted in India where a large number of the world's pharmaceutical companies are located, in particular generic drug manufacturers. Pharmaceutical manufacturing companies in India are one of the world's largest sources of generic drugs, supplying 50% of global demand for a range of vaccines, 40% of generic demand in the US and 25% of all UK medicines.[223] Therefore, a lot of PILs studies emerged from India. Most of them tried to assess the completeness of PIs which are required by the Indian Drugs and Cosmetic regulations, with relatively few seeking patient views. In total there were 23 studies conducted in Arab state countries, where regulation of medicines has recently been harmonised, showing interest in researching the value of PILs is increasing in this region. As in India, most of the studies concerned the content of leaflets, in this case PILs.

Africa is the most affected region by HIV/AIDS in the world, particularly among young women (WHO).[224] Many of the PILs studies in Africa, consequently, focused on patients with HIV/AIDS. Moreover, ten of the African studies were conducted by same research group. For Ros Dowse's research group, most of their studies researched PILs for anti-retroviral therapy in patients with HIV, focussing on pictograms to help patient understanding.[45–47,70,130–132,153,154] Similarly, in the UK, of the many studies found, 20 studies were identified from Knapp/ Raynor's research group.[17,18,21,22,72,74,111,119,120,125,128,129,136,138,151,166,167,198–200] In contrast to Dowse, this group were interested in many aspects of PILs, but studies were still seeking to improve them to help patient understanding.

3.6.2 Summary of findings

3.6.2.1 Source of patient medicine information

There were many studies carried out to explore patient attitude, degree of awareness, level of trust in information, patients' needs and common sources of medicine information, investigating patients' knowledge by using qualitative and quantitative methods (cross-sectional surveys). The

most medicine information sources which participants mentioned they used were PILs, verbal information, and the Internet. Patients indicated that they were most interested in adverse effects, dosing and indications information.[91,101,102,106,108]

The verbal information from health care professionals is the main preferred medicine information source for patients. Individualised information was strongly valued. PILs were generally seen as less helpful than face to face advice. Physicians and pharmacists were the most commonly used sources of information for prescribed medicines.[70,39,40,10,95,97,68,69,69,71,101,225] Pharmacists, and relatives or friends were commonest sources for non-prescription medicines. [70,103] Some studies showed that most patients stated that they were informed fully about their medicines by a hospital doctor, nurse or pharmacist. Receiving medicine information from the staff of community pharmacies was judged important for patients and the majority of them trusted the information received. However, information provided by health professionals was sometimes perceived as too technical, and safety information was limited.[78] Patients may become non-adherent to their medicines if insufficient information is provided.[226]

The Internet plays an important role as an easily accessible medicine information source, both to increase knowledge and facilitate decision making. Patients used websites to answer drug-related questions with queries about adverse effects being the most common query and ease of use being the most common reason for using this source. Some patients found that information was easy to find and understandable. However, some patients perceived it difficult to find reliable information on the Internet .[10]

3.6.2.2 Written medicine information

There were various aspects regarding WMI which is the main focus of this thesis. Many studies were carried out in terms of investigating the impact of written medicine information on patient's knowledge and behaviour. The actual PILs, demonstration PILs, or pictograms were used as principal medium. Furthermore, available PILs were used to evaluate their content, layout and design. Patient's view on the PILs were also investigated.

Impact of written medicine information on patient's knowledge and behaviour

Many studies were conducted based on the hypothesis that PILs could be useful tools for enhancing patient's use of medicines. It was therefore expected that PILs could improve patients' knowledge, understanding and behaviour with regard to medicines.

The interventions involved providing a PIL usually in combination with verbal information or other initiatives such as counselling, or group education, and showed an increase in patients' knowledge

and adherence. In comparison with the control the intervention groups in comparative studies, and also in before and after studies, a benefit from the use of PILs was demonstrated. However, studies also found that some patients may be confused by PILs, such as people with patients with limited literacy skills.[45,52,58] All in all, the researchers have emphasized the need for simple, understandable text in medicines information leaflets.

Development and use of pictograms

Several studies used this kind of method to investigate the use of pictograms. A pictogram is a pictorial symbol for a word or phrase. It is a simple drawing that represents something or conveys an idea or concept through its pictorial resemblance to a physical object. They are in common use today, serving as representational signs, instructions, or diagrams. In relation to medicines, pictograms are standardized graphic images that help convey medication instructions, precautions, and/or warnings to patients and consumers. Pictograms are particularly helpful in passing on important information to patients with a low reading ability. Even though, standardized pictograms can be downloaded from the USP (US Pharmacopeia) website, differentiation in languages and cultures might affect understanding. This mean that PILs require testing in a culturally specific context in order to ensure understanding. Therefore, user-testing is one process in pictogram development.

From the review, the studies conducted user-testing for development of new pictograms in leaflets for use in low-literate patients with HIV, older people, and general patients. All studies found that the pictogram significantly ($p<0.05$) improved the comprehension of medicines. However, it was noticed that the pictogram must be combined with text label, and that verbal counselling was still needed for HIV patients. In agreement with other findings, higher education level was associated with greater comprehension.[126,130–132,134]

However, there were some drawbacks of using PILs, one of which is poor literacy. Studies using pictograms alone found that it was valuable for some groups especially for low-literate patients, but the PILs weren't always easy to understand, and needed much greater care in their development. The studies mostly concluded that PILs should be provided in combination with verbal instruction.

Studies comparing locally made and international pictograms, designing new pictograms for side effects, investigating patients' preferences and comprehension were conducted. Local pictograms were more correctly interpreted. This is because of the effect of culture and context. Literacy skills, education level, age, occupation, and culture must be considered in the early

process of PILs development. The studies demonstrate that patients need to be involved in pictogram development.

Patient information leaflet

Focusing on PILs, some patients claimed they always read their leaflets. Most of them read when first-time of using a medicine.[76,83,86,91,95,97,99,102,110,227] They agreed that reading the leaflet was the way to generate new knowledge and provided positive impact on their behaviours. The adverse drug effects were commonly the principal sections of interest. Over half of PIL users experiencing a suspected side effect had read the PIL.[113,123] Reading the PIL helped most of them to decide that they had experienced a side effect. Many studies revealed that higher educational level and using a chronic medication had impacted on whether or not participants were reading the leaflet.[107,163] From the patients' point of view, they affirmed that they were more likely to take their medicine after reading the leaflet. Also studies showed the suitability of a PIL to help people decide on choice of drug.

Nevertheless, there were many studies that found that some people tended not to read labels or leaflets. PILs were not always received, and seen as not necessary for repeat purchases for OTC medicine. [74,88–90]

A large proportion of participants were dissatisfied with the poor format and language of medicine leaflets. They had some difficulty in comprehension or understanding related to the language used, technical terms, and the small fonts used. Some issues which were included in PIs, as the single source of information given to patients in many countries, were not easy to understand, including pharmacology, chemistry and interactions. Therefore, in these situations, leaflets had less influence on patient knowledge due to low readability and comprehensibility. Moreover, some patients reported that they faced problems in reading leaflets. They felt that PILs raised fears and concerns. Increasing in anxiety was reported in some studies after reading the leaflet. As a result, they decreased their adherence, and reduced their use of the medication. In some cases, patients felt overwhelmed in receiving standard medicine information leaflets together with PILs. [79,84,87,95,107]

Factors affecting reading and usefulness of PILs

Patient's perspective on PILs are different. No matter if it's positive or negative, it can affect their behaviour. Higher health literacy was associated with more thorough reading of drug labels, which was in turn associated with better perceived medication adherence.[105] People who had limited health literacy, had poor awareness of information source, lack of health knowledge and stigma also contributed to a lack of information seeking practice.[80] Therefore, the

recommendations from these studies are that healthcare professionals should pay attention to patients as individuals when providing information, to ensure that their needs are met. There is a need for healthcare professionals to evaluate patient comprehension and need for drug information, especially for patients with low health literacy. Health care providers should also consider other information sources that a patient may be using, such as the Internet, media, family and friends.[83]

PILs Content and design

Many studies attempted to investigate new formats, content and design of PILs by formal user-testing for comprehension. The studies were conducted using internationally accepted methods such as RCTs or before and after surveys. User-testing is a performance based, flexible development method which identifies barriers to readability and understanding and use of the data presented in a PIL, and indicates problem areas which should be amended. It should be used as part of a leaflet development process.[23] All PILs in the EU must be subjected to user-testing, but it is less common in other countries.

Many studies used user-testing to assess verbal, numerical, or percentage in risk explanation, and in using headline section in a PIL. Good design and format enabled information to be found and easy to understand. Users obtained more correct answers quicker.[82-83,89] However, there were only a small number of studies on this issue. Therefore, preferences for format need more investigation.

Many studies aimed to evaluate the content of PILs using validated criteria or in-house schemes. Producing clearly written and easily readable materials is very important. Readability testing reveals the readability level of texts which can then be adjusted if needed, to ensure that PILs are not an unnecessary barrier. Standard readability formulas such as SMOG, FRE, FKG, GFSS, BALD are often used to assess the readability and design of developed information leaflets. In Africa and Asia, there was a small number of studies (5 studies) evaluating PILs with standard tools in comparison with the UK (6 studies).

The SMOG grade is a measure of readability that estimates the years of education needed to understand a piece of writing. SMOG index is calculated using the number of polysyllabic words in three ten-sentence samples near the beginning, middle, and end of a piece of text. If there are fewer than 30 sentences, the formula contains a factor to correct for this.[228]

The Flesch–Kincaid readability tests are readability tests designed to indicate how difficult a passage in English is to understand. There are two tests, the FRE, and the FKGL They are both calculated using the average sentence length (i.e., the number of words divided by the number

of sentences) and the average syllables per word (i.e., the number of syllables divided by the number of words) using different formulas.

The Gunning-Fog Score (GFS) is calculated using the average sentence length and the number of polysyllabic words (i.e., those with three or more syllables). The counted polysyllabic words do not include (i) proper nouns, (ii) combinations of hyphenated words, or (iii) two-syllable verbs made into three with -es and -ed endings.[229]

The BALD method is used to assess the layout and design of the leaflets. The scores are based on the length of the line, distance between the lines, letter font size, graphics used, percent of white space, paper quality. A document which scores 25 or more is considered as the document with good layout and design.[143]

Evaluating the readability and basic elements of PILs or medicine information website revealed that some of PILs achieved a standard readability score. However, a great number of PILs were indicated as difficult to read. They were rated poor in layout and design. The text font size was small which made PILs difficult to read especially for elderly people. Content and design in PILs still needs further investigation and improvement. Some studies reviewed information on websites, for which the quality was well accepted, and the main contents were covered.

Format of risk and benefit presentation

For PILs evaluation, unclear content, impropriate presentation, and lack of serious information were found. Patients had some difficulty recognizing and comprehending certain information items in PILs especially in precaution and side effect sections. Furthermore, three studies revealed that verbal description can lead to significant over-estimations of side effects. Using frequency format achieved greater accuracy in estimating potential side effects.[17–19]

Some studies found that patients overestimated the probability of occurrence of side effects in general and found that textual format was associated with higher estimation of the risks than the numerical format.[20] The use of verbal descriptors to communicate side-effect risk in PILs could lead to high side-effect expectations. However, some studies stated that numeracy was positively related to the perceived influence of the information on the decision to take the medicine and was negatively related to satisfaction with the information. In practice, patients found numerical data difficult to interpret. They preferred textual descriptions.[21,22]

Providing some benefit information in combination with side effect information in a short written explanation about a medicine and PILs provided greater satisfaction with the helpfulness of the information, perception of effectiveness and appropriateness of the medicine, benefit and risk to

health, and intention to adhere to treatment.[115,116] However, some studies found that benefit information may cause shock and reduce faith in a medicine and the form in which it is presented may be difficult to understand.[21,72]

Preferences for WMI format

Studies showed that patients welcomed the concept of tailored information, preferring information tailored to their condition, age and gender, but also desired verbal information. They needed PILs in their own language. Therefore, patients with long experience of using medicines should be involved in the development of PILs. [75,78,86,96]

With regards to format and design, some patients, for example people with learning disabilities who take psychiatric medication, need a larger leaflet, with pictures rather than symbols. There was room for improvement in the use of words and concept.

Regulatory aspects on PILs

There were studies aimed to compare the content of PILs with regulatory guidelines such as medicines and cosmetics regulation, the literature, or best evidence. Moreover, some studies tried to compare PILs which were produced by generic brand and original brand manufacturers, or between countries. Most studies were conducted in India where many local-made drug companies are located.

Regarding PIL provision, in Asia, some studies aimed to access the completeness of available PILs with domestic regulation for example Indian medicines and Cosmetics regulation, or Thai regulations.[191] In the Emirate of Abu Dhabi,[190] they have a set of safety criteria published from the Ministry of Health (MOH).

However, some studies in Singapore, Palestine, and Japan investigated content of PILs using international regulations for example the US FDA Medication Guide regulations. [158, 183–187,188] In the UK, European Medicines Agency (EMA) was the main guideline for PILs evaluation.[198,200]

In general, studies demonstrated that there is still room for improvement in the content, design and layout of PILs. There was incompleteness of information. Clinical data was not compliant with the regulations. There were improvements needed in terms of the size, shape, font size, references, updating information and drug-drug interactions. The side effect issue, which is perhaps the most important section was not well presented, it needed more consideration. Comparing PILs between companies or country of origin, there were discrepancies in many sections for example general medicine information, pharmacogenomics information, and patient

safety information. The discrepancies were by reason of differences in regulatory requirements and historical factors in local and global contexts.

3.6.3 Differentiation of the studies between continents

3.6.3.1 *Medicine information needs and preferences and medicine information sources*

In Africa, almost all studies investigated patients with HIV, and/or non-literate people. There was a paucity research which aimed to investigate patients' medicine information needs, preferences, and medicine information sources more widely. However, one study found that participants had poor awareness of information sources, lack of health-related knowledge and that stigma contributed to a lack of information-seeking practice. Their needs for medicine information and written medicines were still unmet. The main sources of information were health-care professionals, followed by family and friends.[70]

In Asia, studies were conducted in various groups of people such as those with asthma, diabetes mellitus, or hypertension or people with low literacy. Some studies targeted people taking specific medicines, for example, antidepressants or those with drug allergy. Studies investigating patient's information needs and preferences revealed that patients need medicine information in their own languages. The information viewed as most important and needed were adverse effects, dosage, indications, and method of administration, duration of treatment, expiry date, and contraindications.[10,97,106] Doctors and pharmacists were reported to be the most commonly used sources of information for prescribed medicines, but pharmacists and relatives or friends were commonest sources for non-prescription medicines. The Internet was also found as a medicine information source.[10,92,97,103] Similar to the study in Africa, patients still received inadequate drug information. [103]

In comparison, in the UK there was much more variety in the focus of studies investigating patients and medicines than in Africa and Asia. The studies involved patients with asthma, anxiety, learning disability, cancer, acne, rheumatoid arthritis, and other conditions. Patients were familiar with medicine information provided from many sources. With regards to medicine information need and preferences, some studies reported unmet need in verbal information from healthcare professionals, and in written medicine information.[78,111,112,122]

In term of medicine information sources, two studies found that patients from hospitals were informed about their medicines by a hospital doctor, nurse or pharmacist.[113,118] Moreover, studies showed that participants accessed the Internet, which most regarded as trustworthy, while some considered that the information provided by their health professionals was too technical.[77,78]

From the review, it can be concluded that there are knowledge gaps in medicine information needs and preferences and that studies on medicine information sources are still needed to fulfil these gaps. What people in general want, prefer and need in medicine information and their opinions about medicine information sources requires more investigation in many countries across Africa and Asia, and even in the UK.

3.6.3.2 *Patient information leaflet usage*

In Africa, there were merely four studies conducted in Ghana, Egypt, and Nigeria on patient information leaflet usage. In Ghana, only a third of patients received advice to read the leaflet. A study showed that people did not understand why the PIL was provided and a few read the PIL. The PIL appeared to have not much influence on patient knowledge due to low readability and comprehensibility.[79,80]

In Egypt and Nigeria, one third of the patients read PILs selectively but reported that they needed more information. In contrast, the study in Nigeria, found that nine in ten of patients were informed to read the leaflet for identifying the areas of interest as dosage, indications, side effects and safety precautions, but also found that some topics were not easy to understand, such as pharmacology, chemistry and interactions. This reveals that studies to explore how patient use medicine information leaflets, and what people prefer and need on PILs are still needed in this continent.[83,84]

In Asia, there were few studies undertaken to assess PIL usage. The studies in Palestine, Saudi Arabia, Pakistan, and Israel found that half of patients claimed they read their leaflets. Most of them read the leaflet when first using a medicine.[86,87,91,95,107] However, in India, the majority said that they "never" read the package inserts, due to difficulties in comprehension.[88–91] Besides, people prefer to read PILs in their language.[86,96]

However, they thought that the leaflets raised fears and concerns.[87,96,107] Most of PILs had some difficulty in understanding language, technical terms, and the small font. Patients overestimated the probability of occurrence of side effects in general and that verbal format was associated with higher estimation than the numerical format.[20] Patients who stated that reading the leaflet caused anxiety were more likely to reduce their use of the medication. [107]

In comparison, in the UK, there were more studies on patient information leaflet usage which focused on exploring patients' need and preferences than those on the other two continents. The studies showed there were both kinds of people those who read and those who did not read PILs.[73,119,120,125]

Positive and negative views on PILs were expressed. Reading the leaflet could generate new knowledge and may have a positive impact on behaviour.[76,114,119] It could improve the trust between them and their doctors, and they were more likely to take their medicine after reading the leaflet.[119]

However, leaflets were not always received or were not perceived to have a role for repeat purchases.[73,111] Patients felt that purpose of PILs was to protect manufacturers if anything went wrong, or for drug marketing.[78] A large proportion were dissatisfied with the information they received about side effects and interactions .[112]

With regards to PILs development, participants welcomed the concept of tailored information, preferring information tailored to their condition, age and gender, but also desired verbal information with a healthcare professional.[75] Patients with long experience should be involved in the development of medicine information leaflets.[77,78] Although, there were a greater number of this kind of studies in the UK, there is little research in patient information leaflet usage, and for preferences for information sources in general.

There was incompleteness of information in many countries about how people use PILs, their preferences and needs, therefore more studies are required to find out more.

3.6.3.3 *Provision of PILs and PIs and Regulations study*

In Africa, there were no studies which aimed to evaluate provision of PILs and PIs in line with regulations, or even describe these issues directly.

In Asia, there were a great number of studies conducted on provision of PILs or PIs, and meeting regulations; however, these studies were concentrated only in certain countries such as India and Japan. There were 12 studies in India comparing PIs with the Indian Drugs and Cosmetic regulation. In Japan, 5 studies were undertaken to compare the content of 'drug labels', or SmPC between the United States (USA), the United Kingdom (UK) and Japan.

Some studies in other countries aimed to assess the completeness of available PILs with domestic regulation; for example, Thai regulation in Thailand, safety criteria published from the Ministry of Health (MOH) in the Emirate of Abu Dhabi.[190,191] In addition, some studies in Singapore, Palestine, Saudi Arabia investigated content of PILs using international regulations as comparators, for example US FDA Medication Guide regulations.[188,189,192] One finding across several countries was the difference between local and imported products in the quality of the content. The imported products showed better adherence with the regulation than the local products.[141,152,158,189,194,196,197,201,214,215,221]

In the UK, the European Medicines Agency (EMA) was the main guideline for PILs evaluation. The majority of studies focused on PILs evaluation in comparison with this regulation. The issues which studies aimed to investigate consisted of evaluating risk descriptors in verbal and numerical forms, the effect of a headline section, or providing benefit information.[76,77,120,142–144,78,79,82,83,89,138,91,118,119,60,61]

The provision of PILs and PIs, as well as regulations, are the most important because they dictate how PILs and PIs should be. In many countries, PIs appear to be provided, which are designed for health professional use, not PILs, designed for patient use. It is therefore not surprising that patients struggle with understanding their content. Further studies are required to find out more about how to improve the regulations to optimise information for patients.

3.6.3.4 *Quality of PILs (Content, readability, Patient understanding)*

In Africa, most studies focused on PILs featuring pictograms in term of content, its readability, and patient understanding. The studies had been conducted with different methods such as RCT, before and after studies, and surveys. Pictograms seemed to play an important role in patient's preferences and needs in this continent. However, differentiation in languages, cultures and educational level might affect understanding. Apart from pictogram studies, there were two studies which evaluated the readability and basic elements of PILs by using the SMOG, and assessed the readability using Flesch scores and content validity of PILs for malaria medicine and chronic diseases, respectively in Nigeria.[140,141]

In Asia, there were three main focuses on these issues. Firstly, there were studies which focused on content and readability of leaflets by measuring with validated criteria such as FRE, BALD, FRE score for readability, FKGL, Gunning-Fog Index, and SMOG Grading for estimating school grade levels.[142–145] However, language was the major limitation for this kind of study in Asia because the validated tools normally evaluate in English language. Secondly, there were some studies evaluating content and completeness in PILs by comparing local and imported PILs, or available literatures.[86,160,169,174,189,193,210–212,216–218] Thirdly, studies were focused on linguistic evaluation. Because of diversity of languages especially in China, there were a small number of studies invested in this perspective.[162,205,207]

In contrast, in the UK, there were a greater number of studies assessing readability of PILs than in Africa and Asia.[146–151] This is perhaps because of their advantage in terms of language which validated tools support. In addition, the studies also were able to evaluate patient understanding of several aspects of PILs, such as patient understanding in risk description, headline section, providing benefit information.[17–19,22,115,116,121,128,129,136,138]

There were a small number of studies covering these issues in Asia and Africa in comparison with the UK. As aforementioned, provision of PILs or PIs and the regulations which mandate their provision affect research which is possible. Moreover, the studies conducted seemed to depend on researcher interest. There was no systematic research to find the problems with PILs or PIs, and consider how to solve them or to provide an overall picture of their use in any one country.

3.7 Strengths and limitations

The scoping review method was used in this study. This method is more flexible for general question than traditional systematic review and meta-analysis. This is also taking into account for a diversity of relevant literature and studies using different methodologies. A wider range of studies carried out with both qualitative and quantitative methods were included. In order to distinguish between the results, a classification system was implemented. As a result of the overlap in some studies, they may fall under more than one category. The search was limited to the studies written or with an abstract in English. Any published studies in other languages were excluded. One technique using the key phrases "drug information" AND "patient" was applied to many databases to achieve comprehensive searching and ensure the most appropriate databases. However, other engines or search terms e.g. “customer medicine information” were not applied. As this is a scoping review, any detail of the quality of studies was not examined in this chapter. However, some of studies were evaluated for their quality in the next chapter (Chapter 4).

3.8 Future research

Overall, research into PILs is a topic of increasing interest. However, there are knowledge gaps which emerge from this scoping review. Key questions revolve around learning more about what people want, prefer and need from written medicine information, assessing the quality and benefits of making this information available using internationally accepted methods, and the regulations then need more significant improvement.

More intervention studies are needed, but require good quality PILs first, therefore it is essential to concentrate on identifying the most desirable format and content of PILs. More research is required to find out more about if and how people receive and use PILs, and what other sources of information people use and want. The content and format of information people prefer and need also requires ore research in some countries. Both quantitative studies, such as surveys, and qualitative studies, such as focus groups, are needed to explore these needs and preferences, in order to ensure both breadth and depth. Information is important for all medicines, not just those used long-term, therefore studies need to involve the wider public who use medicines

occasionally, not just patients using regular medicines, who may in fact be quite well-informed about the medicines they have used for a long time.

More work is also needed to assess the quality and availability of PILs in different countries in comparison to each other, to help determine whether existing patient information is able to meet peoples' needs.

Chapter 4 Study appraisal

4.1 Introduction

A systematic review is a type of study that aims to conduct a systematic search, appraise, and collate all relevant empirical evidence in order to present a comprehensive interpretation of research findings. [230,231] The systematic review can be tailored to answer various types of research questions for a variety of review users (such as healthcare providers, researchers, and policy makers). [39]

The quality assessment of the included studies is a crucial stage in systematic review.[39] The appraisal aims to understand the validity of the studies.[38] The study designs that are most likely to produce valid results are chosen for appraisal. The research methods used in the primary studies reflect the "quality" of the studies. The quality of the study refers to study design, conduct, and analysis which minimizes the potential for bias. Biased primary studies are obviously more likely to provide misleading results. High-quality studies are presumably conducted with the method that is most likely to produce a genuine assessment of a treatment's or exposure's benefit or harm, the diagnostic accuracy of a test, or a specific prognosis. Quality assessments in systematic reviews are based on evaluating the quality of research on therapy, prevention, diagnosis, prognosis, and harm.[38]

Having completed the scoping review described in Chapter 3, it was considered appropriate to conduct a quality assessment process, in order to assess the quality of the outcomes from both intervention studies and cross-sectional surveys in a systematic review study. Studies were selected due to their common aims and methodologies, which allowed for an assessment of the risk of bias using standard appraisal tools. Therefore, this chapter is a continuing part from Chapter 3 which focuses on study appraisal. As this chapter was conducted in 2018, only studies that were found in 2004-2017 were appraised for their quality.

4.2 Objective

The objective of this study was to assess the quality of intervention studies and surveys identified in the scoping review.

4.3 Methods

After extracting the data, the studies retained were categorised depending on focus and methodology, which included intervention studies and surveys. Then, the studies which had human participants involved in intervention studies, in-depth interviews, or surveys were appraised to assess their quality. This means that all studies categorised as 1A*,2A*, 1A, 1B and 1C category were appraised. The type of quality assessment was dependent on the design of the study as described in chapter 3. The studies in which only an abstract was presented were excluded. The studies categorised in 1A* and 2A* were RCT studies. All 1A* and 2A* papers, then, were appraised using a checklist from the Critical Appraisal Skills Programme (CASP) for RCT.[232]

With regards to studies within the 1A category, they were quantitative studies using tools to measure effect of using PIL (before/ after; cohort; non-randomised studies). Therefore, papers graded as 1A were appraised using a checklist from Methodological Index for Non-Randomised Studies (MINORS).[233] The studies in 1B category were qualitative studies – in-depth analysis. A critical appraisal tool for qualitative study[234] conducted by Centre for Evidence-Based Medicine (CEBM) University of Oxford was used to apprise these studies.[235] The 1C studies which were quantitative studies were appraised by using a checklist; appraisal tool for Cross-Sectional Studies (AXIS). [236] The cross-sectional studies were scored Yes = 1, and No, and N/a = 0. The criteria for RCT, Non-RCT, qualitative, and cross sectional studies are shown in **Error! Reference source not found.**,

Box 4-2,Box 4-3,and Box 4-4, respectively

Box 4-1 Checklist from the Critical Appraisal Skills Programme (CASP)

Section A: Are the results of the trial valid?
1. Did the trial address a clearly focused issue?
2. Was the assignment of patients to treatments randomised?
3. Were all of the patients who entered the trial properly accounted for at its conclusion?
4. Were patients, health workers and study personnel 'blind' to treatment?
5. Were the groups similar at the start of the trial?
6. Aside from the experimental intervention, were the groups treated equally?
Section B: What are the results?
7. How large was the treatment effect?
8. How precise was the estimate of the treatment effect?
Section C: Will the results help locally?
9. Can the results be applied in your context? (or to the local population?)
10. Were all clinically important outcomes considered?
11. Are the benefits worth the harms and costs?

Box 4-2 Checklist from Methodological Index for Non-Randomised Studies (MINORS)

1. **A clearly stated aim**: the question addressed should be precise and relevant in the light of available literature

2. **Inclusion of consecutive patients:** all patients potentially fit for inclusion (satisfying the criteria for inclusion) have been
included in the study during the study period (no exclusion or details about the reasons for exclusion)

3. **Prospective collection of data:** data were collected according to a protocol established before the beginning of the study

4. **Endpoints appropriate to the aim of the study:** unambiguous explanation of the criteria used to evaluate the main outcome which should be in accordance with the question addressed by the study. Also, the endpoints should be assessed on an intention-to-treat basis.

5. **Unbiased assessment of the study endpoint:** blind evaluation of objective endpoints and double-blind evaluation of subjective endpoints. Otherwise the reasons for not blinding should be stated

6. **Follow-up period appropriate to the aim of the study:** the follow-up should be sufficiently long to allow the assessment of the main endpoint and possible adverse events

7. **Loss to follow up less than 5%:** all patients should be included in the follow up. Otherwise, the proportion lost to follow up should not exceed the proportion experiencing the major endpoint

8. **Prospective calculation of the study size:** information of the size of detectable difference of interest with a calculation of 95% confidence interval, according to the expected incidence of the outcome event, and information about the level for statistical significance and estimates of power when comparing the outcomes

Additional criteria in the case of comparative study

9. **An adequate control group:** having a gold standard diagnostic test or therapeutic intervention recognized as the optimal
intervention according to the available published data

10. **Contemporary groups:** control and studied group should be managed during the same time period (no historical comparison)

11. **Baseline equivalence of groups**: the groups should be similar regarding the criteria other than the studied end points. Absence of confounding factors that could bias the interpretation of the results

12. **Adequate statistical analyses:** whether the statistics were in accordance with the type of study with calculation of confidence intervals or relative risk

Box 4-3 Critical appraisal tool for qualitative studies

1. Was a qualitative approach appropriate?
2. Was the sampling strategy appropriate for the approach?
3. What were the data collection methods?
4. How were data analysed and how were these checked?
5. Is the researcher's position described?
6. Do the results make sense?
7. Are the conclusions drawn justified by the results?
8. Are the finding transferable to other clinical settings?

Box 4-4 Appraisal tool for Cross-Sectional Studies (AXIS tool)

Introduction
1 Were the aims/objectives of the study clear?
Methods
2 Was the study design appropriate for the stated aim(s)?
3 Was the sample size justified?
4 Was the target/reference population clearly defined? (Is it clear who the research was about?)
5 Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?
6 Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?
7 Were measures undertaken to address and categorise non-responders?
8 Were the risk factor and outcome variables measured appropriate to the aims of the study?
9 Were the risk factor and outcome variables measured correctly using instruments/ measurements that had been trialled, piloted or published previously?
10 Is it clear what was used to determined statistical significance and/or precision estimates? (p values, CIs)
11 Were the methods (including statistical methods) sufficiently described to enable them to be repeated?
Results
12 Were the basic data adequately described?
13 Does the response rate raise concerns about non-response bias?
14 If appropriate, was information about non-responders described?
15 Were the results internally consistent?
16 Were the results for the analyses described in the methods, presented?
Discussion
17 Were the authors' discussions and conclusions justified by the results?
18 Were the limitations of the study discussed?
Other
19 Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?
20 Was ethical approval or consent of participants attained?

4.4 Results

4.4.1 Randomised controlled trials study

Thirteen studies were randomised controlled trials. The objectives of these studies were to evaluate patients' adherence, knowledge of medicines, interpretation, comprehension, attitude towards and satisfaction with PILs, and pictograms. However, PILs were often used as a tool which was part of an intervention for example to improve patient's knowledge of medicines. These studies were therefore not focused on the PILs but on the overall intervention. Generally, the participants were patients with certain conditions [45–47,50,51,56–59], elderly people [126], workers[52], or the general public[129,136].

All studies assigned patients to an intervention using randomised methods. Twelve studies reported the number of participants that were lost to follow up.

All studies were focussed in terms of the population studied, the intervention given, the comparator given, the outcomes considered. There were two studies in Africa and one study in Asia with no reporting on dropout numbers. There was no intention-to-treat analysis in any study.

Many studies identified a major defect in their design in relation to blinding. While, five studies clarified that blinding between assessors and researchers were enforced[50,56–58,128], one study was not blinded.[59]There were additionally seven studies that did not describe their blinding procedure.[45–47,51,52,126,129]

Within the studies which tested the equivalence of the participants' demographic characteristics between the active and control groups, there was no significant difference in demographic characteristics found in eight studies.[46,47,51,52,56,57,128,129] There were two studies having a difference between groups in their participants prior to the intervention.[50,58] In one study, there was a significant age difference between females and males.[50] In the others, there was an imbalance in the proportion of patients who had not taken medicines previously or received a service from a certain clinic.[58]

There was no baseline of participants' characteristics in one study in Africa, and one Asian study, and one study in the UK.[45,59,126] There was only one study reporting 95% CI confidence limits.[51]

Apart from the experimental intervention, as far as could be determined, participants in both control and intervention groups seem to have all been treated equally in terms of having receiving the normal service with standard care.

The primary outcomes were generally patients' adherence, knowledge, understanding and comprehension, anxiety and patient satisfaction. The PIL, pictogram, or any interventions utilizing

these were evaluated in terms of their impact on these outcomes. Therefore, the primary outcomes were relevant to the proposed objectives of the review.

In term of external validity, the results could generally be applied within the context of the local population. Improvements in patient's adherence, knowledge, understanding and comprehension, anxiety and patient satisfaction were obtained. All interventions appeared to have been without risk, and any benefits were therefore valuable. The RCT study evaluation results are shown in Table 4-1

Table 4-1 the evaluation result of randomise controlled trial study

	1. Did the trial address a clearly focused issue?	2. Was the assignment of patients to treatments randomised?	3. Were all of the patients who entered the trial properly accounted for at its conclusion?	4. Were patients, health workers and study personnel ' blind' to treatment?	5. Were the groups similar at the start of the trial?	6. Aside from the experimental intervention, were the groups treated equally?	7. How large was the treatment effect?	8. How precise was the estimate of the treatment effect?	9. Can the results be applied in your context? (or to the local population?)	10. Were all clinically important outcomes considered?	11. Are the benefits worth the harms and costs?
Manso or & Dowse 2006[45]	Yes, to assess the impact of medicines information on adherence	Randomly allocated on an alternating basis (to a control group receiving no PIL), group A (complex PIL) and group B (simple PIL incorporating pictograms).	no, 7 were 'lost during the study'	No information	no information reported	Yes	Overall mean percentage adherence of the participants in group B (88.3%) was significantly (P <0.05) higher than those in group A (73.6%), and the control group (67.7%).	Not given	Yes, simple text and pictograms resulted in significantly improved adherence to therapy	Yes - adherence measures appropriate	Yes - intervention causes no harm
Dowse et al 2014[46]	Yes, access standard or standard care plus a PIL on antiretroviral drugs (ARV) knowledge and patient self-efficacy in those with limited literacy	Yes, computerized random number generator	No, 52 were 'lost during the study'	Patients - not possible; assessors - not stated	Yes, reported similar at the start	Yes with standard care	No significant change in knowledge was found in the control group over six months (p=0.258) whereas knowledge in the intervention group increased significantly from 62–94% (p<0.001).	Not given	Yes - suggests PIL could be useful	Yes, knowledge and self-efficacy questions relevant to study aim	Yes - intervention causes no harm

	1. Did the trial address a clearly focused issue?	2. Was the assignment of patients to treatments randomised?	3. Were all of the patients who entered the trial properly accounted for at its conclusion?	4. Were patients, health workers and study personnel ' blind' to treatment?	5. Were the groups similar at the start of the trial?	6. Aside from the experimental intervention, were the groups treated equally?	7. How large was the treatment effect?	8. How precise was the estimate of the treatment effect?	9. Can the results be applied in your context? (or to the local population?)	10. Were all clinically important outcomes considered?	11. Are the benefits worth the harms and costs?
Manson & Dowse 2007[47]	Yes - it is assessing the provision of a PIL, with or without pictograms on knowledge in low-literate HIV-positive patients on co-trimoxazole	Yes, but no details given, so inadequate	No, 7 were 'lost during the study'	Patients - not possible; health workers not applicable; assessors - not stated, but seems unlikely, since those receiving PIL were asked not to refer to it during assessment	Yes for most variables, but proportion reading English in different groups not stated	Yes	Knowledge scores, but no primary outcome specified; control 43.3%, group A 50.9%, group B 76.3% (increase of 33%)	Not given	Yes - suggests pictograms could be useful	Yes - knowledge questions relevant to study aim, not aiming to study actual behaviours	Yes - intervention causes no harm
Ng AWY at al 2017[126]	Yes, to access the benefits of pharmaceutical pictograms for improving comprehension of medicine information for older people.	Simple random	No information	No information	No information	Yes	Pictograms improved the comprehension of medicine information for older people.	Not given	Yes, Pictogram improved comprehension by older people	Yes, Comprehension by older people	Yes - intervention causes no harm

	1. Did the trial address a clearly focused issue?	2. Was the assignment of patients to treatments randomised?	3. Were all of the patients who entered the trial properly accounted for at its conclusion?	4. Were patients, health workers and study personnel ' blind' to treatment?	5. Were the groups similar at the start of the trial?	6. Aside from the experimental intervention, were the groups treated equally?	7. How large was the treatment effect?	8. How precise was the estimate of the treatment effect?	9. Can the results be applied in your context? (or to the local population?)	10. Were all clinically important outcomes considered?	11. Are the benefits worth the harms and costs?
Kheir N et al 2014[52]	Yes, to evaluate comprehension of the pictograms or conventional text supported with verbal instructions in foreign workers with low literacy skills.	Yes, computer-generated random numbers	Yes	No information	Yes	Yes	There were statistically significant differences in the average level of comprehension of medicine labels between the three groups ($P \leq 0.05$) for 10 of the 11 medicine instructions	Not given	Yes, pictogram labels and verbal instructions. Could be useful for foreign workers with low literacy skills.	Yes, comprehensive	Yes - intervention causes no harm
Al-Saffar et al 2005[51]	Yes, access medication adherence by using self-report and tablet counting.	Randomised sequentially by day	No, 22 patients withdrew	Can't tell	Yes	Medicine was dispensed from the pharmacy as normal.	Good medicine adherence at 2 and 5 months was more common in patients who were given a PIL (OR 3.0, CI 1.7–5.3) or a PIL plus counselling (OR 5.5, CI 3.2–9.6).	95% CI	Yes, information leaflets and counselling could be useful	Yes, Adherence	Yes - intervention causes no harm
Demiraley 2004[56]	Yes, the effect of asthma education on asthma knowledge, behaviour and morbidity in asthmatic patients.	Yes, closed envelope technique	No, 8 were lost during the study	Yes, Double blind fashion	Yes	Yes	There were no differences in the knowledge scores among the groups (P = 0.291), but the mean change in the knowledge score was higher in the verbal-written education group than those of the verbal and written education groups.	Not given	Yes, Patients with asthma need more information	Yes, rate of compliance , the rate of correct inhaler use and the rate of hospital admissions.	yes - intervention causes no harm

	1. Did the trial address a clearly focused issue?	2. Was the assignment of patients to treatments randomised?	3. Were all of the patients who entered the trial properly accounted for at its conclusion?	4. Were patients, health workers and study personnel ' blind' to treatment?	5. Were the groups similar at the start of the trial?	6. Aside from the experimental intervention, were the groups treated equally?	7. How large was the treatment effect?	8. How precise was the estimate of the treatment effect?	9. Can the results be applied in your context? (or to the local population?)	10. Were all clinically important outcomes considered?	11. Are the benefits worth the harms and costs?
Al-Saffar et al 2008[50]	Aim not clearly stated, but is assessing the effect of method of information provision (verbal/written) on knowledge in depressed patients	Yes, sequential by day of recruitment, seems to be concealed	Drop-out rate is reported by group	Patients - not possible; health workers not applicable; assessor - yes for initial interview, not stated for follow-up interview	No information reported	Yes	Several aspects of knowledge assessed separately; no primary outcome measure; effects variable	Not stated	yes	Limited knowledge questions, no overall score	Unclear - pharmacist time expensive for limited benefit
Knapp et al 2014[128]	Yes, to access. Combining verbal and numerical expressions increase perceived risk of medicine side-effects	Random	No, 22 lost	Participants and researchers were 'blinded'.	Yes, similar proportions of participants on each of the demographic variables.	Yes	The combined verbal and numerical risk expressions resulted in higher estimates of side-effects, four of which reached statistical significance ($P < 0.05$),	Not given	Yes, significant risk overestimations when compared to numerical frequency bands alone.	Yes, patient's expressions perceptions	yes - intervention causes no harm
Oldman et al 2004[57]	Yes, patient information leaflets in anaesthesia: effect on anxiety and patient satisfaction	Randomization was by numbered sealed envelope from a computer generated randomization sequence.	No, 1 lost	Health worker blinded	Yes, no significant difference	Yes	Significantly more patients who received drug patient information leaflets felt that they had received too much information (0% Group 1 vs 18% Group 2, P=0.003).	Not given	Yes, sometimes, patients felt that they had received too much information. Giving manufacturers' patient information leaflets for anaesthetic drugs to patients before anaesthesia does	Yes, on anxiety and patient satisfaction	Yes - intervention causes no harm

	1. Did the trial address a clearly focused issue?	2. Was the assignment of patients to treatments randomised?	3. Were all of the patients who entered the trial properly accounted for at its conclusion?	4. Were patients, health workers and study personnel ' blind' to treatment?	5. Were the groups similar at the start of the trial?	6. Aside from the experimental intervention, were the groups treated equally?	7. How large was the treatment effect?	8. How precise was the estimate of the treatment effect?	9. Can the results be applied in your context? (or to the local population?)	10. Were all clinically important outcomes considered?	11. Are the benefits worth the harms and costs?
									not increase anxiety.		
Knapp etal 2013[129]	Yes, to evaluate the interpretation of, and preferences for, numerical information on side-effect incidence when presented in three different formats.	Random	No, 129 people (25.8%) completed the study.	No information	yes, The study allocations had similar proportions of participants on each of the demographic variables.	Yes	Three formats did not influence participants' ratings of the information or their side-effect estimates.	Not given	Yes, the participants preferred the combined (frequency and percentage) format of side effect information	Yes, patient's perceptions	Yes - intervention causes no harm
Myhill el al 2017[59]	Yes, the use of supplementary patient education material increases treatment adherence and satisfaction	Yes, randomization list was generated by a statistician.	No, 15 lost	No	No information reported	Yes	Better adherence was observed in the Adapalene 0.1%/benzoyl peroxide 2.5% gel (A/BPO) supplementary patient education material (SEM) group	Not Given	Yes, SEM may increase adherence of acne patients	Yes, Adherence	Yes - intervention causes no harm
Homer et al 2009[58]	Aim not clearly stated, but is assessing the effect of method of information (individual/group counselling)	Yes, adequate method, concealed	Yes - 9 were no longer eligible at allocation, so excluded	Patients - not possible; consultants - not stated; assessors - probably ('PI blinded to questionnaire data until all data from primary	No - differences in proportion with previous DMARD use, contact with nurse-led clinics	In group method, FAQs at early sessions were incorporated into later sessions, no similar option described for individual sessions	Adherence was primary outcome measure, by pill counts monthly for 4 months: 69% versus 90% (21% increase - not significant); secondary measures were satisfaction with information about medicines (SIMS) and	Not stated, but pilot study, therefore not powered to detect difference	No - group counselling not a standard option for most pharmacists	Yes - adherence measures appropriate for aim	This study could be described as a non-inferiority RCT - it is aiming to determine whether group counselling is no worse than individual counselling, it

	1. Did the trial address a clearly focused issue?	2. Was the assignment of patients to treatments randomised?	3. Were all of the patients who entered the trial properly accounted for at its conclusion?	4. Were patients, health workers and study personnel ' blind' to treatment?	5. Were the groups similar at the start of the trial?	6. Aside from the experimental intervention, were the groups treated equally?	7. How large was the treatment effect?	8. How precise was the estimate of the treatment effect?	9. Can the results be applied in your context? (or to the local population?)	10. Were all clinically important outcomes considered?	11. Are the benefits worth the harms and costs?
	provision on adherence in patients starting disease-modifying anti-rheumatic drugs (DMARDs)			outcome available')			adherence with monitoring schedules, no significant differences				suggests that group counselling is economically a viable alternative

4.4.2 Non-randomised studies (1A)

There were four studies; (prospective before and after studies) included in this category all of which were conducted in Asia. The purpose of the studies was to test an intervention rather than conducting readability tests which occur on one occasion. Generally, the studies aimed to assess the development, testing, implementation, and evaluation of new leaflets.[64–66] The combination of a PIL with pharmacist's counselling was also tested.[68] The outcomes included participants' knowledge[64–66,68] , adherence[66] , understanding[68], and behaviour in preventing recurrent drug allergy.[68] All studies stated their research questions which were relevant to their objectives.

Participants were patients with certain diseases[64–66] or conditions.[68] Only two studies defined the participant's inclusion criteria, and these were appropriate for the study objectives. The data collection process was planned before the studies had started.

No study reported an intention-to-treat analysis or prospective calculation of the study size. In terms of pre-post design, the studies reported the follow-up period of between one week to one month without more details.

The outcomes were appropriate to the question addressed by the studies. None of studies used blind evaluation. The percentage of loss to follow up varied from 8%[65] to 77.15%[66]. No studies described how control and intervention group were managed during the same time period. All statistics were used appropriately and in accordance with the type of study. The evaluation results are shown in Table 4-2

Table 4-2 the evaluation result of non-randomised controlled trial study

ID study	A clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to the aim of the study	Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of the study	Loss to follow up less than 5%	Prospective calculation of the study size ..	An adequate control group	Contemporary groups	Baseline equivalence of groups	Adequate statistical analyses
Kumaran et al 2009[64]	Yes	No	Yes	Yes	No	N/A	No	No	-	-	-	-
Kumaran et al 2010[65]	Yes	Yes	Yes	Yes	No	N/A	No	No	-	-	-	-
Gupta et al 2005[66]	Yes	No	Yes	Yes	No	Yes	No	No	Yes	No	Yes	Yes
Jarernsiripornkul et al 2015[68]	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	No	Yes	Yes

4.4.3 Qualitative studies (1B)

There were nine studies conducted using qualitative research methods.[21,70,72–78] Most of them were carried out in the UK, one in South Africa[70] and none in Asia. The objectives of the studies were to explore certain behaviours, beliefs, attitudes, information preferences and needs for medicine information. Face to face interviews and focus group discussions were used. One study collected data by telephone interview (UK701).[76] Purposive sampling was adopted to include a wide spectrum of participant's demographics and cover target participants such as age, gender, and having had experience in taking some certain medicines. Content analysis and thematic analysis were applied in all studies. Most studies described the researcher's position as an interviewer, modulator, or data assessor. The evaluation results are shown in Table 4-3.

Table 4-3 the evaluation result of qualitative studies

ID study	Was a qualitative approach appropriate?	Was the sampling strategy appropriate for the approach?	What sampling strategy	What were the data collection methods?	how interview	How were data analysed and how were these checked?	Analysis	Is the researchers position described?	Do the results make sense?	Are the conclusions drawn justified by the results?	Are the finding transferable to other clinical settings?
Patel& Dowse 2013[70]	Yes	Yes	purposive and convenience sampling	Yes	Four focus group discussions	Yes	Content analysis	Yes	Yes	Yes	Yes
Hamrosi et al 2013[72]	Yes	Yes	purposive sampling	Yes	Eight focus group discussions	Yes	Content analysis	Yes	Yes	Yes	Yes
Arkell et al 2013[73]	Yes	Yes	purposively sampled	Yes	Two focus groups	Yes	Content analysis	No	Yes	Yes	Yes
Dickinson et al 2017[21]	Yes	Yes	purposive sampling	Yes	21 face-to-face interviews	Yes	Content analysis	Yes	Yes	Yes	Yes
Tong etal 2017[74]	Yes	Yes	purposive sampling	Yes	76 Face-to-face semi structured interviews	Yes	Thematic analysis	Yes	Yes	Yes	Yes
Dickinson et al 2013[75]	Yes	Yes	purposive sampling	Yes	Eight focus groups	Yes	Content analysis	Yes	Yes	Yes	Yes
Smith etal 2017[76]	Yes	Yes	purposive sampling	Telephone	12 Telephone interviews	Yes	Thematic analysis	Yes	Yes	Yes	Yes
Balmer 2012[77]	Yes	Yes	purposive sampling	Yes	15 Face-to-face semi structured interviews	Yes	Content analysis	Yes	Yes	Yes	Yes
Raynor 2004[78]	Yes	Yes	purposive sampling	Yes	Four focus group discussions	Yes	Content analysis	Yes	Yes	Yes	Yes

4.4.4 Cross sectional survey studies (1C)

There were 34 studies identified as cross-sectional research surveys. The studies scored between 11 and 19 (total score = 20) using the AXIS tool. There were 15 studies conducted in the UK (score range between 12-19), 16 in Asia (score range between 11-15), and three in Africa (score range between 14-16).

All included their objectives for which they surveyed patients' needs and common sources of medicine information, knowledge, awareness regarding information in drug package inserts, or the frequency of receiving medicine information. All study designs were correlated with their aims. Many studies (n=30) did not report the sample size calculation.

All studies defined their target population, and the sampling frame and selection process mostly represented the target population. The participants were either general public or patients, but one study collected data in undergraduate students which are not typical of the general consumers as indicated in the study aim.[106] All except two of the studies described their sampling process.[89,90] The studies approached their participants by using purposive sampling (n= 7), convenience sampling (n = 17), systematic random sampling (n= 3), or proportional quota sampling (n =2), non-probability sampling (n=1), and simple random sampling (n=2).

The number of non-responders were addressed in only eight studies.[10,86,87,91,98,107,111,125] which was between 5% and 37.5%. The outcome variables proposed were appropriate to the aims of all studies. There were 22 research studies conducted with measurements which had been trialled, piloted or, used data published previously.[10,20,22,80,83,86,90–92,96,98,103–105,107,112,113,116,121–124] For example, some studies used questionnaires which were adapted and modified from, or calculated their sample size based on, the previous literature.[90,98,121]

Most studies (n=24) determined statistical significance if it was appropriate for their analysis. Most formal published studies included details of their approach to statistical analysis of their data. The basic data were adequately described in terms of participants' characteristics. None reported either concerns relating to the response rate which might raise the non-response bias or described the non-response impact. The results in all studies were presented for all the analyses described in the methods, and they were referred to in the discussions and conclusions. Nearly half of the studies (n= 15) considered the limitations of their studies. Any funding sources or conflicts of interest were declared by all authors in 20 of the studies. There were 17 studies that recorded that they were approved by an ethics committee. The evaluation results are shown in Table 4-4

Table 4-4 the evaluation result of survey study

ID study	1. Were the aims/objectives of the study clear?	2. Was the study design appropriate for the stated aim(s)?	3.Was the sample size justified?	4.Was the target/reference population clearly defined? (Is it clear who the research was about?)	5.Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?	6.Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?	7.Were measures undertaken to address and categorise non-responders?	8.Were the risk factor and outcome variables measured appropriate to the aims of the study?	9.Were the risk factor and outcome variables measured correctly using instruments/measurements that had been trialled, piloted or published previously?	10. Is it clear what was used to determined statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)	11.Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	12.Were the basic data adequately described?	13.Does the response rate raise concerns about non-response bias?	14.If appropriate, was information about non-responders described?	15.Were the results internally consistent?	16.Were the results presented for all the analyses described in the methods?	17.Were the authors' discussions and conclusions justified by the results?	18.Were the limitations of the study discussed?	19.Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	20.Was ethical approval or consent of participants attained?
Kyei et al 2014[79]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Amin et al 2010[83]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	yes	No
Ankrah and Ofei 2010[80]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No
Saleem et al 2015[95]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	No	No	Yes	yes	Yes	No	No	No
Kaikade & Jha 2015[88]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	No	Yes	Yes	Yes	No	No	No
Singh et al 2016[89]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	No	No	No	Yes	Yes	Yes	No	No	Yes
Al-Ramahi et al 2012[86]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	No
Sweileh et al 2004[87]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	No	No	No	Yes	Yes	Yes	No	No	No
Dawoodi & Bhosale 2016[90]	Yes	Yes	No	Yes	Yes	yes	No	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	No	No	No

ID study	1. Were the aims/objectives of the study clear?	2. Was the study design appropriate for the stated aim(s)?	3.Was the sample size justified?	4.Was the target/reference population clearly defined? (Is it clear who the research was about?)	5.Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?	6.Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?	7.Were measures undertaken to address and categorise non-responders?	8.Were the risk factor and outcome variables measured appropriate to the aims of the study?	9.Were the risk factor and outcome variables measured correctly using instruments/measurements that had been trialled, piloted or published previously?	10. Is it clear what was used to determined statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)	11.Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	12.Were the basic data adequately described?	13.Does the response rate raise concerns about non-response bias?	14.If appropriate, was information about non-responders described?	15.Were the results internally consistent?	16.Were the results presented for all the analyses described in the methods?	17.Were the authors' discussions and conclusions justified by the results?	18.Were the limitations of the study discussed?	19.Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	20.Was ethical approval or consent of participants attained?
Jarernsiri pornkul et al 2015[98]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Perera et al 2012[104]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes
Song et al 2017[105]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes
Ho et al 2009[10]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes
Nader et al 2008[103]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	No
Rahim et al 2015[96]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes
Bawazir et al 2003[91]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	No
Juffali et al 2013[20]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	No
Vinker et al 2007[107]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	Yes
Abanmy et al 2012[92]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No
Kim&Ahn 2013[106]	Yes	Yes	No	Yes	Yes	No	No	Yes	No	No	Yes	Yes	No	No	Yes	Yes	Yes	No	No	No
Whiskey at al[119]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes

ID study	1. Were the aims/objectives of the study clear?	2. Was the study design appropriate for the stated aim(s)?	3.Was the sample size justified?	4.Was the target/reference population clearly defined? (Is it clear who the research was about?)	5.Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?	6.Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?	7.Were measures undertaken to address and categorise non-responders?	8.Were the risk factor and outcome variables measured appropriate to the aims of the study?	9.Were the risk factor and outcome variables measured correctly using instruments/measurements that had been trialled, piloted or published previously?	10. Is it clear what was used to determined statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)	11.Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	12.Were the basic data adequately described?	13.Does the response rate raise concerns about non-response bias?	14.If appropriate, was information about non-responders described?	15.Were the results internally consistent?	16.Were the results presented for all the analyses described in the methods?	17.Were the authors' discussions and conclusions justified by the results?	18.Were the limitations of the study discussed?	19.Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	20.Was ethical approval or consent of participants attained?
Raynor, et al 2007[120]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	No	Yes	Yes	Yes	No	No	Yes
Webster, etal 2017[121]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes
Auyeung et al 2011[122]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No required
Kraka&Morecroft 2012[123]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes
Duggan at al, 2007[124]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes
Raynor et al 2005[125]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Parham et al 2009[112]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No
Krska et al 2013[113]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Symonds etal 2011[114]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Bersellini & Berry 2007[115]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes

ID study	1. Were the aims/objectives of the study clear?	2. Was the study design appropriate for the stated aim(s)?	3.Was the sample size justified?	4.Was the target/reference population clearly defined? (Is it clear who the research was about?)	5.Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?	6.Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?	7.Were measures undertaken to address and categorise non-responders?	8.Were the risk factor and outcome variables measured appropriate to the aims of the study?	9.Were the risk factor and outcome variables measured correctly using instruments/measurements that had been trialled, piloted or published previously?	10. Is it clear what was used to determined statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)	11.Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	12.Were the basic data adequately described?	13.Does the response rate raise concerns about non-response bias?	14.If appropriate, was information about non-responders described?	15.Were the results internally consistent?	16.Were the results presented for all the analyses described in the methods?	17.Were the authors' discussions and conclusions justified by the results?	18.Were the limitations of the study discussed?	19.Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	20.Was ethical approval or consent of participants attained?
Bersellini & Berry 2007[116]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	N/a	No
Gardner etal 2011[22]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No
Olofinjana & Taylor 2005[111]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	No

4.5 Discussion

With regards to RCTs, most of the studies reviewed achieved most of the criteria on the CASP checklist for RCTs. However, the African and Asian studies failed to report blinding of assessors in comparison with studies in the UK. Some studies reported that blinding measures had been taken rather than providing the detail of how this had been achieved. Failure to blind could presumably have led to bias in perception of benefit, improved performance, assessment, and evaluation.[237] An inequality treatment might occur; this could be the major defect. Even though some studies reported random sampling, there was a difference between groups of their participants at the beginning, and some studies omitted this information entirely. This may reflect a selection bias which happened at the point of allocating participants, as a result of systematic differences in the characteristics of the participants.[237]

Publication bias should also be taken into account. This bias occurs when the results of published studies change systematically from the outcomes of unpublished studies. Those with statistically significant or positive outcomes are more likely to be published than studies with insignificant or negative outcomes.[238,239] Therefore, published studies may be different from those of unpublished studies.

All of the RCTs identified and reviewed had positive outcomes this implies that medicine information always benefits patients, for example by increasing their knowledge and awareness of medicine side-effects or their adherence to treatment. Publication bias means that this conclusion may not actually be valid. Furthermore, the practicality of applying these to the real world is questionable particularly with respect to the time required to deliver the intervention. For instance, when verbal information was provided by pharmacists on an individual basis this was time consuming. One of the studies demonstrated the benefit of a group counselling approach which may be an economically viable alternative.

In terms of non-randomised studies, none described methods to adopt blinding. No studies described how the control and the studied group were managed. In terms of the follow-up period, this was specified in two of the four studies; one week[24] and one month[25]. These studies were assessing adherence and understanding about medicines, respectively, and whilst the chosen follow up period may have been appropriate to reduce loss of participants to follow up, no justification was provided by the researchers of either study. The one-week gap might be appropriate for evaluating the impact of a PIL on the knowledge of medicines on a short-term basis but doesn't indicate whether any increased knowledge is sustained. The other study which

aimed to evaluate patients' knowledge, understanding and behaviour in preventing their drug allergy employed a pre and post-test period of one month. However, since drug allergy is fortunately a relatively rare occurrence, perhaps a longer follow up period would have been able to determine the true impact of this intervention.

Performance and detection bias might have been experienced. High drop-out or loss to follow up rates were found in a number of the studies without intention-to-treat analysis. These could result in possible attrition bias due to systematic differences in the withdrawals or exclusion of participants between study groups.[237] Overall of intervention studies, the interventions were tested in some specific group of people or patients. The measurement of outcomes was also highly varied; therefore, the results could be applied in certain contexts, but not for the population more generally. External validity could also be questioned. With regards to qualitative studies, most of them were conducted in the UK. The advantage of a qualitative approach is to gather an in-depth understanding of specific issues by interviewing, individually or as a group, as wide a selection of people as possible to provide a full breadth of viewpoints. However, in reality this is difficult to achieve, as those who volunteer for studies are more likely to be of a more privileged social class and have higher educational achievements than non-participants. Rarely does the demographic characteristics of participants reflect wider society. Furthermore, during group interviews individuals with strongly held views may dominate the discussion and/or during one to one interview participant may inform researchers of what they think they would like to hear. The analysis of interviews is also subject to possible bias due to the interpretation of transcripts by the researcher. The researcher must be fully aware of the impact of their own context and beliefs on the research process (reflexivity). For these reasons whilst the results of the studies were probably valid within the specific context of the study, they are not generalisable.

With regards to cross-sectional survey studies, most of the studies reviewed achieved most of the criteria on Appraisal tool for Cross-Sectional Studies (AXIS tool). However, many studies had neither information on the sample size calculation nor had reported refusal rates. None reported information about non-responders. Identifying their limitations in term of sample size, characteristics of participants, or the specific focus of the survey were also omitted in many of the studies. These could result in potential sources of bias and question the generalizability of the results of the studies outside of the context within which they were conducted.

4.6 Strengths and limitations

The studies were categorised, and their quality evaluated using published tools, specific to the study design. This approach has standardised the critical appraisal and facilitated a systematic evaluation of all of the studies identified in the scoping review (chapter 3). Again, the search was limited only to articles entirely written or with an abstract in English. Those written in other languages were excluded. Another limitation was that the study in the 2A category was not included for quality assessment. All studies were not attempted to combine results from the intervention studies in a meta-analysis because it isn't possible, due to the highly varied methods and outcome measures used.

4.7 Conclusion

Overall, the quality of the studies varied. The majority of RCTs and the qualitative studies conducted in the UK adhered to RCT and qualitative study standards, respectively. With regards to non-RCT and cross-sectional surveys, there was a lack of critical information, for example, blinding measures, sample size calculation, characteristic of participant, refusal rates, and follow-up period. The high dropout rate was also a source of concern. The quality of the studies were sometimes doubtful. In terms of the qualitative studies, the quality of the study was more likely to meet the standard. In comparison to the cross-sectional surveys, in which the results were broader, the results from qualitative studies were deeper. However, participants in qualitative studies were usually specific groups of people. The results were therefore only valid within the specific context.

From Chapters Three and Four, no study identified the causes of dissatisfaction with the PILs, although many highlighted criticisms. The provision of PILs should be reviewed. Although there were many studies which examined content and format of PILs, no study examined both these aspects together with readability, from either the UK PILs or Thailand. This lack led to the comparison study of UK PILs and Thai PIs for Ibuprofen being evaluated in terms of content and design quality. Furthermore, there was also little information on the general public's needs for medicine information in the UK or Thailand. Hence a further empirical study was undertaken to address this gap.

Chapter 5 Comparison of provision on PILs from the EU, US, Australia and Thailand

5.1 Introduction

The PILs regulations have been established across the world to provide guidelines regarding how medication information for patients should be written, designed, and delivered. This chapter reviews PILs regulatory guidance from the European Union (EU), United States (US), Australian, and Thai authorities in terms of what is expected for content provided, layout and design. This section describes the related documents which were selected for review, and the purpose of each document.

In EU countries, PILs have been provided with all medicines since 1999. All patient information leaflets in each EU country were required to be reviewed and approved by their relevant authorized organization e.g. Medicines & Healthcare products Regulatory Agency (MHRA) in the UK before being supplied with the medicine.[1]

There are two main documents related to developing the PILs. First, the document which provided the template of information required is named the "QRD template v10.2" (revised on 1/01/2021). The European Medicines Agency's (EMA) Working Group on Quality Review of Documents (QRD), had reviewed and updated the templates for product information for use by applicants and marketing authorisation holders for human medicines.[16,240] The purpose of this template was to ensure that the basic regulatory requirements must be included in the text versions of all packaging components in the order specified, and written in a language understandable by the patient.

Second, the document which provides guidance about the design and layout of the PILs is the Guideline on the Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use.[15] The design and layout are key elements for the readability of the final printed material. The purpose of this document is to provide guidance on how to ensure that the information on the package leaflet is accessible to and can be understood by those who receive it, so that they can use their medicine safely and appropriately.[15]

In the United States, the medicine leaflet for the general public is called Consumer Medication Information (CMI). This is written information about prescription drugs developed by organizations or individuals other than a drug's manufacturer. CMI is intended for distribution to consumers at the time of drug dispensing.

The main document providing guidance in developing CMI is "Guidance on Useful Written Consumer Medication Information (CMI)", provided by U.S. Department of Health and Human Services, Food and Drug Administration Centre for Drug Evaluation and Research (CDER), Centre for Biologics Evaluation and Research (CBER).[241] This guidance is proposed to guide individuals or organizations (e.g., pharmacies, private vendors, healthcare associations) in developing useful written CMI. In the US, neither the Food and Drug Administration (FDA) nor a drug's manufacturer reviews or approves CMI, therefore the FDA recommends that the developers of WMI use the guidance contained in this document to help ensure that their CMI is useful to consumers.

In Australia, as in the US, the leaflet for consumer and patient is called Consumer Medicine Information (CMI). The CMI must be provided with all new medications required by law. The pharmaceutical company (sponsor) is responsible for creating the content of their CMIs and ensuring that they are effective. There are four documents related to producing the CMI. All documents are produced by the Therapeutic Goods Administration (TGA), Department of Health, Australian Government. The first document is Creating the CMI summary page, Guidance for sponsors.[242] This document provides guidance about preparing the summary page for CMI documents. It is intended for sponsor who supplied the medicines to the Australian market and other interested stakeholders.

The second document is Using the TGA CMI template Guidance for sponsors.[13] As with the first document, the purpose of this guidance document is to provide sponsors of medicines supplied to the Australian market and other interested stakeholders information about preparing CMI documents that comply with current regulations. The focus of this resource is providing instructions for using the TGA CMI template for prescription medicines and non-prescription medicines. The third document is tga-consumer-medicine-information-prescription-medicine-template.[243] This is the actual template which provides the design, format, example statements, and compulsory information topics. The sponsor can adapt and adopt the template to create their own CMI.

The fourth document is "Consumer Medicine Information (CMI)– How to use the improved CMI template".[244] This document is intended to be a companion resource to the Creating the CMI summary page, Guidance for sponsors, and the Using the TGA CMI template Guidance for

sponsors. This document provides general information and guidance regarding the new templates and effective writing for consumers.

The guideline provides general information, main topics, example statements, and guidance regarding CMI templates for all Australian guidelines. There are two forms provided: full and summary templates. The summary version is intended to be used in conjunction with the full CMI and it is not, therefore, required to be comprehensive. When a summary version is required or voluntary, it must be limited to one page. During user testing, the summary version received very positive feedback. In general, the guideline states that the exact wording in the headings and body text is recommended rather than required, but the type of information indicated under each heading must be included. However, details regarding the specific information provided to patients is not clearly defined.

In Thailand, the guideline for patient information leaflet development was introduced in 2013.[27] Then, the updated guideline version was published in 2019.[28] The first and the second guideline do not differ much apart from adding some information and editing the format. The main purpose was still the same. This guideline covers the production of two types of WMI. The first of these is medicine information for health care professionals. This can be provided in two forms: a SmPC, and PIs. The second covers WMI for patients, called PILs, which are specifically designed for the general public.

5.2 Objectives

1. To examine the guidelines on PILs in the EU, the United States, Australia, and Thailand.
2. To compare the requirements between the guidelines for similarities and differences.

5.3 Methods

Data searching

Registered websites of health-related organisations or government agencies were searched in order to identify guidelines.

a. The EU guideline was available at European Medicines Agency website**.** **https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/product-information/product-information-templates-human**
b. The US guideline was available at U.S. Food and Drug Administration website.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/useful-written-consumer-medication-information-cmi

c. The Australian guideline was available at Therapeutic Goods Administration Australian Government website. **https://www.tga.gov.au/improved-consumer-medicine-information-template**

d. The Thai guideline was available at Thai Food and Drug Administration website. **https://www.fda.moph.go.th/sites/oss/Shared%20Documents/SmPC-PIL_HPEP%20guideline_updated%20May2019.pdf**

Data extraction

The guidelines from the four countries were read, all recommendations with regard to content and design were identified and the areas covered were identified. All topics covered by the guidelines were tabulated to enable identification of similarities and inconsistencies. Both content and layout and design were analysed, and compared.

5.4 Results

5.4.1 Content

Generally, all regulations addressed the main headings that needed to be shared with the patients. Most compulsory headings were similar to each other e.g. name of medicine, indication, contraindication, and side effects. The regulations review compared each country's regulations in terms of similarities and differences between them with respect to the criteria on content. The comparison of guidance relating to content for EU, USA, Australia and Thailand is shown Table 5-1

Regarding medicine name, both generic name and brand name were required to be included at first with all regulations. The phonetic spelling of the brand name was also required in the US and Australian guidelines. The pharmaceutical form was mentioned only in EU and Thai regulations, while the example of CMI in the US guideline presented the dosage form as well. The medicine strength was mentioned in all regulations except the Australian guidance.

The Thai regulations required that the medicine strength be written in the Metric system with no abbreviation e.g. 200,400 milligrams or other international units, while the other guidelines did not specify.

In terms of indication and contra-indications, the EU and Thai regulations suggested referring to the pharmaceutical references e.g. SmPC, Micromedex EMA, and their authorized organisation references e.g. FDA. Despite including contraindications, the EU and Thai regulations also suggested providing information about what patients need to know before taking the medicine. The US FDA suggested stating what to do if any of the contraindications apply to the patient, such as contacting the healthcare provider before taking the medicine, and including a statement of precautions about any circumstances in which the use of the medication could lead to serious injury or death.

In regard to dosage, the US FDA and Thai regulations recommends stating the "usual dosing instructions" or "it is important to follow the dosing instructions provided by the patient's healthcare provider". This means that the CMI could refer patients to the prescription label for specific dosing instructions.

Specific to how to use, how to administer and the route of administration, the EU regulation also indicated that when the medicine was licensed in different age groups with a different dose, method of administration, frequency of administration or duration of treatment, specific instructions for use for each age group should be clearly identified. The route(s) of administration according to "Standard Terms" published by the Council of Europe and an additional patient-friendly explanation may be used if necessary.

The US regulations mentioned the information if specified in the PI, the information on how to use the medication, route of administration, special information for taking the medicine e.g. taking with or without food or special instructions such as for inhalers should be included in the CMI. Also the statement "it is important to follow the dosing instructions provided by the patient's provider" should be added.

For the Australian guideline, the main information required was how much to take/use, when to take / use [medicine name], how to [insert appropriate verb] [medicine name] (relevant for devices). A statement was suggested to add "Follow the instructions provided and use [medicine name] until your doctor tells you to stop, or for antibiotics, replace with 'Follow the instructions provided when [medicine name] was prescribed, including the number of days it should be taken.'

The Thai guidance suggested to provide information about how often you should use this medicine, route(s) and/or method of administration, instructions describing how to administer the medicine. They advise that some pictures may be needed. It might also be relevant to add a

statement "it is important to follow the dosing instructions provided by the patient's healthcare provider".

All of the regulations required information advising patients what they should do when they miss a dose or take more than a scheduled dose (overdose). Especially, for overdoses the leaflet needs to describe the signs and symptoms that a patient may experience so that they can identify these, and know when to meet their doctor. In addition to missed doses and overdose, the EU regulation also mentions that patients should be informed about stopping the medicine and whether they could expect any withdrawal effects.

In terms of monitoring the effectiveness of treatment, all regulations suggested that some kind of statement that "you must contact a doctor or pharmacist if your symptom worsens or do not improve" needed to be added to help patients monitor the effectiveness.

With regards to warnings and precautions, and boxed warnings, the US and EU regulations suggested referring to information stated in the SmPC and package leaflet. This also covered patient activities and behaviours to avoid. The US FDA guideline also stated that information contained in boxed warnings in the PI should be presented prominently in CMI and be consistent with or derived from the PI.

The side-effects were considered to be important information. The EU and Thai regulations suggested that there were two types of side effects: the most serious which require that patients must stop taking the medicine and seek medical advice, and other side effects which patient may experience but should not lead them to stopping the medicine. The list of side effects should be listed by frequency and start with the most frequent. The US FDA did not require that CMI contain a full listing of all possible side effects, but they recommended that the most serious potential adverse reactions are included, plus a list of the symptoms of the most frequently occurring (common) adverse reactions. The FDA also suggested further that the statement "Side effects given are not a complete list and that patients should be instructed to ask their doctor or pharmacist for more information" be included. The Thai regulation suggested that the information should be referred from US FDA, Micromedex, and EMA.

The Australian guideline suggested that the side effects information should be grouped and prioritised in CMI (and summary) by their seriousness, as indicated by the actions that the consumer needs to take. Another suggestion was that it may be possible and helpful to group a number of potential side effects by type, such as 'stomach complaints', 'skin problems', or 'breathing issues'. The guidance also nominated the website that patient can report the side

effects which is the Therapeutic Goods Administration online at www.tga.gov.au/reporting-problems. Similarly, in the EU guidance, the reporting of side effects was also mentioned by suggesting to report side effects directly via the national reporting system e.g. https://yellowcard.mhra.gov.uk/ in the UK.

In terms of drug interactions section, the EU regulations suggested referring to the SmPC of the medicine. The US FDA suggested that the leaflet should not present every possible interaction, but explain that the list is incomplete, and suggest that patients who are taking other medicines should keep a list of all these medicines and discuss them with their doctor or pharmacist.

The Australian guidance provided the example statement related with this topic for example 'Tell your doctor or pharmacist if you are taking any other medicines, including any medicines, vitamins or supplements that you buy without a prescription from your pharmacy, supermarket or health food shop.' The CMI may show subdivisions and list the medicines depending on the nature of their interaction.

In the Thai guideline, the drug-drug interaction information was included in contra-indications ;What you need to know before taking the medicine topic. The suggested statement was "This medicine should not be used in with certain medications, herbs, or dietary supplement because it may have therapeutic effects or be risk." The list of drug-drug interaction should only include the medicines which were important items and are widely used in Thailand.

All regulations indicated specific information for special populations e.g. children, adolescents, elderly, pregnancy, breast feeding, and fertility. In the US, the regulations state that patients with compromised immune systems or people with impaired kidney or liver function need to be provided with specific information. In the EU, Australia, and Thailand, guidance about driving and using machines were separated from the side effect topic so that this would be provided as special information. Advice regarding storage conditions was provided as nearly the last topic in all of the regulations. The EU and Australian regulation provided the storage condition in more detail e.g. expiry date, shelf life after reconstitution, dilution or after first opening the container. The EU, Australian and Thai regulations suggested the statement "keep away from children". The EU advised that the contents of the pack must be provided. EU, Australian and Thai regulations suggested to disclose all excipients.

Focusing on the US regulation, additional statements, not required by other authorities were advised to be included. For instance, a statement "medicine should only be used by the patient for whom it is prescribed and should not be given to other people", a statement "discussion with

a healthcare professional about the prescription medicine", and a statement "This leaflet summarizes the most important information about <insert medication name>. If you would like more information, talk with your doctor."

With regards to Marketing Authorisation Holder (MAH) and manufacturer information, these were written in the last part of the patient leaflet suggested by EU, Australian, and Thai regulation, while the US regulation suggested providing the CMI publisher's name and address. The date that the leaflet was last revised or published was recommended to be provided by all regulations.

In terms of other information, there were some further differences between the regulations. For the EU regulation, references should be included to other sources of information which will be useful for the patient. The US regulation concerned that the CMI should be considered a stand-alone document in meeting this criterion. The content and tone of the CMI text should be written with unbiased information and accepted scientific literature standards.

The text of the CMI should be unbiased in content and tone and should meet the accepted standards of scientific literature. A disclaimer stating that the CMI is a summary and does not contain all possible information about the medicine should added.

The Australian regulation suggested explaining how consumers can access the medicine, and describing what the medicine looks like in simple language and include the registration number for the medicine. The disclaimer "The PILs is a summary and does not contain all information, ask doctor or pharmacist for more information. " was recommended to be added in the last part of the patient leaflet by Thai regulation. The comparison of guidance relating to content for EU, USA, Australia and Thailand is shown in Table 5-1.

Table 5-1 Comparison of guidance relating to content for EU, USA, Australia and Thailand

Content	EU	USA	Australia	Thailand
Name	✓ + therapeutic group	✓ + phonetic spelling	✓ phonetic pronunciation optional	✓
Pharmaceutical form	✓	Not specified	Not specified	✓
Strength	✓	✓		✓ In metric system with no abbreviations
Indication	✓	✓	✓ in plain English	✓
Contra-indications	All	All	Significant	Includes drug interactions
Before taking medicine	✓ Contraindications, Appropriate precautions for use; special warnings, Interactions with other medicines	Not specified	Not specified	✓ Absolute contraindication warning, precaution, caution, relative contra-indication
Other information for contraindication		Directions about what to do if any of the contraindications apply to the patient		When should you consult your doctor?
Dosage	✓	✓ “ It is important to follow the dosing instructions provided by the patient’s healthcare provider”	✓	✓ "It is important to follow the dosing instructions provided by the patient’s healthcare provider"
How to use	✓	✓	✓	✓
How to administer	✓	✓	✓	✓ Pictures may be needed.

	EU	USA	Australia	Thailand
Route of administration	✓	✓	Not specified	✓
Missed Doses	✓	✓	✓	✓
Overdoses	✓	✓	✓	✓
Stopping taking	✓	Not specified	Not specified	Not specified
Monitoring effectiveness of treatment	✓	✓	✓	✓
Warnings and precautions	✓	✓	✓	✓
Boxed warnings	NA	✓	✓ If the product is under to the Black Triangle Scheme or a boxed warning, then retain the relevant wording provided on the summary template, or at the top of the first page of the full CMI.	
Side-effects	✓ The most serious side effects need to be listed prominently first with clear instructions to the patients on what action to take, and then a list of all other side effects, listed by frequency and starting with the most frequent.	✓ Not expected to contain a full listing of all possible side effects.	✓ Side effects should be grouped and prioritised in CMI (and summary) by their seriousness,	✓ There are two types of side-effects included: SE which patient must stop taking medicine and see the doctor immediate, SE which patient do not stop taking medicine, but patient must contact a doctor or pharmacist if the symptoms worsen.
Tolerance/ dependence/ Withdrawal of treatment	Not specified	✓	✓	Not specified
Drug Interactions	✓	✓	✓	✓

	EU	USA	Australia	Thailand
Food interactions	✓	✓	✓	✓
Special populations	Children Adolescents Pregnancy Breast feeding Fertility	Children Elderly patients People with compromised immune systems People with impaired kidney or liver functioning Pregnancy Breast feeding Labour	Elderly Children, infants People with specific pathological conditions. Pregnancy Breast feeding	Children Adolescents Elderly patients Pregnancy Breast feeding
Driving and using machines	✓	✓	✓	✓
Storage	✓ Keep this medicine out of sight and reach of children	✓	✓	✓ Keep away from children
Package labelling	Not specified	✓	Not specified	Not specified
Person-centred advice			Provide targeted information that directly relates to a person or their situation so they can take action or make a decision. Provide targeted information and step by step guidance.	
Contents of the pack and other information	✓	Not specified	Not specified	Not specified
All excipient(s)	✓	Not specified	✓	✓

	EU	USA	Australia	Thailand
	What X contains What X looks like and contents of the pack			Appearance, colour, active ingredient, All excipients
Sign post to HCP to encourage patient discussion with a healthcare	✓	✓	✓	✓
Sign post to further information	✓ Provide reporting of side effects websites + alternative reporting details	Not specified	✓ Provide direct information on where links go and use short URL links to external information.	Not specified
Marketing Authorisation Holder	✓	Not specified	✓	✓
Manufacturer	✓	Not specified	Not specified	✓
CMI publisher	Not specified	✓	Not specified	Not specified
Date of publish/ revision	✓	✓	✓	✓
Other info	A statement that “Keep this leaflet. You may need to read it again.” A statement that <- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.>	A statement that the medicine should only be used by the patient for whom it is prescribed and should not be given to other people. A disclaimer stating that the CMI is a summary and does not contain all possible information about the medicine.	Explain how consumers can access the medicine. Describe what the medicine looks like in simple language and include the registration number for the medicine.	A disclaimer " PIL is a summary and does not contain all information, ask doctor or pharmacist for more information. "

5.4.2 Layout and design

Apart from content, the layout and design are also important components of PILs. The main principle of setting guidelines for the layout and design was to enable readers to distinguish key information and ensure that the text is readable. All regulations had common agreement with the issues that mattered most.

The font size should in general be measured 8- 11 points; EU recommends Times New Roman and Thailand Tahoma font. Capitals should be used for emphasis with no italics and ornate typefaces employed. The text colour should be contrasted with the paper colour. The space between the lines should be more than 2.2 mm. EU suggest a space between lines should be at least 3 mm. The bold type face or a different colour of high contrast style should be used for the headings. The EU regulations also advised that the paper should be sufficiently thick to avoid transparency.

Furthermore, the text size of 14 points, bold centred in the box was suggested for heading in Thai regulation. Short paragraphs, numbering, bulleting and tables were suggested as ways to improve the navigation through the leaflet in all regulations. Justification of text was prohibited in the EU regulations. A line length of approximately 40 letters long was advised in the US regulations.

The Thai regulations recommend separating text into three columns in A4 landscape paper. Plain language with short sentences and paragraphs, direct, including step by step guides and active style should be written. The use of acronyms should be minimised. Symbols and pictograms were recommended to be used in EU and Australian regulations. The Thai language must be used for Thai leaflets. However, for the EU regulation, where a multi-lingual leaflet was proposed there should be clarification between the different languages used. More importantly, all regulations required that medical terms should be avoided and translated into plain language.

The readability test was indicated in the US CMI guidance. It was indicated that CMI could be provided at the sixth to eighth grade reading level. In addition, user testing was required to conduct in EU, and recommended to carry out in Australian, and Thai guidance, while only EU and Thai guidance provided the user testing guide. The Australian CMI template was subjected to user testing. The comparison of guidance relating to layout and format for EU, USA, Australia and Thailand is shown in Table 5-2. The full table of comparison of PILs guidance shows in Appendix 2

Table 5-2 Comparison of guidance relating to layout and design for EU, USA, Australia and Thailand

Layout and design	EU	USA	Australia	Thailand
Font – size	✓ > 8 point	✓ >10-point	Not specified	✓ Main topics: 14 points General: > 11 points
Font- type	✓	✓	Not specified	✓
Font colour	✓	✓	Not specified	✓
Line spacing	✓	✓	Not specified	✓
Headings	✓	✓	✓	✓
How to emphasise certain points	✓	✓	✓	✓
Use of Capital letters	✓	✓	Not specified	Not specified
Use of Italics	✓	✓	Not specified	Not specified
Use of underlining	✓	✓	Not specified	Not specified
Use of highlighting	N/A	✓	Not specified	Not specified
Justification of text	✓	Not specified	Not specified	Not specified
Length of line	Not specified	✓ Approximately 40 letters long	Not specified	Not specified
Layout of columns	✓ landscape layout	Not specified	Not specified	✓ 3 columns (suggestion) Landscape
Multi-lingual leaflets	✓	Not specified	Not specified	Not specified
Sentence construction	✓ An active style should be used	✓ unbiased in content Neutral; without comparative adjectives	✓ Use plain English Use active voice Clearly legible	✓ Use plain language

	EU	USA	Australia	Thailand
Sentence length	✓	Not specified	✓	✓
Paragraphs/ Bullet points/ Tables	✓	✓	✓	✓
Scientific symbols	✓	Not specified	Not specified	Not specified
Numbers	Not specified	Not specified	Not specified	✓ All Arabic
Abbreviations/ acronyms	✓	Not specified	✓	Not specified
Symbols/ Pictograms	✓	Not specified	✓	✓
Language	Not specified	Not specified	Not specified	✓ Thai language
Medical terminology	✓	Not specified	✓	✓
Links within the document	Not specified	Not specified	✓	Not specified
Paper Size/ orientation	✓	✓	Not specified	✓
Paper quality and colour				
Layout	✓	Not specified	Not specified	Not specified
Readability	Not specified	✓ CMI could be provided at the sixth to eighth grade reading level.	Not specified	Not specified
Guide for user testing	✓	Not specified	The templates were subjected to user testing. Sponsors are encouraged to do user testing. No user testing guide.	✓

5.5 Discussion

The main purpose of the guidelines was to provide guidance on how to ensure that the information contained in medicine leaflets for patients is accessible to and could be understood by those who receive it, so that they could use their medicine safely and appropriately. They were established to guide individuals or organizations (e.g., pharmacies, private vendors, healthcare associations, manufacturers) in developing usable patient information leaflets.[241] However, the detail and information contained in guidelines and regulations varied between the different countries, dependent on their contexts and backgrounds.

In the EU and Australia, the provision of PILs and CMI has been mandatory before the release of prescription medicines, some non-prescription medicines, and some biologicals to the market.[15,245] There was no legal requirement for the manufacturers to produce this in the United States or Thailand.[28,241,246] This could have both advantages and disadvantages.

Advantages of not being required by guidance to provide the manufacturer's information leaflet was that health professionals could choose which information to provide to patients.[247] The regulation was a guide which health professionals and manufacturer can adopt and adapt to suit their medicine and patient. This allows flexibility for creation. Although, manufacturers' guidelines to use for the production of information leaflets were in place, the leaflets still remain substandard.[199,247]

However, compulsory provision of medicine information leaflets was an important step towards improving patient safety. This also assured the reliability of the information provided by the manufacturer, ensuring the information provided was standardised and uniform, and met legal requirements. Restriction of the guidance, however, may cause a reduction in innovation.

With regards to content, there were the same issues and variations between the regulatory authorities' documents. They had a common interest in the following key topics: medicine name, indication, contraindication, precaution, dosage, administration, missed and overdoses, monitoring effectiveness of treatment, drug interaction, side effects information, storage and date of publish/ revision. They all also recommend putting up statements to encourage patients to discuss concerns with their health care providers. However, there were differences in terms of providing all information versus some information e.g. contraindications – all in EU and US, only those considered significant in Australia. This could take into account differences depending on the type of medicine. For prescription medicines, the medicines were selected and dispensed by health care professionals to selected patients, therefore it may not be considered necessary to supply the entire list of contraindication information. On the other hand, these medicines are

likely to carry more risks than OTC medicines, so perhaps more likely to need information on contra-indications. Regarding to OTC medicine, however, all contraindicative information was essential because these medicines could be purchased from patients by themselves. In this case providing only partial information about contraindications could harm the patient.

In term of side effect information, the same recommendation existed for the provision of EU, Australia, and Thailand side-effect information, in that this information should be grouped and prioritised. For example, in the EU, the most serious side effects need to be listed prominently first with clear instructions to the patients on what action to take, and then a list of all other side effects, listed by frequency and starting with the most frequent. In Thailand, the side effects were divided in two groups; must stop the medicine and see the doctor immediately, and do not stop taking the medicine, but must talk with health care provider if the symptoms worsen. However, in the US guidance, there were no requirements to provide an entire list of side effects. Instead it is recommended to include an affirmation that patients do not have a full list of side effects and that patient should ask for more information from their doctor.

From previous studies, the side effect information section was the most frequent interesting information which patients read in PILs and took into account. Despite the guidance on providing side effects information, some patients argued that they felt that PILs raised fears and concerns.[79,84,87,91,95,107,248–250] Some research showed that if people though that the information in the leaflet was not clear, then patients stopped their medicine.[250] Another study proposed that, in order to make informed decisions about medicines, patient leaflets should use a tone for the potential side effect information in the language that engenders less fear while maintaining the information content needed.[251] These results from the research should be taken into account in developing and revising the guidelines.

With regards to layout and design, similar aspects of formatting were included in guidelines between the EU, US, and Thailand, for instance, font size, font-type, line spacing, heading, and emphasising certain points. In Australian guidance, there was a template available that covers all formatting and style issues, and also suggested sentences for CMI. It was subjected to user testing. Therefore, the guidance omitted details of design and layout.

The main suggestion for all guidelines in the construction of sentences was to control the tone, the voice and the phrase. Recommendation in language used was plain language, nonbiased content and active voice phrases. The most distinguishing recommendation was readability, only mentioned in the US guideline, which required that CMI should be provided at sixth to eighth grade reading level. This could help to ensure that patients can comprehend the medicine information provided.

While all guidelines have been drawn up to cover both appearance and content in all aspects, the leaflets then have also been prepared in accordance with well-established guidance, patient satisfaction has, however, not been achieved.

Internationally, studies repeatedly find problems with WMI given to patients (Chapter 3). The survey in the UK (chapter 7) also found that the leaflets were often difficult to comprehend with small font and text size, and contained information that was outdated, basic and general to population rather than specific to individual conditions. There were problems in term of language used, including medical terms. Problems with leaflets have also been reported by the BBC, suggesting that there was too much focus on the potential side-effects of medicines. The benefits of the medicines and mechanism of action information were understated compared with potential harms.[252–254]

In the USA, private vendors create CMI which is expected to be given with the first dispensing of all medicines. However, these leaflets had varying quality.[199] One problem was that manufacturers provided huge amounts of information in the leaflets so that 'all the basics' were covered, primarily to prevent any legal issues.[247] A previous study found that the more information contained in package inserts, the worse patients feel informed. Increasing the amount of content decreased the ability to focus on the information provided, significantly.[255] In contrast, a prior study found that the failure to provide extensive information on contraindications, precautions, and interactions in U.S. CMI had an impact on consequences for safe and effective medication use.[199]

With respect to general public views, studies have shown that people in many countries were dissatisfied with poor format, lack of information patients seek, and language used in medicine leaflets. They had some difficulty in comprehension or understanding related to the language used, technical terms, and the small font size used. They felt that PILs raised fears and concerns.[79,84,87,91,95,107,248] All of these affected the willingness of patients to read the leaflets.[249]

Thus it could be assumed that the guidance provides some recommendations which did not correspond to the satisfaction of patients. The leaflets were held to be not written from the viewpoint of the consumer.[252] In addition, the leaflets were not always helpful in finding, understanding and recalling information they had read. Patients were not motivated to read the instructions in the leaflets and follow them.[24] The guidance may need to be updated and revised.[24]

Apart from preparing leaflets by following the guideline, user testing has also played an important role in testing the performance of the leaflets. It is required by the EU before launching the leaflet

to the market. User-testing is a flexible development tool designed to determine whether the information presented was transmitted correctly to end-users.[15] However, user testing did not improve the quality of the information provided, but indicated where problem areas need to be resolved.[15] Again, even though leaflets were well prepared and tested before they were made available to the general public, most of them didn't satisfy the needs of people.[249] Aforementioned, the quotation from BBC news about the leaflet "They aren't written from a consumer's perspective," reflected what people have been thinking about their leaflet.[252]

A previous study has also revealed that the appearance of the leaflet could attract or distract patients.[247] Creating good design principles to improve readability, understanding and information capability could help to meet and satisfy the patient's needs.[249] The patient involvement in the development of the leaflets must start both with the content and the design. Patient participation could be added up to the standard of user testing in creating regulations or guidelines, as well as templates, which could help regulatory authorities or manufacturers to improve leaflet quality. Furthermore, during the user testing, patients could be tested on their degree of emotional response when reading risk information to allow them to weigh the benefits and risks of their medication.[251] This could lead to more acceptable and patient-centred leaflets.[247]

Furthermore, customized information leaflets on medicine should be considered, although in practice this is difficult to achieve. Leaflets tailored to patient characteristics and requirements would potentially increase efficiency. In previous studies patients have also welcomed the concept of tailored information, preferring information tailored to their condition, age and gender. [75,249]

5.6 Conclusions

All important aspects of medicine information which patients should know were covered in all regulations. In all guidelines, the content and layout of the leaflet were considered in more or less detail. The details provided in each guideline varied between different countries, depending on their circumstances and background.

5.7 Recommendations

In addition, all leaflet guidance in all countries could be updated to ensure adequate standard and appropriate formats by following the results of research studies. All stakeholders involved: regulatory body, manufacturing sector, and general public or patients should be involved in developing and improving the guideline and leaflets for patient. Then, the content, design and layout of available leaflets can be routinely assessed whether they are following the guideline, so that patients are better informed.

Chapter 6 Patient information leaflets and package inserts of Ibuprofen provided in the UK, and Thailand: A comparative assessment

6.1 Introduction

As aforementioned in earlier chapters, the PILs are considered as tools which healthcare professionals usually use to communicate and educate patients about their medicines. The purpose of a PIL is to advise patients about the indication, mode of administration, precautions and side effects of their prescribed medication.[251] Patient information with medicines was introduced in the United Kingdom since 1977.[1] It is, by EU regulations, a legal requirement that all licensed medicines must be provided with a PIL inside the pack. The content of the PILs must include the following headings; 1. What X is and what it is used for, 2. What you need to know before you take X, 3. How to take X, 4. Possible side effects, 5. How to store X, 6. Contents of the pack and other information.[16]

More recently, PILs are becoming increasingly required in a wide variety of healthcare settings worldwide including in developing countries, such as Thailand and other Association of Southeast Asian Nations (ASEAN) and African countries.[24,25]

In Thailand, submission of a SmPC or PIs with or without a PIL is a prerequisite for drug registration with the Thai FDA. Guidelines for leaflet development for drug research and Innovation were introduced in Thailand in 2013,[26,27] with an updated guideline version (minor change) published in 2019.[28] In theory, there is a recommendation for the provision of a Thai PIL with medicines. However in practice, because the provision of PILs in Thailand is optional and they are still voluntarily produced and supplied by pharmaceutical companies, there is a very limited number of PILs available.[25]

In contrast, Thai PIs are compulsory and all medicines must be provided with PIs in the Thai language. Therefore, the leaflet provided with medicines is often a package insert, designed for use by health professionals, rather than a PIL, designed specifically for use by patients.[25] When written information is provided to patients, this is usually in the form of a Thai PI.

Thai guidelines classify leaflets into two main groups; leaflets for the health care professionals and leaflets for patients, so-called PILs. Leaflets for the health care professionals are further subdivided into SmPC, and package PIs.[28]

A Thai PI presents information including: 1. name of the Medicinal Product, 2. name and strength of active ingredient (s), 3. product description (list of excipients), 4. pharmacodynamics / pharmacokinetics, 5. indication, 6. recommended dose, 7. mode of administration, 8. contraindication, 9. warning and precautions, 10. interactions with other medicaments, 11. pregnancy and lactation, 12. undesirable effects, 13. overdose and treatment, 14. storage condition, 15. dosage forms and packaging available, 16. name and address of manufacturer / marketing authorization holder, 17. date of revision of package insert.

The Thai guidelines permit that both the SmPC and PI can be presented in either long or short form. The long and short versions differ in terms of pharmacodynamics and pharmacokinetics properties information, which may be abridged in the short version. Pre-clinical trial data can also be removed from the short form of the SmPC.[28]

For ibuprofen, there are further details which must be included because of its medicinal class; notification issue 55 of Minister of Public Health (MoPH) provides specific requirements for non-selective NSAIDs. This notification was first announced in 1990, then first updated in 2012. The most recent version was announced in 2015. These additional requirements, which are shown in Box 6-1, state that specific warnings must be provided on the label and in the leaflet.[256] These facts include all of the precautions, contraindications, side effects and drug interaction information. The guidelines do not specify whether the leaflet is a PIL, PI or SmPC and therefore all of these documents must contain this information. In this study, these additional requirements will be referred to as the '12 facts' of Ibuprofen.

Box 6-1 specific warnings provided on the label and in the leaflet for NSAIDs

No.	Fact
1	It is contraindicated in patients who have previously exhibited hypersensitivity to the drug or in individuals with the syndrome of asthma urticaria or rhinitis in response to aspirin, or other non-steroidal anti-inflammatory drugs (NSAIDs).
2	It is especially important not to use the drug during third trimester of pregnancy unless specifically directed to do so by a physician.
3	It is contraindicated in patients with active or history of recurrent gastrointestinal bleeding or peptic ulceration.
4	It is contraindicated in patients with severe hepatic failure or renal failure.
5	It is contraindicated in patients with dengue haemorrhagic fever.
6	If rash or cold like symptom occurred after using this drug, stop using it and consult with your doctor immediately.
7	NSAIDs may cause an increased risk of serious gastrointestinal adverse events including bleeding ulceration and perforation of the stomach or intestines.
8	NSAIDs may cause an increased risk of resinous cardiovascular thrombotic events, myocardial infarction and stroke. This risk may increase with high dosage and duration of use.
9	Fluid retention and peripheral oedema have been observed in some patients receiving the drug before the drug should be used with caution in patients with a history of cardiac decompensation or renal function impairment.
10	Caution is advised when the drug is required in hypertension and elderly.
11	The drug may decease platelet aggregation and prolong bleeding time. Because prolonged bleeding effect may be exaggerated in patients with underlying haemostatic defects, it should not be used in suspected patient with dengue haemorrhagic fever or persons with intrinsic coagulation disorders and those on anticoagulant therapy.
12	After using this drug, if the following symptom occur: fever, rash, papule peel off of the skin and tissue such as oral cavity, throat, nose, genital organ, and conjunctivitis. Stop using and consult with you doctor immediately because this may be attributable to Stevens Johnson syndrome.

* These 12 facts about taking Ibuprofen were presented in a collected Thai PI which has an English version.

In the UK, PILs are prepared and provided by the medicine manufacturer by following a standardised template which must consist of the same information. However, despite substantial regulatory efforts to improve readability and comprehensibility, including the requirement for user-testing, the leaflets are still suboptimal and do not meet the needs of patients. A study analysing PILs of frequently prescribed medications reported in 2008 that only very few manufacturers complied with European guidelines; nearly half of PILs gave no information of the possible adverse effects occurring whilst the remainder presented long lists of adverse effects in paragraphs of continuous text.[198] However, a later study found improvement in the presentation of side effect information in European PILs.[200]

Typically PILs that contain long texts are written in small font size with unsuitable design,[257] include difficult medical terms and poorly presented statistical information. This leads to rising patient anxiety of adverse effects and consequently poor decisions and adherence on the medically prescribed treatment[198]

Recent results from a survey of the general public in the UK and Thailand support this finding. (chapter 7 and 8). PILs were often considered difficult to read with small font and text size and contained information that was basic and directed at the general population rather than specific to individual conditions. They also were problematic in terms of the language used, including the use of medical terms which were difficult to understand. Some people recognized that the PILs were written by the manufacturer which, for some people raised doubts about their trustworthiness, while others thought this was a strength. The information written with technical terms in the leaflet made some feel worried.

Similar findings have been reported in a large number of studies where people in many countries were dissatisfied with the poor format and language used in medicine leaflets (Chapter 3). Comprehension of technical terms, and the small font size used within leaflets were common issues and PILs were highlighted as potentially raising patients fears and concerns.[79,84,87,91,95,107,248] The quality of PILs could be improved by having critical assessment of factual and visual aspects, and consideration of key linguistic features.[258] Leaflet evaluation is still needed.

Ibuprofen is now widely used in many countries, often as a first line treatment for the relief of symptoms of pain, inflammation and fever at both prescription as well as non-prescription dosage.[259] It can also be used to relieve headaches, rheumatic and muscular pain, backache, dental pain, and neuralgia. It can also be used to reduce fever and relieve the symptoms of colds and flu. PILs for Ibuprofen, a non-steroidal anti-inflammatory drug (NSAID), were selected for this study because ibuprofen is frequently used for relief of pain and inflammation by Thai patients, and can be dispensed by a pharmacist with or without a prescription. Additionally, one-third of major cause of Adverse Drug Events which were reported to the Health Product Vigilance Centre between 1984 and 2019 in Thailand were attributed to Ibuprofen.[191,260] In the UK, Ibuprofen is used without a prescription and can be purchased directly from retail outlets or pharmacies.

A critical evaluation and comparison PILs of Ibuprofen between the UK, where medicine information systems are well established, and all the various medicine leaflets and Thailand where the system is developing, could therefore be useful to both countries in term of bench-marking, and future improvement in PILs development.

The comparative assessment was conducted in order to evaluate the appropriateness of layout and design, readability, the regulatory compliance of Ibuprofen PILs in both countries, and the quality of the information provided.

6.2 Aim and objectives

This study aimed to evaluate the quality of a sample of UK PILs and Thai PIs of Ibuprofen provided in the UK and Thailand.

6.2.1 Objectives:

1. To use Baker Able Leaflet Design (BALD) criteria to evaluate the layout and design of a sample of UK PILs and Thai PIs.
2. To assess the readability of the samples of UK PILs and Thai PIs by using FRE and FKGL Flesch Reading Ease score and Flesch-Kincaid Grade Level, and Text Readability Checker for Thai Documents programme (TRC4Thai), respectively.
3. To scrutinize provision compliance of UK PILs against relevant EU, and Thai PILs regulatory standards, and Thai PIs against Thai PILs and Thai PIs regulatory standards.
4. To use US Keystone Criteria to assess the overall quality of the contents contained within all collected leaflets.

6.3 Methods

6.3.1 Layout and design evaluation

The BALD criteria were used for assessing the design of the leaflet. The BALD is a validated tool which consists of 16 criteria used to rate the design and layout of leaflets on a rating scale with a total maximum score of 32.[261,262] The 16 criteria cover the important aspects of leaflets. These are then weighted selectively to reflect the relative contribution of each to the overall design. The scores are based on the length of the line, distance between the lines, letter font size, graphics used, percent of white space, and paper quality. The leaflet which achieve the maximum score must be written in lines that are 50-89 mm long. The separation between the lines should be more than 2.8 mm. The paragraph ideally should be unjustified and the information printed with Serif typeface, and a font size of at least 12 points. The first line should be indented. The titles (headings) should be lower case and italics should not be used. The tone of information should be positive advice ('Do' instead of 'Do not'). The headings should stand out from the body of the text. Numbers should all be Arabic. There should be a maximum of one box containing text. Words cannot be replaced by pictures, although use of pictures should be considered where possible. Use of four different colours is recommended. White space around the text must account for more than 40% of total paper. Ideally the thickness of the paper should be more than 90 gsm.[262] These criteria and the associated scoring system are provided in Table 6-1

Table 6-1 The Baker Able Leaflet Design (BALD) assessment form©

Name of CPI:	**Value**			
Design characteristics	**3 points**	**2 points**	**1 point**	**0 points**
1. Lines 50-89 mm long			Yes (Y)	No (N)
2. Separation between lines	> 2.8 mm	2.2-2.8 mm		<2.2 mm
3. Lines unjustified			Yes (Y)	No (N)
4. Serif typeface		Yes (Y)		No (N)
5. Type size	≥ 12 points	10-11 point	9 points	< 9 points
6. First line indented			Yes (Y)	No (N)
7. Titles (headings) lower case			Yes (Y)	No (N)
8. Italics		0 words	1-3 words	≥4 words
9. Positive advice ('Do' instead of 'Do not')		General positive		Negative common
10. Headings stand out		Yes (Y)		No (N)
11. Number all Arabic			Yes (Y)	No (N)
12. Boxed text			0 -1 box	> 1 boxes
13. Picture (not including cover picture)	Words could not replace	In between	In between	non or superfluous
14. Number of colours	4	3	2	1
15. White space (% of page area, e.g. cm^2)	> 40%	30-39%	20-29%	<20%
16. Paper quality	Thick (> 90 gsm*)	Average (75-90 gsm)		Thin (<75 gsm)

*gsm - grams per square metre. Standard bond paper or photocopying paper is 80 gsm.

6.3.2 Readability assessment

With regards to readability assessment, there are several standard tests such as SMOG, FOG, the Fry Readability Formula and the Flesch Reading Ease Index, which estimates reading grade level for the written educational materials.[263] The Flesch Reading Ease FRE Index and Flesch-Kincaid Grade Level FKGL (FKGL) were chosen for this study.

The Flesch Reading Ease (FRE) score is a tool for calculating the approximate reading level of English-language texts. The results are based on the structure of the English language. The reading ease scores on FRE scale are graded from 0 to 100. If the score of a written text is less than 60, the document is considered to be difficult to read by the general public. The ideal PIL should have a readability score of more than 80.[261] When calculating the Flesch readability score, both the length of the sentence and the length of the words inside the sentence are counted.[264] The Flesch-Kincaid Grade Level (FKGL) readability score examines and ranks texts on a grade-school level in the United States, based on the average number of syllables per word and words per sentence. The FRE and FKGL formulas are commonly used and available in Microsoft word.[261] Therefore, the leaflets in this study were evaluated their readability by FRE and FKGL. Readability test were conducted on each PIL to assess readability with FRE score (Table 6-2) and FKGL. The text was analysed by using Microsoft Word Office software. To calculate FRE, FKGL using the computer, the text of the PIL should be typed in a Word document, and then using the tool bar click on readability, the calculated readability scores of the document appear on the screen.

Table 6-2 Flesch reading ease Scores

Score	School level	Notes
100.0–90.0	5th grade	Very easy to read. Easily understood by an average 11-year-old student.
90.0–80.0	6th grade	Easy to read. Conversational English for consumers.
80.0–70.0	7th grade	Fairly easy to read.
70.0–60.0	8th & 9th grade	Plain English. Easily understood by 13- to 15-year-old students.
60.0–50.0	10th to 12th grade	Fairly difficult to read.
50.0–30.0	College	Difficult to read.
30.0–10.0	College graduate	Very difficult to read. Best understood by university graduates.
10.0–0.0	Professional	Extremely difficult to read. Best understood by university graduates.

For Thai language, the one and only computer programme which can be used for evaluating the difficulty of the language in a document is TRC4Thai. The programme works by assessing extracted loanwords to evaluate the readability of the Thai texts. [265,266] This tool was, therefore, used to evaluate Thai leaflets. The readability is determined by using the programme to compare the documents of interest. The test measures readability by comparing at least two sentences. This means that there is no independent score for each text, but by comparing one text to another the comparative difficulty of a document with another document or group of documents can be evaluated. The different sentences were pasted into the programme, then their degree of readability classified by comparing others pasted in at the same time. The assumption of Thai readability was that the degree of readability depended on the number of loanwords, Pali, Sanskrit, and orthography. The loanword is a word adopted from one language and incorporated into another language without translation. For example, in English language, loanwords were borrowed from French, Greek, Spanish, and Italian. In Thai, loanwords are mainly borrowed from Pali, Sanskrit, Khmer, Chinese, and English. Generally, original Thai words are one syllable and have a complete meaning. The loanwords in the Thai language were more sophisticated than the original Thai word in terms of writing and meaning. Therefore, the more of these words there are in a sentence, the more difficult it is to read. All Thai leaflets in this study were examined their readability by TRC4Thai. The readability is classified as one of five levels (very easy (1), easy (2), neutral (3), difficult (4), very difficult (5)) depending on the number of loanwords it contains.[265]

The texts within each of the following sections: indications, precautions, and side effects, from the different Thai PIs were applied to the TRC4Thai programme. As the Thai readability was tested by comparing leaflets to each other, it was not applicable to assess the text relating to the 12 precautions and side effect messages suggested by the Thai FDA, which were included in all Thai Ibuprofen leaflets.

6.3.3 Regulation compliance

There are two core guidelines related to producing a UK PIL. First, the document which provided the template of information provided is the QRD template v10.2 (revised on 1/01/2021).[16] the second document which guides about design and layout of the PILs is the Guideline on the Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use.[15]

In Thailand, there are two main documents related to Thai PI for Ibuprofen. The first document was the guideline for patient information leaflet development which introduced in 2013.[27] Then, the updated guideline version was published in 2019.[28] The second was the notification issue 55 of Minister of Public Health (MoPH) provides specific requirements for non-selective NSAIDs.[256]

With regards to the regulatory compliance, UK PILs were compared with both EU[15,16] and Thai PIL regulations.[28] All Thai PIs were evaluated against of Thai PIs and PILs regulatory standards including issue 55 of MoPH guidance.[28,256] Thai leaflets and UK PILs were assessed for compliance with each item on the checklist and scored as presence (1) or absence (0).

6.3.4 *Content evaluation*

The quality of the information provided was evaluated based on the U.S. Keystone Criteria (Table 6-3) related to the structure and content of leaflets and used by Svarstad and colleagues. These criteria were developed through a structured process of consensus by a large number of stakeholders.[199,267]

The checklist was adapted from two previous studies. The eight criteria referred to the "Keystone Consensus Criteria" were used with the relevant sub-criteria.[267] These criteria required that the leaflet include the following clinical content: (1) drug names and indications for use; (2) contraindications and what to do, if applicable; (3) specific directions for using, monitoring, and getting the maximum benefit from the medication; (4) specific precautions on how to avoid harm while using the drug; and (5) symptoms of frequent or serious adverse reactions and actions to take if they occur. The leaflet must also (6) include general information, a disclaimer, and encouragement to ask questions; (7) be scientifically accurate, unbiased, and up to date; and (8) be written in a format that is legible and comprehensible to the consumer. The sub-criterion for evaluating drug information quality specific to Ibuprofen was adopted into the main criteria.[268] Criteria which were duplicated or overlapped with other aspects of the evaluation were excluded.

Table 6-3 U.S. Keystone Criteria

No	U.S. Keystone Criteria
1	Include drug names and indications for use
2	Include contraindications and what to do if applicable
3	Include specific directions about how to use, monitor, and get most benefit
4	Include specific precautions and how to avoid harm while using
5	Include symptoms of serious or frequent adverse reactions and what to do
6	Include general information, disclaimer, and encouragement to ask questions
7	Be scientifically accurate, unbiased, and up to date
8	Be written in a format that is legible and comprehensible to consumer

6.3.5 Study Design:

This study was a cross-sectional study carried out by collecting the available leaflets for Ibuprofen, and evaluating their features in several aspects.

6.3.6 Settings:

The study was conducted in Songkhla, Thailand and Canterbury, England between November 2019 until December 2020.

6.3.7 Instruments*:*

1. Baker Able Leaflet Design (BALD) Criteria
2. Word for Microsoft programme[269], and Text Readability Checker for Thai Documents programme (TRC4Thai).[270]
3. EU and Thai PI and PIL guideline.
4. U.S. Keystone Criteria

6.3.8 Sampling

The Thai PIs and UK PILs for ibuprofen produced by different manufacturers were collected from community pharmacies and/or retail outlets (UK) in the urban areas of Songkhla, Thailand, and Canterbury, UK. Convenience sampling of community pharmacies/ retail outlets were carried out to obtain the leaflets by purchasing a pack of ibuprofen.

6.3.9 Procedures:

1. All collected leaflets were scanned, and kept in a computer file.
2. The BALD score was used to categorise the leaflets based on their design and layout quality. The length of the line, the space between the lines, the font size, and the white space were all measured with a standard ruler. A thickness micrometre was used to measure paper thickness (millimetres), which was then converted to paperweight (grams/square metre (gsm)).[271] As a result, the total scores were computed.
3. The Microsoft Word for Mac version 16.49 programme was used to calculate the FRE and FKGL readability score. The calculation began with the preparation of the texts to be computed, then selecting preferences from the Word menu. In the Authoring and Proofreading, “Tools” section was clicked. Then, “Spelling & Grammar” were pointed on the “Tools” menu and select “Spelling & Grammar”. After Word has finished checking spelling and grammar, it displays information about the document's reading level as a readability statistics box.

4. The TRC4Thai programme was used to assess the readability of Thai texts. The group of texts was run once in the TRC4Thai programme, followed by a text-ordering click. When comparing indication information, for example, all indication information from each Thai PI was applied once in separate boxes in the programme. After applying the selected texts from the Thai PIs to the TRC4Thai programme, the programme extracted and counted the number of loanwords, and the texts were classified by their level of difficulty in readability. Then the difficulty level was ordered, and the score of each information was displayed.
5. With regards to the regulatory compliance, again, all UK PILs were compared with both EU and Thai PIL regulations. All Thai PIs were evaluated against Thai PIs and PILs regulatory standards including issue 55 of MoPH guidance. The elements of all guidance were extracted. The assessment form was created using Microsoft Excel. Thai leaflets and UK PILs were scored as present (1) or absent for compliance with each item on the checklist (0). The total score was then computed.
6. The US keystone was used to assess the content of the leaflets. The assessment form was constructed using Microsoft Excel. The Thai leaflets and UK PILs were scored as present (1) or absent (0) for compliance with each item on the checklist. The total score was then computed.

6.3.10 Ethical approval

There were no ethical concerns raised as a result of the lack of human participation in this study. Therefore, the Ethical approval process was bypassed.

6.4 Results

6.4.1. General information

In the UK, 18 different PILs were collected from retail shops such as Boots, Tesco, and Wilko. Apart from pain relief, and relieve the symptoms of colds and flu, the information on the outer packaging indicated that the medicine was for relief of migraine or period pain. The information written on UK PILs was mostly in two columns printed with black or dark blue typeface on white colour paper. The leaflets varied in size and were between 12x19 to 29.5 x19 cm. (228.0 - 560.5 $cm.^2$). All the leaflets divided their text into the sections which are required by EU regulation which was mentioned in the introduction of this chapter.

In Thailand, Thai PILs are not generally provided with Ibuprofen. Therefore, the package inserts (PIs) were collected instead. Eighteen different Thai PIs were collected from 20 community

pharmacies in Hatyai district, Songkhla province, Thailand. These would have been supplied with either strips of the medicine in an envelope dispensed by the Pharmacy, or in the original pack. Where, the original pack was supplied the information on the outer packaging indicated that the medicine was for pain and inflammation, migraine and period pain relief. Even though some Thai PIs were the same trade name and written by the same drug company, they were all included into the study because their content was slightly different, and not all included the date of publication. Therefore, in real practice, patients could receive different versions of the leaflet when purchasing the same product.

Similarly to PILs in the UK, the Thai PIs contained information which was generally separated into two columns. The information was normally printed with black or dark blue on white paper, but one was printed in pink. The leaflets were between 8 x 10 – 21 x 29.5 cm. (80 - 619.5 cm^2.)

While, the UK PILs contained the similar pattern of information provided, the actual amount of information contained in Thai PIs was considerably different. Therefore, in this study, the collected Thai PIs (n=18) were classified into three different types of information provided; full information version (n=1), short information version (n=8), and very short information version (n=9). These were as follows:

(i) The full version of Thai PIs contained all of the information required by the regulations which was mentioned in the introduction, and the 12 facts of taking Ibuprofen (Box 6-1).

(ii) The short version contained most of the same information as the full version and the 12 facts of taking Ibuprofen (Box 6-1). However, they either excluded or shortened the pharmacodynamics and pharmacokinetics properties information.

(iii) The very short version included the name of the medicine product, indication, other information and the 12 facts about taking Ibuprofen. The amount of information in the very short version was much less than in the short and full versions.

Eleven of the Thai PIs contained both Thai and English version, while eight Thai PIs were only written in Thai language. The general information of UK PILs and Thai PIs are shown in Table 6-4 and Table 6-5, respectively. The headings provided in each of the Thai PIs are shown in Table 6-6.

Table 6-4 General information of the UK Leaflets

Leaflet code	Strength	Stated Indication	Manufacturer
UK01	200	Pain relief	Boots
UK02	342	Migraine relief	Wrafton Laboratosies
UK03	200	Pain relief	Pfizer
UK04	200	Pain relief	Galpharm
UK05	342	Pain relief	Boots
UK06	200	Period pain relief	Reckitt Benckiser Healthcare international
UK07	200	Pain relief	Reckitt Benckiser Healthcare international
UK08	342	Pain relief	Wrafton Laboratosies
UK09	200	Pain relief	Wave Pharma
UK10	300	Pain relief	Boots
UK11	200	Pain relief	Patheon Softgels B.V.
UK12	342	Pain relief	Wrafton Laboratosies
UK13	342	Migraine relief	Wrafton Laboratosies
UK14	200	Migraine relief	Reckitt Benckiser Healthcare international
UK15	200	pain relief	Relonchem limited
UK16	200	Pain relief	Reckitt Benckiser Healthcare international
UK17	200	Pain relief	Reckitt Benckiser Healthcare international
UK18	200	pain relief	Reckitt Benckiser Healthcare international

Table 6-5 General information of the Thai Leaflets

Leaflet code	Strength	Stated Indication	Manufacturer	Language	Version
TH01	200,400	pain relief	Osoth Inter Labotarories Co., Ltd.	Thai, English	Short
TH02	400,600	Pain relief	Greaterpharma	Thai	Very short
TH03	400	Pain relief	Asian pharmaceutical	Thai	Short
TH04	200,400	pain relief	Pond Chemical Company Limited	Thai, English	Very short
TH05	400	pain relief	Boots	Thai	Very short
TH06	200,400, 600	Pain relief	Avance Pharmaceutical Manufacturing Co., Ltd	Thai, English	Very short
TH07	200,400, 600	Pain relief	Avance Pharmaceutical Manufacturing Co., Ltd	Thai, English	Very short
TH08	400	pain relief	MEGA life science	Thai	Short
TH09	200,400	pain relief	Geltec Private Limited	Thai, English	Short
TH10	600	Pain relief	Seven Stars Pharmaceutical Co., Ltd	Thai, English	Full
TH11	200,400	Pain relief	Thai Nakorn Patana Co.,Lth	Thai, English	Very short
TH12	200,400	pain relief	Thai Nakorn Patana Co.,Lth	Thai, English	Very short
TH13	400	pain relief	Thai Nakorn Patana Co.,Lth	Thai, English	Very short
TH14	200,400	Pain relief	President Inter Pharma Co.,Ltd	Thai, English	Short
TH15	200,400	Pain relief	Zambon group S.p.A Vicenza (Italy)	Thai, English	Very short
TH16	400	pain relief	T.O. Chemical	Thai	Short
TH17	400	Pain relief	Softgel Healthcare Private Ltd	Thai	Short
TH18	400	pain relief	Patheon Softgels B.V.	Thai	Short

Table 6-6 Headings and information shown in Thai PIs

Criteria (Thai)	TH01	TH02	TH03	TH04	TH05	TH06	TH07	TH08	TH09	TH10	TH11	TH12	TH13	TH14	TH15	TH16	TH17	TH18
1. Name of the medicine product	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2. Qualitative and Quantitative composition	1	1	1	0	1	0	0	1	1	1	1	1	0	1	1	0	1	1
3. List of excipients	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
4. Pharmacodynamics properties	0	0	1	0	0	0	0	1	1	1	0	0	0	1	0	1	1	1
5. Pharmacokinetics properties	1	0	1	0	0	0	0	1	1	1	0	0	0	1	0	1	1	1
6. Indication	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7. Dosage	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8. Administration	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9. Contraindication	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10. Precaution	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11. Drug interaction	1	0	1	0	0	0	0	1	1	1	0	0	0	1	1	1	1	1
12.Pregnancy,breast-feeding, and fertility	1	0	1	0	0	0	0	1	1	1	0	0	0	1	0	0	1	1

Criteria (Thai)	TH01	TH02	TH03	TH04	TH05	TH06	TH07	TH08	TH09	TH10	TH11	TH12	TH13	TH14	TH15	TH16	TH17	TH18
13. Possible side effects	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14. Overdose	1	0	1	0	0	0	0	1	1	1	0	0	0	1	0	1	1	1
15. Storage conditions	1	1	1	1	1	1	1	1	1	1	0	0	0	1	0	1	1	1
16. Dosage form, and Contents of the pack and other information	1	0	1	0	0	0	0	1	1	1	0	0	0	1	0	0	1	1
17. Name of manufacturer, importer, or Marketing Authorization Holder; MAH	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
18. The date that the PIs was published	1	0	1	0	0	1	0	1	1	1	0	0	0	0	0	0	1	1
19. 12 facts of taking Ibuprofen	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1

6.4.2. Assessing layout and design of the leaflets by BALD criteria.

With regard to UK PILs, the maximum BALD score was 13 (n=2) while the minimum was 9 (n=1). Most leaflets scored either 10 (n=6) or 11 (n=5). Some BALD criteria were achieved by most UK PILs. For example, 16 of 18 UK PILs were written in lines that were between 50-89 mm long. All of them were written using unjustified lines without any italic typeface or letters. All headings stood out in all UK PILs (n=18), and all of the numbers used were Arabic (n=18). Not more than one boxed text was used in all UK PILs. However, there were 10 of the 18 leaflets having only 20-29% (n=7) or less than 20% (n =3) of white space. Only eight UK PILs kept white space to 30-39% (n=7) of the page and the ideal target of or 40% or more was achieved by a single example (n=1). There were 11 UK PILs where the titles (heading) were typed in lower case.

For all UK PILs, (n=18) the separation between the lines of text was less than 2.2 mm and they were all (n=18) printed in non-Serif typeface. Twelve UK PILs were written with 9-point font size, and only four included 10-11-point font size. The first line was indented in only one UK PIL. The information and advice in all UK PILs (n=18) was written in a negative rather than the recommended positive tone, and this was especially relevant to the precaution section. None of the UK PILs contained pictures. Either black or dark blue ink was chosen to print in all UK PILs (n=18), therefore only one colour was used. Low paper quality (less than 75 gsm) was utilised in all examples reviewed (n=18). The assessment of quality of design and layout according to the total BALD score with the UK leaflet are shown in Table 6-7. The number of UK leaflets that achieved specific BALD criteria are shown in Table 6-9.

Table 6-7 BALD scores for the UK PILs.

Leaflet code	BALD score (Max Score = 32)
UK01	12
UK02	11
UK03	10
UK04	11
UK05	12
UK06	11
UK07	10
UK08	12
UK09	11
UK10	10
UK11	10
UK12	10
UK13	10
UK14	13
UK15	11
UK16	9
UK17	12
UK18	13

With regard to Thai PIs much greater variability in the BALD score was observed with a maximum of 16 (n=1), and a minimum of 7 (n=2). Most leaflets scored either 8 (n=5) or 9 (n=5). The Thai language usually contains only one size of letters without lower or uppercase. Therefore, the BALD assessment relating to using titles (headings) in lower case was not applicable. Furthermore, although some Thai font claims to have been adapted from Serif typeface, a serif which is a small line or stroke regularly attached to the end of a larger stroke in a letter or symbol within a particular font or family of fonts is not obvious within Thai letters. Therefore, serif typeface criteria for Thai PIs was also graded as non-applicable, and the total maximum possible BALD score for Thai PIs was 29.

Fourteen leaflets were written in lines 50-89 mm long, while four leaflets were typed in lines more than 90 mm long. No italics were found in any of the Thai leaflets (n=18). All headings stood out in all leaflets (n=18). They were separately typed from the content, but some of them were written in relatively small characters. The numbers used were all Arabic (n=18). No more than

one boxed text was present in all leaflets (n=18). Eight of the totals were printed with adjusted-line formats.

With regard to failed criteria, there were 13 of 18 leaflets written with a space between the line of less than 2.2 mm. Only four and one were set with separation of text between the lines between 2.2 - 2.8 mm, and more than 2.8 mm, respectively. Most leaflets (n=15) were printed with less than 9-point type size. One leaflet was typed with font size of 9-point and two with 10-11-point font size. A non-indented format for the first line of the sections was used in most leaflets. Because the Thai PIs were written for health professionals, written positive advice was not considered to be an important issue. Therefore, positive advice was not used in any of the leaflets (n=18). No pictures were included in any of the leaflets (n = 18). Whilst leaflets were written in black, pink or dark-blue each was written in only one colour.

Most leaflets (n=8) were set with white space covering only 20-29%. Three contained less than 20% of white space, four between 30-39% and only three more than 40%. All leaflets had been written on low paper quality (< 75 gsm). The assessment of quality of design and layout according to the BALD score with Thai leaflet are shown in Table 6-8. The number of Thai leaflets that achieved the various BALD criteria are shown in Table 6-9.

Table 6-8 BALD scores for the Thai PILs

Leaflet code	BALD score (Max Score = 29)
TH01	8
TH02	9
TH03	9
Th04	11
TH05	8
TH06	9
TH07	8
TH08	8
TH09	7
TH10	9
TH11	7
TH12	10
TH13	9
TH14	8
TH15	14
TH16	13
TH17	10
TH18	16

Table 6-9 Number of leaflets which achieved individual BALD criteria.

	Criteria	Score	Number of UK leaflets passed the criteria (n=18)	Number of Thai leaflets passed the criteria (n=18)
1	Line 50-89 mm long	1 (YES)	16	14
		0 (NO)	2	4
2	Separation between lines	3 (>2.8 mm)	0	1
		2 (2.2-2.8 mm)	0	4
		0 (<2.2 mm)	18	13
3	Line Unjustified	1 (YES)	18	8
		0 (NO)	0	10
4	Serif typeface	2 (YES)	0	
		0 (NO)	18	N/A
5	Type size	3 (≥ 12 point)	0	0
		2 (10-11 point)	4	2
		1 (9 point)	12	1
		0 (< 9 point)	2	15
6	First line indented	1 (YES)	1	2
		0 (NO)	17	16
7	Titles (headings) lower case	1 (YES)	11	
		0 (NO)	7	N/A
8	Italics	2 (0 words)	18	18
		1 (1-3 words)	0	0
		0 (≥ 4 words)	0	0
9	Positive advice ('Do' instead of 'Do not')	2 (General positive)	0	0
		0 (Negative)	18	18
10	Headings stand out	2 (YES)	18	18
		0 (NO)	0	0
11	Number all Arabic	1 (YES)	18	18
		0 (NO)	0	0
12	Boxed text	1 (0-1 boxes)	18	18
		0 (> 1 boxes)	0	0
13	Picture (not including cover picture)	3 (Words could not replace)	0	0
		2 (In between)	0	0
		1 (In between)	0	0
		0 (non or superfluous)	18	18
14	Number of colours	3 (4colours)	0	0
		2 (3colours)	0	0
		1 (2colours)	0	0
		0 (1 colour)	18	18
15	White space (% of page area, e.g. cm2)	3 (>40%)	1	3
		2 (30-39%)	7	4
		1 (20-29%)	7	8
		0 (<20%)	3	3
16	Paper quality	3 (Thick > 90 gsm*)	0	0
		2 (75-90 gsm)	0	0
		0 (<75 gsm)	18	18

6.4.3. Readability evaluation

Readability of a sample of PILs of Ibuprofen in the UK were evaluated with FRE Flesch Evaluating Reading Ease score and the FKGL, and Thai PIs were evaluated with TRC4Thai.

All of the 18 UK PILs were assessed with respect to their readability. From FRE Flesch Reading Ease scores, a document scoring 50.0 – 30.0 is suitable for individuals with college level qualifications while documents scoring 60.0 – 50.0 are suitable for those in 10^{th} to 12^{th} grade and are therefore fairly difficult to read. The FRE Flesch Reading Ease score of the UK PILs ranged from 44.6 to 57.7, with a median score of 52.2. This means that the documents are difficult to read. The percentage of passive sentences ranged between 6.4% and 19.6%. The FKGL Flesch–Kincaid Grade Levels ranged from 8.7 to 10.6, with a median score of 9.6. The FRE Flesch Reading Ease scores and FKGL are shown in Table 6-10.

Table 6-10 Flesch Reading Ease scores and Flesch–Kincaid Grade Levels of UK PILs

Leaflet code	Flesch Reading Ease Score	Flesch-Kincaid Grade	Passive Sentences (%)
UK01	52.9	9.8	19.6
UK02	51.7	9.6	12.3
UK03	44.6	10.6	12.5
UK04	51.4	9.6	9.5
UK05	55.9	9.0	14.0
UK06	52.0	9.6	11.2
UK07	50.9	10.1	12.1
UK08	51.6	9.7	11.1
UK09	50.0	9.5	6.4
UK10	55.3	9.4	12.1
UK11	52.3	9.7	11.4
UK12	50.8	10.0	11.4
UK13	53.1	9.6	12.5
UK14	54.0	9.6	13.4
UK15	54.4	9.3	10.1
UK16	53.3	9.4	13.6
UK17	48.9	10.2	13.2
UK18	57.7	8.7	12.6

For Thai PI readability, the indication section was defined as very difficult and difficult to read in seven and four leaflets, respectively. Regarding precautions, there were four leaflets categorised as very difficult to read. Five leaflets contained side effect information that was classified as very difficult to read. The results of the readability assessment for Thai PIs are shown in Table 6-11. The number of Thai PIs in each level of readability is shown in Table 6-12.

Table 6-11 Results of readability test for Thai PIs

	Readability level*		
Leaflet code	Indication score	Precaution score	Side effects score
TH 01	5	1	5
TH 02	5	3	n/a
TH 03	1	5	5
TH 04	4	n/a	4
TH 05	5	4	n/a
TH 06	n/a	n/a	n/a
TH 07	n/a	n/a	n/a
TH 08	3	2	5
TH 09	5	2	1
TH 10	4	2	5
TH 11	2	n/a	n/a
TH 12	2	n/a	n/a
TH 13	5	n/a	n/a
TH 14	4	3	1
TH 15	5	5	3
TH 16	5	5	1
TH 17	3	5	5
TH 18	4	2	2

* Readability level 5 = very difficult, 4 difficult, 3= neutral, 2= easy, 1 very easy, n/a = not applicable

Table 6-12 Number of Thai PIs in each level.

Readability scale	Number of Thai PIs (n=18)		
	Indication	Precautions	Side effect
Very easy	1	1	3
Easy	2	4	1
Neutral	2	2	1
Difficult	4	1	1
Very difficult	7	4	5
n/a	2	6	7

6.4.4. Investigating the UK PILs against EU regulation

All of the UK ibuprofen PILs complied with EU regulation in terms of content. However, layout and design were slightly varied. The seven UK PILs used all capital letters for the main topics e.g. “WHAT THIS MEDICINE IS FOR?”. None of the leaflets achieved a space between lines of text of at least 3 mm. The paper used for all leaflets were not sufficiently thick to reduce transparency. Symbols and pictograms were not printed in any of the leaflets. The requirement that a multi-lingual leaflet should provide a clear demarcation between the different languages used was not applicable. The results of the analysis of the UK PILs against the EU regulations are shown in Table 6-13.

Table 6-13 Comparison of the UK PILs against the EU regulations

	Criteria	**Number of UK leaflets passed the criteria (n=18)**
Design	1. > 8 point as measured in font Time new Roman	17
	2. Space between lines of at least 3 mm.	0
	2. Consideration Using different sizes or enable key information to stand out	18
	3. Don't use widespread use of capitals	11
	4. Don't use italics and underlining	18
	5. Don't use justified	18
	6. Space between one line and the next should be at least 1.5 times the space between words on a line.	11
	7. Where a multi- lingual leaflet is proposed there should be a clear demarcation between the different languages used (n/a)	(n/a)
	8. bold type face for the heading or a different colour,	18
	9. Same level headings should appear consistently (numbering, bulleting, colour, indentation, font and size) to aid the reader.	18
	10. No more than 2 levels when multiple levels of heading	18
	11. A different type size or colour is one way of making headings or other important information clearly recognisable.	18
	12. Long sentences should not be used.	18
	13. starting with the highest frequency, is recommended/ Not setting side effects by organ/system/class	16
	14. an active style should be used	17
	15. Instructions should come first, followed by the reasoning	18
	16. Similarly scientific symbols (e.g. > or <) are not well understood and should not be used.// Abbreviations use	18
	17. Medical terms should be translated into language which patients can understand.	18
	18. The paper is sufficiently thick to reduce transparency // Use the uncoated paper	0
	19. Make sure that when the leaflet is folded the creases do not interfere with the readability of the information.	18
	20. Symbols and pictograms can be useful provided the meaning of the symbol is clear and the size of the graphic makes it easily legible.	(n/a)
Content	21. The name, the active substance(s), the pharmaceutical form, strength of the product should be stated.	18
	22. Therapeutic indications	18
	23. Information necessary before taking the medicine	18
	24. Dosage	18
	25.Warnings and precautions	18
	26.Possible side effects	18
	27.Children <and adolescents>	18
	28.Pregnancy <and> <,> breast-feeding <and fertility>	18
	29.Storage conditions	18
	30 Contents of the pack and other information	18
	31. Name and address of the Marketing Authorisation Holder (MAH) and manufacturer	18

6.4.5. Investigating the UK PILs and Thai PIs against Thai PILs regulation

Most UK PILs and Thai PIs achieved the basic criteria: for example; presenting the medicine name, dosage form, trade name, indication, dosage, contraindication, and precaution. They all provided the side effect information. The name/ logo of the manufacturer, importer, or Marketing Authorization Holder was also present.

With regards to content and language used, all UK PILs and Thai PIs were written in English and Thai language, respectively. However, all the UK PILs were written in plain language rather than the Thai PIs which were written in formal language. None of the UK PILs and seven Thai PIs gave information about the strength using the Metric system with no abbreviation 200, 400 milligrams. All UK PILs and nine Thai PIs provided the details of all ingredients (qualitative and quantitative composition). Only two Thai PIs showed the salt name combined with the active ingredient. There were nine UK PILs and one Thai PIs that showed information on what to do when a patient missed a dose, while the information about over dosage and signs and symptoms of over-dosage were described in all the UK PILs and nine of Thai PIs. All the UK PILs and Thai PIs informed patients about how they should take care when taking Ibuprofen, for example by including statements such as: “to reduce the chance of side effects, use the lowest effective dose for the shortest possible time”, “NSAIDs may cause an increased risk of serious gastrointestinal adverse events including bleeding ulceration and peroration of the stomach or intestines”. Only four Thai PIs suggested how to monitor the drug for efficacy and when patients should see their doctor if their symptoms did not improve. Only nine Thai PIs recorded the date of leaflet revision.

With respect to the layout and design, most UK PILs (18) and Thai PIs (17/18) were printed using contrasting colours between the text (black or dark blue) and the paper colour (white). Only one Thai PI was used with soft pink text printed on the white paper. However, other criteria showed greater deviation from the BALD criteria. The Thai PILs criteria recommend that the medicine name strength, dosage form, and trade name are printed with 14 points bold centred. This was met for 11 of 18 the UK PILs and none of Thai PIs. The main topic should also be written with 14 points bold centred in the box; only two the UK PILs and none of the Thai PIs achieved this criterion. Only four UK PILs and one Thai PI were generally written with the same size of Tahoma 11 font. Five Thai PIs were designed to keep the space between lines and the next to be at least equal to a newspaper line (>2.2 mm), but none of the UK PILs were more than 2.2 mm. That the information should be written within 3 columns on A4 paper and landscape orientation was not applied to leaflets (PILs or PIs) from both countries. The disclaimer statement “summary and does not contain all information, ask doctor or pharmacist for more information." was not compulsory for either the UK PILs and Thai PIs and therefore unsurprisingly none of these included this

statement. A summary of how the UK PILs and Thai PIs measured up against the Thai PILs regulations is shown in Table 6-14.

Table 6-14 Results of UK PILs and Thai PIs against Thai PILs regulation

Criteria	Number of UK leaflets passed the criteria (n=18)	Number of Thai leaflets passed the criteria (n=18)
1. Thai language (English for UK PILs): short sentences and paragraphs, common words	18	18
2. Number all Arabic	18	18
3. Use plain language e.g. "take, swallow"	18	0
4. Text contrast with the paper colour	18	17
5. Tahoma 11 (General)	4	1
6. line: easy to read/ Space between one line and the next should be at least equal a newspaper line (>2.2 mm US)	0	5
7. 3 columns (suggestion)	0	1
8. A4 paper with Landscape	0	0
9. Introduction: 14 points bold centre in the box for medicine name, strength, dosage form, trade name	11	0
10. Main topic: 14 points bold centre in the box for topic	2	0
11. Subtopic: bold, Align left	18	18
12. Medicine name, dosage form, trade name	18	18
12.1 strength (using Metric system with no abbreviation e.g. 200,400 milligram)	0	7
13. What is in the medicine? (+ salt)	18	2
14. What is this medicine used for?	18	16
15. When should you not take this medicine?: bullet list	18	18
16. What other medicines or food should be avoided whilst taking this medicine?	18	10
17. How much & how often should you use this medicine?:	18	17
17.1 Add statement "it is important to follow the dosing instructions provided by the patient's healthcare provider"	18	10
18. What should you do if you miss a dose?	9	1
19. What to do when you have taken more than the recommended dosage? (Over dosage)	18	9
20. Sign & symptom of over dosage?	18	9
21. Care that should be taken when taking this medicine	18	18
22. When should you consult your doctor? (Follow 21)	18	4
23. Undesirable effects	18	18
24. When should you consult your doctor? (Side Effect)	18	18
25. How should you keep this medicine?	18	13
26. Description of product, what is in the medicine? (Qualitative and Quantitative composition)	18	9
27. Name/ logo of manufacturer, importer, or Marketing Authorization Holder; MAH	18	18
28. Date of revision of PIL	18	8
29. Disclaimer " CMI is a summary and does not contain all information, ask doctor or pharmacist for more information. "	0	0

6.4.6. Investigating Thai PIs against Thai PI regulation

The 18 Thai PIs were assessed for presence or absence of the information required by Thai PI regulations. All Thai PIs showed the name of the medicine product, dosage, administration, contraindication, precaution, possible side effects, and name of manufacturer, importer, or Marketing Authorization Holder (MAH). However, the detail contained in the leaflets varied. Eight of the 18 leaflets contained pharmacodynamics properties. Half of the Thai PIs included pharmacokinetics properties. Eight Thai PIs were written regarding cautions relating to pregnancy and breast-feeding, and fertility, dosage form and contents of the pack and other information, and the published date. However, the precaution in avoiding using in third-trimester pregnancy was included in the 12 facts about taking Ibuprofen which was presented in 17 Thai PIs. A list of excipients was described in only two leaflets. How the Thai PIs compared to the Thai PIs regulations are shown in Table 6-15.

Table 6-15 Investigating the Thai PIs against Thai PI regulation

Criteria	Number of Thai leaflets passed the criteria (n=18)
1. Name of the medicine product	18
2. Qualitative and Quantitative composition	13
3. List of excipients	2
4. Pharmacodynamics properties	8
5. Pharmacokinetics properties	9
6. Indication	18
7. Dosage	18
8. Administration	18
9. Contraindication	18
10. Precaution	18
11. Drug interaction	10
12.Pregnancy,breast-feeding, and fertility	8
13. Possible side effects	18
14. Overdose	9
15. Storage conditions	14
16. Dosage form, and amount of the pack and other information	8
17. Name of manufacturer, importer, or Marketing Authorization Holder; MAH	18
18. The date that the PIs was published	8

6.4.7. Assessment of the quality of content provided in UK PILs and Thai PIs by comparison to the U.S. Keystone Criteria.

Overall, there were a greater number of the UK PILs achieved some U.S. Keystone Criteria than Thai PIs. All of the leaflets both the UK and Thai showed generic and brand names. However, phonetic spelling was not applied to any U.K. and Thailand because phonetic spelling is not the requirement for UK PILs, and Thai leaflets are written in the Thai language. Most leaflets described the indication which was a requirement of the Keystone criteria: relieve mild to moderate pain; pain, stiffness and swelling associated with rheumatoid arthritis, osteoarthritis, and primary dysmenorrhea; also reduces fever. The drug class: nonsteroidal anti-inflammatory drug or NSAIDs was written in all UK leaflets, while only seven Thai PIs indicated the medicine class even though they were the PI for health professionals. Allergy to NSAIDs is a major caution with ibuprofen, therefore, all leaflets provided this. For other diseases or conditions, the UK leaflet was clearer in identifying cautions such as ulcer disease, heart disease, high blood pressure, kidney or liver dysfunction, than the Thai PIs. All UK leaflets indicated that ibuprofen should be used with caution in pregnant women, but 16 UK leaflets showed this in a separate section with bold title. Using of the medicine in children under 6 months of age was not included. However, all the UK leaflets provided the statement “Do not give to children under 12 years”. Less half of Thai leaflets (8/18) included information about using in pregnant or nursing women in a stand-alone section. The rest of the Thai leaflets mentioned using in pregnancy in the 12 facts of taking Ibuprofen. Less than half of the UK leaflets (7/18) mentioned about taking Ibuprofen with meals or milk to prevent gastrointestinal effects, while most of Thai leaflet (16/18) suggested this action. None of leaflets mentioned using in arthritis, as included in the Keystone criteria. Only eight of the 18 the UK leaflets, and only one Thai leaflet described how to deal with missing doses, and indicated about long-term use with proper monitoring especially in patients at risk for kidney problems, heart failure, liver dysfunction, those taking diuretics, and elderly patients. All UK PILs and 11 of the 18 Thai PIs included the precaution not to take more than 3,200 mg daily. Ten of the Thai leaflets included the sentence “Stop taking and call provider immediately if severe gastrointestinal (GI) effects occur”, but none of Thai leaflets included the sentence “other side effects may occur, check with provider”. The publisher name and date of publication or most recent revision were shown in all UK PILs, but for Thai PIs, although all presented the publisher name, only eight stated the date of publication.

In terms of language used, layout and design, Thai PIs were designed for health care professionals, the language used e.g. polysyllabic jargon or medical terms were used. Therefore, none of Thai PIs could not meet the criteria about being written clearly; avoiding long sentences or avoiding or explaining polysyllabic terms. This included the 12 facts about ibuprofen, drafted by the FDA.

Other layout and design criteria in terms of bullets, brief reinforcement separate from main text, headings, boldface type, or box, font size, good contrast, and adequate space between lines and paragraphs, were covered by the BALD criteria. The readability test was also not applied as this was assessed separately.

However, some criteria were not applicable to any UK PILs and Thai PIs. For example, showing the disclaimer statement "Leaflet does not contain all possible information, provider can give additional information." and stating that the medicine should only be used by the patient and not given to others, and advising that patients 'may request non–child-resistant caps' were not applied to leaflets from both countries. Table 6-16 shows the U.S Keystone sub-criteria for Ibuprofen and the number of leaflets that met each sub-criterion.

Table 6-16 Comparison of UK PILs and Thai PIs against U.S Keystone criteria for Ibuprofen

Criteria	Number of UK leaflets passed the criteria (n=18)	Number of Thai leaflets passed the criteria (n=18)
1.Include drug names and indications for use		
1.1. Generic (ibuprofen) and brand name (if dispensed a brand name, e.g., Motrin [McNeil]), phonetic spelling.	18	18
1.2 Used to relieve mild to moderate pain; pain, stiffness and swelling associated with rheumatoid arthritis, osteoarthritis, and primary dysmenorrhea; also reduces fever.	18	16
1.3 Drug class (nonsteroidal anti-inflammatory drug, often abbreviated NSAID).	18	7
2. Include contraindications and what to do if applicable		
2.1. Do not take if allergic to aspirin or other NSAID (e.g., indomethacin, naproxen).	18	18
2.2. Make sure provider knows about other medical problems that may affect use of ibuprofen, especially ulcer disease, heart disease, high blood pressure, kidney or liver dysfunction, coagulation defects/use of anticoagulants, impending surgery.	18	10
2.3. Check with provider if pregnant or nursing; not to be used in children under 6 months of age.	16	8
3. Include specific directions about how to use, monitor, and get most benefit		
3.1. Take with meals or milk to minimize gastrointestinal (GI) effects; take with liquid; may combine with antacids.	7	15
3.2. If taken for arthritis, take regularly as prescribed; pain relief occurs within hour but anti-inflammatory effect occurs after 1–2 weeks of adequate dosage.	0	0
3.3. Take missed dose as soon as possible; skip if almost time for next dose.	9	1
4. Include specific precautions and how to avoid harm while using		
4.1. Not recommended to combine with aspirin because there is no known benefit.	18	18
4.2. Long-term use without proper monitoring should be avoided; patients at risk for kidney problems are those with impaired kidney function, heart failure, liver dysfunction, those taking diuretics, and the elderly.	18	1
4.3. Use caution when taking other over-the-counter (OTC) products that contain ibuprofen, do not exceed 3,200 mg daily.	18	11
5. Include symptoms of serious or frequent adverse reactions and what to do		
5.1. Stop taking and call provider immediately if severe GI effects occur (e.g., bleeding, ulceration, black or bloody stools); effects m ay result in hospitalization, may be fatal. (SE)	18	10

Criteria	Number of UK leaflets passed the criteria (n=18)	Number of Thai leaflets passed the criteria (n=18)
5.2. Tell provider about rash, if other side effects do not go away or are bothersome, including GI disturbances, blurred vision, weight gain, or water retention. (SE)	18	18
5.3. Other side effects may occur, check with provider.	18	1
6. Include general information, disclaimer, and encouragement to ask questions		
6.1. Store at room temperature, away from excess heat or moisture, and away from children.	18	14
6.2. Includes disclaimer that this leaflet does not contain all possible information, provider can give additional information.	0	0
6.3. Includes information stating that medicine should only be used by patient and not given to others, may request non–child-resistant caps.	0	0
6.4 Indication for use consistent with U.S. Food and Drug Administration (FDA) labelling: relieves mild to moderate pain; pain, stiffness, and swelling associated with rheumatoid arthritis, osteoarthritis, and primary dysmenorrhea.	18	18
6.5. Notes that medication may be used for other purposes; communication with provider is encouraged.	0	0
6.6. General guide does not include information about non approved uses.	18	18
7. Be scientifically accurate, unbiased, and up to date		
7.1. Neutral in content and tone.	18	18
7.2. Does not contain promotional messages about product or compare to other brands (may compare chemical entities).	18	18
7.3. Fair balance regarding benefits and risks.	18	18
7.4. Includes publisher name and date of publication (not date printed for prescription use) or most recent revision.	18	8
7.5. Any additional information is consistent with current FDA-approved labelling or federally recognized compendia	N/A	N/A
8. Be written in a format that is legible and comprehensible to consumer.		
8.1. Written clearly; avoids long sentences; avoids or explains polysyllabic terms.	18	0
8.2 black box warning information printed in bold-face type or box (not UK or AUS)	N/A	N/A
8.3 minimal use of italics or ornate typefaces that are hard to read	18	18
8.4 upper and lower case lettering	18	N/A
8.5 headings placed on separate lines (not on same line as text).	18	18

Criteria	Number of UK leaflets passed the criteria (n=18)	Number of Thai leaflets passed the criteria (n=18)
8.6 Bullets used to enhance readability	18	18
8.7 information is well organized and easy to find	18	18
8.8 adequate space between lines (> 2.2 mm; this is approx. 2.2mm)	0	4
8.9 used no smaller than 10-point type (this is 10-point)	4	1
8.10 good ink-paper contrast.	18	17
8.11 written at 6-8th grade level (excluding drug names)	a	b

[a] presented in table 7 Flesch Reading Ease scores and Flesch–Kincaid Grade Levels of UK PILs

[b] presented in table 8 readability test for Thai PIs

6.5 Discussion

6.5.1 General information

In general, the UK leaflets were fairly uniform. They had the same pattern in format and information provided because, in EU countries, it is a requirement by law that all licensed medicines must be provided with a PIL inside the original packaging and must include the exact headings. The UK leaflets were not much different in paper size. The uniformity of the PILs reflects that their content of the PIL is approved as part of the medicine's license approval process.[16,200]

Regarding Thai PIs, the Thai leaflets were much more varied in terms of format, contents, and paper size. Again, by the definition from the guideline, all of the collected Ibuprofen leaflet in this study were PI for the health care professionals. The full version and short PI version contained the information required by the Thai guideline together with the 12 facts about taking Ibuprofen. Most of the information written in the short version was the same as the full version, but the short version excluded or shortened the information on pharmacodynamics and pharmacokinetic properties. This was allowed by the Thai FDA.[28]

The very short version contained much less information, but showed the 12 facts about taking Ibuprofen. According to the very short version, Ibuprofen is an old-fashioned medicine that has been used for a long time. It is reasonable to assume that some Ibuprofen and their leaflets were registered, and the leaflets designed prior to the publication of the leaflet guideline (before 2013). As a result, their leaflets were written based on the very first version of the notification from the

Ministry of Public Health regarding specific requirements for non-selective NSAIDs, which was first introduced in 1990. Despite the fact that some very short version Thai PIs have recently been updated, their contents have largely remained unchanged. Again, even the very short version PI for Ibuprofen was approved by the Thai FDA.

This diversity of Thai leaflets reflects the situation in Thailand, which could present problems for patients and affect their attitudes towards reading the leaflets. A previous survey has found that content length was seen as a reason for not reading the leaflet among Thai people. Some consumers found that the content was slightly too short, but some expressed that it was fairly long to read.[272]

This result also relates to findings from prior studies that show, in Thailand, the available leaflets obtained from pharmacies were not aimed at patients, but at health professionals.[25] This study also found that, as the PILs are voluntarily produced and supplied by pharmaceutical companies, there is a very limited number of available PILs for medicinal products dispensed in Thailand. Inevitably, therefore, the amount of PILs distributed to patients is less than in the EU countries, where PILs are widely provided to patients. This is supported by the findings of a recent survey of Thai outpatients, in which 76% of patients had never heard of PILs, but most (91%) had received a PI. [273] In contrast, 97% of UK patients were aware of PILs in a survey carried out in 2007.[120]

6.5.2 Layout and design

The text design and format of the UK leaflet met the BALD criteria, but most failed the criteria on font size, white space and paper quality. The small font and less space between the lines made leaflets difficult to read. The text design and format of Thai leaflet were more varied, but they similarly failed the same criteria of small font, less space between the lines and paper quality.

These findings relate to many studies in the past which found that the leaflets were often difficult to read with small font and text size. People in many countries were dissatisfied with poor format and language used in medicine leaflets. They had some difficulty in comprehension or understanding related to the language used, technical terms, and the small font size used. [79,84,87,91,95,107,248]

6.5.3 Readability test

Readability of a sample of PILs of Ibuprofen in the UK was evaluated with Flesch Evaluating Reading Ease score and the Flesch-Kincaid Grade Level The median score of 52.2 and grade level of 8 to >10 showed that the leaflets were difficult to read.

More than half of the indication section in the Thai PIs was defined as very difficult or difficult to read when compared with others. Some of the precautions sections, and side effect information sections were also categorised as very difficult to read in comparison with others.

A previous study reported that two-thirds to three-quarters of those reading at the lowest reading level, i.e. a below basic level, which is a 5th grade level or below, report that they read "well" or "very well."[274] A prior study suggested recommended reading-level range of fifth-to-seventh grade for the written information.[275] Previous studies in the UK, Australia, New Zealand, US, Canada, Ireland, and Nigeria have also found that only a minority of PILs met recommended reading-level criteria. Many studies in the past have found that readability of the collected leaflets showed the mean reading level is substantially higher than the recommended reading level for consumers, which is fifth to seventh grade. The language in the PILs collected in these studies was too complex, and require high literacy to read.[141,144,147,151,275,276] One study indicated that the leaflets were written poorly; but also suggested it is possible that standard readability scales are not appropriate for use with medical information.[275]

6.5.4 Regulations compliance

In terms of EU regulations, in EU countries, the information provided must be related to SmPC and is approved when the medicine is licensed by the regulatory authority.[16]

For the layout and design, the guideline on the readability of labelling and package leaflet of medicinal products for human use must be followed. The main purpose of this guideline is to provide instruction which can assure that the information on the leaflet is accessible to and can be understood by those who receive it, so that they can use their medicine safely and appropriately.[15]

All contents of the UK ibuprofen PILs complied with EU regulation. However, layout and design were slightly varied. Some UK PILs used all capital letters for the main topics. None of the leaflets achieved a space between lines of text of at least 3 mm. The paper used for all leaflets was not sufficiently thick to reduce transparency.

Most UK PILs and Thai PIs achieved the basic Thai PILs criteria in terms of content. With regards to language used, all UK PILs and Thai PIs were written in English and Thai language, respectively. However, all the UK PILs were written in plain language rather than the Thai PIs which were written in formal language.

Regarding to the layout and design, both UK PILs and Thai PIs were printed using contrasting colours between the text (black or dark blue) and the paper colour (white), although one Thai PI

was printed in pink, which was harder to read. Overall size of the leaflets varied in both the UK PILs and Thai PIs, but the UK leaflets were uniform in terms of the format, pattern and the information presented, while the Thai PIs were more varied. The Thai PILs guideline recommended printing the main information with 14 points bold. This size was easy to capture by eyesight, but there was a minority of both leaflets printed with 14 points bold.

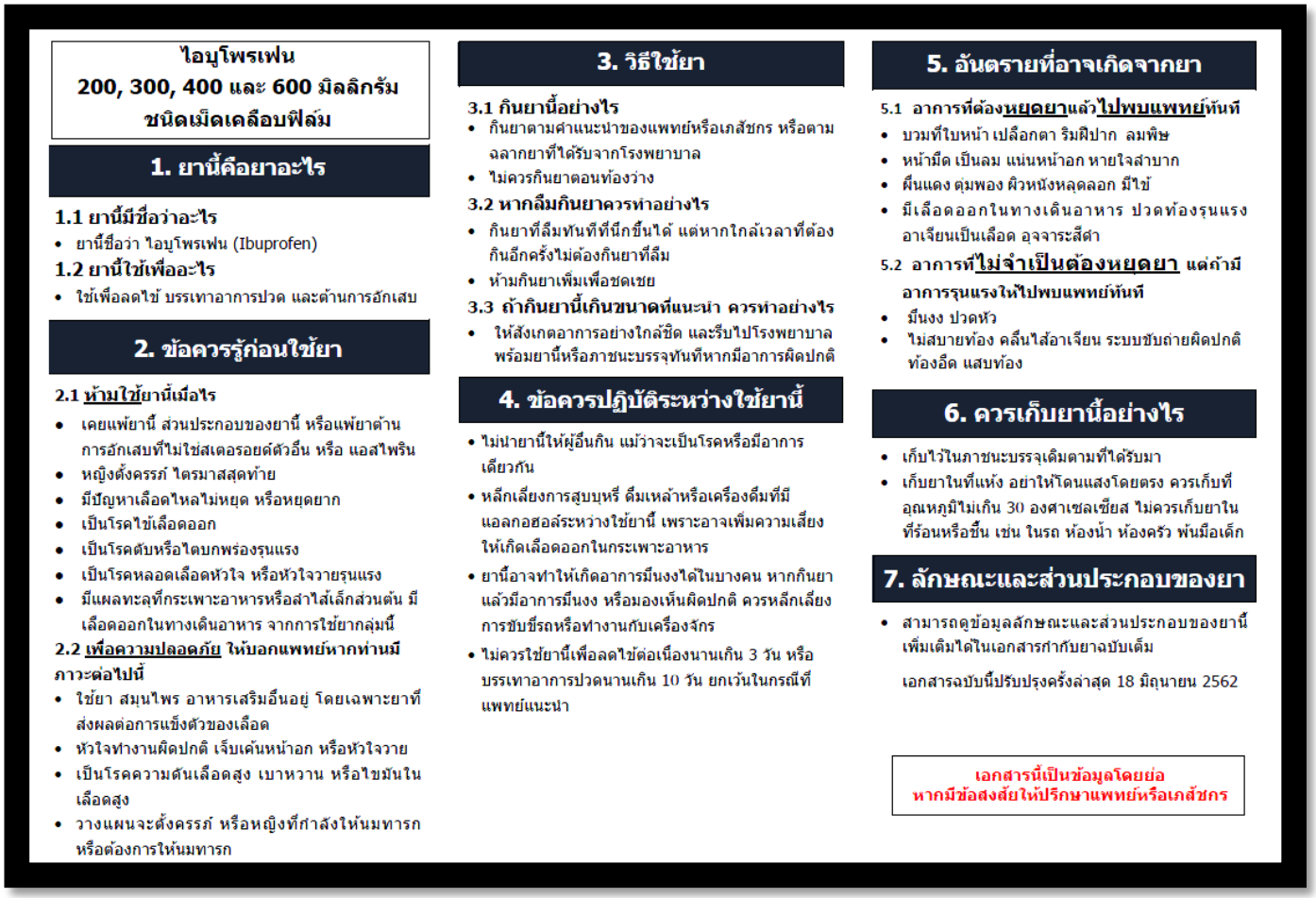
Not surprisingly, the evaluation showed that Thai PIs could not achieve the majority of the Thai PILs criteria because they are designed for a different objective. However, it does show that the Thai PIs were not suitable for being a good patient medicine information source in terms of both content and design.

There is a demonstration version of an ibuprofen Thai PIL which has been created by the Thai FDA. This is available on the Thai FDA website[277] and follows good design principles. The topics of the demonstration ibuprofen PIL consist of: what is in the medicine, what you need to know before taking the medicine, how to take the medicine, what you should do while taking the medicine, possible side effects, how to store the medicine, contents of the pack and other information. The information is presented in A4 paper size with landscape format, divided into three columns. The font and text are written in a larger size than that of a standard leaflet. However, the demonstration leaflet does not contain the 12 facts about ibuprofen. The demonstration ibuprofen PIL is shown in Box 6-2.

When comparing Thai PIs to the Thai PIs regulation, it was discovered that much of the information required by the regulation was present in the majority of Thai PIs. However, a significant proportion of very short version of Thai PIs omitted critical information about drug interactions, pregnancy, breastfeeding, and fertility. This was the major weakness that put the patients at risk. If the patient must take ibuprofen, extra information may be required.

In Thailand, ibuprofen must be provided by health care professionals, it cannot be purchased from grocery stores, as in the UK. Therefore, it may be expected that the patients obtaining ibuprofen would be asked their health history in terms of their allergy, pregnancy status, other medicines being used and other medical problems before dispensing or supplying the medicine. It is also expected that they should be informed about how to take the medicine as well as the possible side effects.

Box 6-2 The Thai demonstration ibuprofen PIL



ไอบูโพรเฟน
200, 300, 400 และ 600 มิลลิกรัม
ชนิดเม็ดเคลือบฟิล์ม

1. ยานี้คือยาอะไร

1.1 ยานี้มีชื่อว่าอะไร
- ยานี้ชื่อว่า ไอบูโพรเฟน (Ibuprofen)

1.2 ยานี้ใช้เพื่ออะไร
- ใช้เพื่อลดไข้ บรรเทาอาการปวด และต้านการอักเสบ

2. ข้อควรรู้ก่อนใช้ยา

2.1 ห้ามใช้ยานี้เมื่อไร
- เคยแพ้ยานี้ ส่วนประกอบของยานี้ หรือแพ้ยาต้านการอักเสบที่ไม่ใช่สเตอรอยด์ตัวอื่น หรือ แอสไพริน
- หญิงตั้งครรภ์ ไตรมาสสุดท้าย
- มีปัญหาเลือดไหลไม่หยุด หรือหยุดยาก
- เป็นโรคไข้เลือดออก
- เป็นโรคตับหรือไตบกพร่องรุนแรง
- เป็นโรคหลอดเลือดหัวใจ หรือหัวใจวายรุนแรง
- มีแผลทะลุที่กระเพาะอาหารหรือลำไส้เล็กส่วนต้น มีเลือดออกในทางเดินอาหาร จากการใช้ยากลุ่มนี้

2.2 เพื่อความปลอดภัย ให้บอกแพทย์หากท่านมีภาวะต่อไปนี้
- ใช้ยา สมุนไพร อาหารเสริมอื่นอยู่ โดยเฉพาะยาที่ส่งผลต่อการแข็งตัวของเลือด
- หัวใจทำงานผิดปกติ เจ็บเค้นหน้าอก หรือหัวใจวาย
- เป็นโรคความดันเลือดสูง เบาหวาน หรือไขมันในเลือดสูง
- วางแผนจะตั้งครรภ์ หรือหญิงที่กำลังให้นมทารก หรือต้องการให้นมทารก

3. วิธีใช้ยา

3.1 กินยานี้อย่างไร
- กินยาตามคำแนะนำของแพทย์หรือเภสัชกร หรือตามฉลากยาที่ได้รับจากโรงพยาบาล
- ไม่ควรกินยาตอนท้องว่าง

3.2 หากลืมกินยาควรทำอย่างไร
- กินยาที่ลืมทันทีที่นึกขึ้นได้ แต่หากใกล้เวลาที่ต้องกินอีกครั้งไม่ต้องกินยาที่ลืม
- ห้ามกินยาเพิ่มเพื่อชดเชย

3.3 ถ้ากินยานี้เกินขนาดที่แนะนำ ควรทำอย่างไร
- ให้สังเกตอาการอย่างใกล้ชิด และรีบไปโรงพยาบาลพร้อมยานี้หรือภาชนะบรรจุทันทีหากมีอาการผิดปกติ

4. ข้อควรปฏิบัติระหว่างใช้ยานี้

- ไม่นำยานี้ให้ผู้อื่นกิน แม้ว่าจะเป็นโรคหรือมีอาการเดียวกัน
- หลีกเลี่ยงการสูบบุหรี่ ดื่มเหล้าหรือเครื่องดื่มที่มีแอลกอฮอล์ระหว่างใช้ยานี้ เพราะอาจเพิ่มความเสี่ยงให้เกิดเลือดออกในกระเพาะอาหาร
- ยานี้อาจทำให้เกิดอาการมึนงงได้ในบางคน หากกินยาแล้วมีอาการมึนงง หรือมองเห็นผิดปกติ ควรหลีกเลี่ยงการขับขี่รถหรือทำงานกับเครื่องจักร
- ไม่ควรใช้ยานี้เพื่อลดไข้ต่อเนื่องนานเกิน 3 วัน หรือบรรเทาอาการปวดนานเกิน 10 วัน ยกเว้นในกรณีที่แพทย์แนะนำ

5. อันตรายที่อาจเกิดจากยา

5.1 อาการที่ต้องหยุดยาแล้วไปพบแพทย์ทันที
- บวมที่ใบหน้า เปลือกตา ริมฝีปาก ลมพิษ
- หน้ามืด เป็นลม แน่นหน้าอก หายใจลำบาก
- ผื่นแดง ตุ่มพอง ผิวหนังหลุดลอก มีไข้
- มีเลือดออกในทางเดินอาหาร ปวดท้องรุนแรง อาเจียนเป็นเลือด อุจจาระสีดำ

5.2 อาการที่ไม่จำเป็นต้องหยุดยา แต่ถ้ามีอาการรุนแรงให้ไปพบแพทย์ทันที
- มึนงง ปวดหัว
- ไม่สบายท้อง คลื่นไส้อาเจียน ระบบขับถ่ายผิดปกติ ท้องอืด แสบท้อง

6. ควรเก็บยานี้อย่างไร

- เก็บไว้ในภาชนะบรรจุเดิมตามที่ได้รับมา
- เก็บยาในที่แห้ง อย่าให้โดนแสงโดยตรง ควรเก็บที่อุณหภูมิไม่เกิน 30 องศาเซลเซียส ไม่ควรเก็บยาในที่ร้อนหรือชื้น เช่น ในรถ ห้องน้ำ ห้องครัว พ้นมือเด็ก

7. ลักษณะและส่วนประกอบของยา

- สามารถดูข้อมูลลักษณะและส่วนประกอบของยานี้เพิ่มเติมได้ในเอกสารกำกับยาฉบับเต็ม

เอกสารฉบับนี้ปรับปรุงครั้งล่าสุด 18 มิถุนายน 2562

เอกสารนี้เป็นข้อมูลโดยย่อ
หากมีข้อสงสัยให้ปรึกษาแพทย์หรือเภสัชกร

The main topics are

1. What is in the medicine
2. What you need to know before taking the medicine
3. How to take the medicine?
4. What you should do while taking the medicine
5. Possible side effects
6. How to store the medicine?
7. Contents of the pack and

6.5.5 Content

To evaluate the content of the leaflets, the US keystone criteria were used as an international standard. Overall, a greater number of the UK PILs adhered to the US keystone criteria than Thai PIs. This relates to previous studies that evaluated certain medicines based on the U.S. Keystone Criteria which found that UK leaflets performed relatively well compared to leaflets from other English-speaking countries and scored highly across all criteria.[151,199]

All Thai and the UK leaflets performed well in terms of including drug names and indications, although some Thai leaflets lacked information on the drug class. Thai leaflets provided less information on contraindications and what to do if applicable and also on monitoring during long term use.

Less than half of the leaflets in both countries gave information about missed doses, most likely because it was not compulsory by their own regulations. While the Thai leaflets stated that ibuprofen should be taken with meals or milk to minimize gastrointestinal (GI) effects, less than half of the UK leaflets presented this information. However, the recommendation from both the NHS and the BNF suggested that patients should take ibuprofen tablets and capsules with food or a drink of milk to reduce the chance of an upset stomach.[278,279]

While both types of leaflet included symptoms of serious or frequent adverse reactions and what to do, Thai PIs were less likely to suggest “talking with provider” because the PIs were aimed at healthcare professionals.

Most other criteria were met, although dates of publication were not presented in some Thai PIs, even though Thai PI guideline also required this information. The legibility and format criteria were met by most leaflets, although these were more rigorously assessed by readability testing and BALD criteria.

However, importantly, half of the Thai leaflets obtained were the very short versions. Even through these were allowed by the FDA. This suggests that patients may frequently receive leaflets lacking important information. As a result, this may have an impact and cause harm to patients because Ibuprofen was attributed to one-third of the major cause of Adverse Drug Events reported to the Health Product Vigilance Centre in Thailand between 1984 and 2019.[191,260] These very short versions should be prohibited and replaced by the short or full version. Even Though, in practice, sometimes patients may be given strips in a plastic envelope without any PI.

6.6 Conclusion

Overall, UK leaflets were generally consistent in terms of information provided and format. The layout and design met the BALD criteria except font size, line space and paper quality. The information was difficult to understand. The UK ibuprofen PILs had all of the required information by EU regulation, however layout and design may be improved. A great number of the UK PILs provided contents that adhered to the US keystone criteria.

In respect of Thai PIs, they differed in both information provided and appearance. The Thai PIs had a wide range of text design and format. They also failed to meet the same criteria of small font, less space between the lines and paper quality. The content was deemed difficult to comprehend. The information required by the Thai PI regulation was written in the majority of Thai PIs. The major weakness was that essential information concerning drug interactions, pregnancy, lactation, and fertility were discarded from a large proportion of Thai PIs. The evaluation showed that Thai PIs were not appropriate to be used as patient information, according to the Thai FDA guidelines. Patients may require additional information from health care professionals.

6.7 Strengths and limitations

All of the leaflets were randomly collected from various pharmacies. As a result, the findings may be reflective of the current situation of the Thai and UK pharmaceutical markets. The Ibuprofen leaflets were evaluated in terms of layout and design, as well as content. The findings clearly revealed that some substandard Ibuprofen leaflets were distributed to the general public particularly in Thailand. However, only the Ibuprofen leaflet, a small quantity of leaflets, and collecting in one region were investigated in this study. Findings cannot be generalised to other prescription medicine leaflets, as well as leaflets from other districts.

6.8 Recommendation for practice

The layout and design of UK leaflets still needed improvement in terms of font size, line space and paper quality. Before releasing, a revision and re-written contents leaflet version, as well as a readability test, may be required.

In the case of Thai PIs, before disseminating Thai PIs to the general public, the authorising organisation must ensure that the contents, layout, and design are all uniform. The information in Thai PIs was difficult to comprehend. Some of the Thai PIs lack crucial information. This is

important as PIs may be intended for use by HCP as well as patients; the content of some PIs have to be improved.

More significantly, PIs could not replace patient-specific leaflets, in particular regarding the contents provided and the language used. The PILs must become compulsory to be made available to the public in Thailand. Even though PILs have been in use in some countries for a long time, there was no guarantee that patients would regard them as satisfactory. Regulation revision, guideline update, and end-user comprehension and satisfaction surveys are all required for continuous improvement. Patients' perspectives are important in real situations.

Chapter 7 Sources of medicine information in the UK: A public perspective

7.1 Introduction

As mentioned in the earlier chapters, patients are able to access information about their health care products easily. They increasingly anticipate being able to make decisions about their health from available evidence.[1] Correctly providing medicine information is a crucial aspect of service delivery for enhancing patient safety. To improve quality of care and patient safety, HCPs could provide medicine information and encourage patients to search for related information using trustworthy sources.

In the UK and Europe, patients are exposed to a broad range of drug information sources of varied reliability. As described in Chapter 6, an information leaflet is regularly provided to patients with every medicine supplied, enforced by European regulations. Verbal information also plays an important role in medicine information and is a responsibility of health professionals involved in prescribing, supplying and administering medicines. In addition, information about medicines is more available than ever before because of the large number of health-related websites on the Internet. Other information sources include newspapers, magazines, TV, advertisements, advice from family and friends. While these offer a great deal of information about medications, they may contain conflicting, inaccurate, poorly written, or non–evidence-based information.[5] Patient preferences for sources and their levels of desire for medicine information are different depending on their age, sex, ethnic and cultural background, the length of time that the patient has been on a medication, or their experiences.[10] This diversity therefore raises the question what are the relevant, desirable and appropriate medicine information sources for patients. A systematic review on the role and value of written medicine information published in 2007 highlighted the need for more research to determine the best content, layout and delivery of written medicine information, in particular PILs, and evaluation of medicines information on the Internet.[44]

From the scoping review in Chapter Three, studies exploring patient's views or attitudes and behaviour using questionnaire-based surveys revealed that PILs play an important role as a medicine information source.[95] Many patients claim that they always read their PILs regularly.[86,87,95,107] Some of them understood the insert and perceive the benefit of PILs in term

of improved judgements and intention to take a medicine.[115] PILs of good quality are in turn associated with better medication adherence.[280]

In contrast, some studies found that patients never read the leaflet provided with their medicine[88,90,103,113] and some have negative views on the format,[91] often because it is not designed for patient use. Patients have indicated they have some difficulty in understanding the language, technical terms, and reading the small font, and that the technical language acted as a barrier to effective use.[89,95] Some studies found that PILs appeared not to have much impact on patient knowledge due to low readability and comprehension.[79] Others found that patients expressed a preference to read medicine information in their own language[86,96] and that the majority did not understand the information in leaflets.[281] One study revealed that an increase in anxiety was reported after reading the leaflet, resulting in decreased adherence.[107] Patient views of PILs might therefore contrast with health professional perspectives. A perfect PIL prepared by health care professionals or manufacturers might not meet patient's need.

In terms of verbal information, physicians and pharmacists are the most commonly used sources of drug information for patients, but not all receive the information they want due to misunderstandings regarding the information needs of the patients. A study in Singapore found that pharmacists and relatives or friends were commonest sources of information for non-prescription medicines[10,97] ,while a study in Iran found that the majority often relied on friends and family as information sources.[103]

Patients view the Internet to be a convenient source with a broad range of information. Studies have found that it was perceived difficult to find reliable information on the Internet. Patients faced both the inability to find needed information and uncertainty about information reliability when searching for medicine information on the Internet.[10,92]

As more countries increased the availability of medicines information for patients, as well as, from the scoping review, there was much more variety in the focus of studies investigating among patients on their view and experiences. It is important to take account of needs and preferences of general public. While more studies are needed in Thailand, it is also important to gather views on PILs and other information sources from a highly developed country, since studies suggest that, despite years of development, PILs still do not meet patients' needs and are often ineffective.[249]

7.2 Aim and objectives

The aim of the study was to identify medicine information sources used, and views on different sources and perceived needs for medicine information among the general public in a region of England with experience of using medicines.

7.2.1 Objectives

1. To identify medicine information sources used by general public
2. To describe how the general public, use the medicine information
3. To find out the perceptions of the general public on different medicine information sources
4. To determine preferences for the content and format of medicine information among the general public

7.3 Method

This study was a cross-sectional questionnaire-based survey study. The study surveyed the general population in term of their medicine information source, and their preferences on each source.

7.3.1 Instrument development

1. Questionnaire construction

   Searching and reviewing relevant literature was conducted to identify key issues on medicine information sources, and methods of gathering perceptions of the general public on different sources. Then, brainstorming discussions were held repeatedly to share ideas about which questions were necessary until the questionnaire reached research team consensus. In general, questions were designed to be easy to answer, and the questionnaire attempted to ensure minimal complexity, while still ensuring key responses could be obtained. Technical terms were avoided throughout the questionnaire. Once finalised, the questionnaire was uploaded onto an on-line platform (SurveyMonkey) and formatted to provide easy navigation, avoiding skipped questions automatically.

2. Content

The questionnaire had four sections. The first section asked about demographic information including gender, age, ethnicity, first language, ability to read English (since medicine information in England is provided in English), highest level of education, regular use of medicines. In the second section was questions on views on different medicine information sources which participants have experienced in the previous 3 months. In the third section, questions seek views on different medicine information sources which participants would perhaps use in the future. The fourth section included questions about preferred way of getting this information.

3. Testing content validity

After drafting, the questionnaire was presented to Public Involvement in Pharmacy Studies (PIPS) which was a group of members of the public established by Medway School of Pharmacy. The objective for doing this was to seek the views of the general public, and to gain comments on the questionnaire. This public hearing contributed to validating the questionnaire in term of the suitability of questions and possible answers. After public hearing, some additional questions and more possible answers were added into the questionnaire.

4. Cognitive interviewing

A sample of up to 10 individual members of the public known personally to the research team such as friends, family member or PhD students who were not study in health sciences, or members of the public engagement group (PIPS) were invited to take part in cognitive interviewing with the principal researcher to further assess face and content validity. The researcher offered an information sheet (Appendix 3) to potential participants. Written informed consent (Appendix 4) was obtained from every participant prior to interview. The researcher asked for permission from the participants to use audio recording during the interview. Then, the researcher asked the participants to think-aloud about the online questionnaire. Those comments were used to improve and amend the questionnaire. Audio-recordings were used as a reminder of specific comments. No transcripts were made.

5. Pilot testing

The on-line questionnaire (Appendix 5) was piloted prior to use in a sample of up to 30 members of the public, and the time taken to complete, using the face-to-face technique, were assessed. This was conducted by all of the research students who would assist in administering the survey. This could ensure that the research students develop and hone their conversation skills as well as ensuring suitability of the questions. Potential participants were general persons in general public as same as in the main survey. Participants were provided with a participant information sheet (Appendix 6). Verbal informed consent was provided from every participant prior to interview. All comments were used to improve and amend the questionnaire.

7.3.2 Participant inclusion and exclusion criteria

The adult population in Kent and Medway were used as a sampling frame. Quota sampling was used to maximise diversity and ensure a representative sample of demographic factors particularly gender, age and socio-economic status.

a. Inclusion Criteria
   1. Participants were older than 18 years old.
   2. Participants were able to communicate in English.
   3. Participants currently used at least one regular medicine, or have used a medicine in previous 3 months.

b. Exclusion criteria
   1. Participants who had no experience of using a medicine themselves in the previous 3 months.
   2. Participants who were unable to communicate in English.
   3. People who did not want to take part in the study.
   4. Participants who were health professional or training in health care sciences.
   5. Participants who had taken part in cognitive interview and pilot testing.

7.3.3 Main survey - General method

1. The survey was a collaboration between the principal researcher and three undergraduate pharmacy students. The survey was conducted in general public places such as high street shopping centres, city centre bus stations, and public parks in Kent between September and December 2019. It involved face-to-face administration of the on-line questionnaire in an interview, conducted in these public places. Visits were made

to each site on different days and at different times of day to ensure a diversity of potential participants. The day and exact time of survey was matched up with student availability.

2. Before commencing the survey, all interviewers completed on-line National Institute for Health Research (NIHR) module on informed consent. Moreover, they were trained by the principal researcher and study supervisor(s) to make it more likely that they could perform effectively. Mock data collection was tried by the researchers among themselves, then piloting of the questionnaire as outlined above, before using it in the real situation. The purpose of training interviewers was to teach the research principles, objectives of study, skills, basic procedures, and problem solving needed to conduct face-to-face interviewing in a manner that achieves high-quality, reliable, and valid information for research.

3. In order to obtain entrance to places where permission was needed such as shopping centres, a formal permission request was provided to places. This was addressed the objectives of study, basic procedures, exact times and places to the relevant manager. Only if permission was obtained, then the data collection could be started in such places.

4. To conduct the survey, passers-by were approached by one of the researchers and invited to participate by completing the face-to-face interview. Those willing to listen were asked some screening questions to ensure eligibility. Any not fulfilling these inclusion criteria would be advised of this and thanked for their time.

5. For those who are approached and fulfil screening criteria, the researcher offered an information sheet, and a short verbal explanation of the study indicating how long the interview took (no more than 15 minutes). Verbal informed consent was asked and be recorded on the questionnaire by every participant prior to continuing with the interview.

   The researcher conducted the interview. The data were collected using an on-line version of the questionnaire uploaded onto a tablet computer. This was shared with the participant, who entered their preferred response to each question. The researcher also entered the participant's verbal responses into the questionnaire directly. After completion of the interview, participants were thanked and invited to keep the paper information sheet for future reference.

7.3.4 Sample size calculation

Sample size calculation was calculated by using precision-based sample size calculations. The quantity of information is dictated by the size sample, which, in turn, is influenced by the precision or level of confidence in sample estimates. An estimate always has an amount of uncertainty associated with it, which is determined by the data's underlying variability as well as the sample size. The more variable the population, the greater the uncertainty in estimate. Similarly, the larger the sample size the more uncertainty reduces. In general, a 95% confidence interval is used to calculate the sample size because 95% confidence intervals are usually based on the normal distribution or a t-distribution —for a normal distribution the value is 1.96. This is a 95% confidence interval, which means that there is 95% probability that this interval contains the true proportion.[282,283]

Calculating for sample size by using following formula:

$n = N*X / (X + N - 1)$, where,

$X = Z_{\alpha/2}^2 * p*(1-p) / MOE^2$,

and $Z\alpha/^2$ is the critical value of the Normal distribution at $\alpha/2$ (for a confidence level of 95%, α is 0.05 and the critical value is 1.96), MOE is the margin of error, p is the sample proportion, and N is the population size.

Adult population size in the Kent and Medway were 1,182,000 persons, but only 50% of them use a regular medicine, therefore the population size were 591,050 persons. For the sample proportion, one study found that 75% of people in England read the PIL (p=75%)[113] Therefore, assuming that taking a confidence level of 95%, α was 0.05 and the critical value was 1.96, MOE is 5%, minimum sample size computed was 288. However, the sample size was adjusted to 300 respondents.[284]

For quota sampling, areas were selected to ensure variation in deprivation: high, medium and low, while taking account of possibility to travel to and safety of the researchers. Then, the population in each area were classified by gender, age.[285] Subsequently, sampling units were selected to ensure sufficient numbers of participants are included in each quota.

7.3.5 Participant recruitment procedures

The researchers worked in pairs and were located at various selected public places, with frequent numbers of passers-by. Individual passers-by were approached by one researcher, and invited to

participate by completing the face-to-face interview. The study was briefly explained verbally and he/she was asked some screening questions. If he/she met the inclusion criteria and accepts to be a participant, he/she was recruited into the study.

7.3.6 Ethical issue and informed consent

This study was approved by the Medway school of Pharmacy Ethic Committee (Appendix 7).

Participants were provided with a participant information sheet (Appendix 6) to take away, giving details of who to contact if they had any concerns about the study and informing them the purpose of the study, the risks and benefits to taking part, and how these anonymous data was used. Verbal informed consent was requested and in addition, participants were asked to indicate their consent as an integral part of the questionnaire.

7.3.7 Data analysis

The data analysis was performed using the statistical programme Statistical Package for the Social Science (SPSS). Data from the Surveymonkey programme was exported directly into SPSS and downloaded. Any data cleaning required was conducted first, following by recoding. Then, frequency distributions and means were used to describe categorical and continuous variables, respectively. The main hypotheses to be tested were that sources of medicine those sources of medicine information used, views on different medicine information sources, and preferred ways of getting this information were different depending on age, gender, and education. The chi-squared test or Fisher's exact test were used to determine whether there were any significant differences between sub-groups.

7.4 Results

7.4.1 General information

The study was conducted between October and December 2019 in three areas: Gillingham, Canterbury and Sevenoaks. These areas were chosen by their index of multiple deprivation (IMD): high, medium and low. Numbers of participants were based on population size in each area. The total sample size required was 300 respondents, 78 in Gillingham, 130 in Canterbury, and 92 in Sevenoaks.

Table 7-1 The target numbers and participants recruited in each area.

			18-30		31-60		>60	
IMD		Male	Female	Male	Female	Male	Female	Total
High (Gillingham)	Target	9	9	20	20	10	10	78
	Achievement	9	10	20	20	10	9	78
	Difference	0	-1	0	0	0	1	0
Medium (Canterbury)	Target	20	18	25	26	19	22	130
	Achievement	18	26	22	25	20	19	130
	Difference	2	-8	3	1	-1	3	8
Low (Sevenoaks)	Target	7	7	22	24	15	17	92
	Achievement	2	5	10	31	11	33	92
	Difference	5	2	12	-7	4	-16	0

Table 7-1 shows the difference between the target and number of recruited participants. The major differences were in Sevenoaks. The target sample in each group was not achieved because of time restrictions. The survey was conducted in the winter. People passing by were not willing to stop and be included into the survey. Conversely, the researchers spent more time collecting data in Gillingham and Canterbury which are closer to the campus therefore they could manage to achieve nearly the required numbers.

A total of 300 participants were included in the survey. The majority of the respondents were female (n=178, 59.3%), with white ethnicity (n=217, 72.3%). This compares to a population of 50.8% females (2018), and 88.5% white (British) ethnicity (2011) in Kent and Medway. The percentage of female and white ethnicity were lower than average number of females and white (British) ethnicity in Kent and Medway area.

English language was the first language for most of them (n=228, 76.0%). Most had either a University (n=119, 39.7%) or a technical college education (n=104, 34.7%). In this study, 63.8% of 24-35 years old, and 41.0% of 35-65 years old have a university degree, while Organisation for Economic Co-operation and Development (OECD) data from 2018 states that that 50.8% of 24-35 year olds and 36.6% of 35-65 year olds in the UK have a tertiary education.[286] The percentage of participants who have tertiary education was higher than the percentage of people who have tertiary education in the UK. All participants were able to read English. A high number of participants (n=243, 81.0%) had used any medicines regularly (on most days) in the past 3 months

and most (n=208, 69.3%) stated that they had regularly used 1-5 medicines. The general characteristics of participants are shown in Table 7-2.

Table 7-2 Demographic characteristics of participants

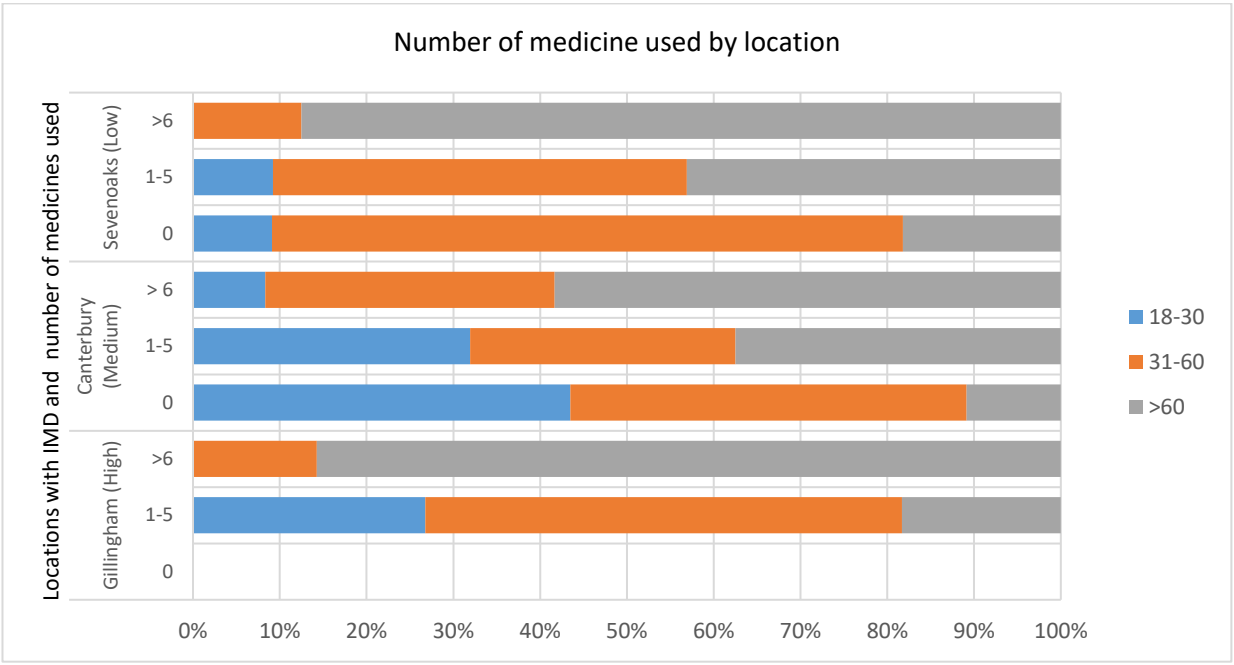
Demographic	Number (%)			
	Age 18-30 (n=70)	Age 31 – 60 (n=128)	Age >60 (n=102)	Total (n=300)
1. Gender				
Male	29 (41.4)	51 (39.8)	41 (40.2)	121 (40.3)
Female	41 (58.6)	76 (59.4)	61 (59.8)	178 (59.3)
Gender diverse	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.3)
2. Ethnicity				
Asian	17 (24.3)	18 (14.1)	9 (8.8)	44 (14.7)
Black	9 (12.9)	10 (7.8)	1 (1.0)	20 (6.7)
Mixed	9 (12.9)	7 (5.5)	3 (2.9)	19 (6.3)
White	35 (50.0)	93 (72.7)	89 (87.3)	217 (72.3)
3. First language				
English	51 (72.9)	89 (69.5)	88 (86.3)	228 (76.0)
Others	19 (27.1)	39 (30.5)	14 (13.7)	72 (24.0)
4. English readable				
Yes	70 (100)	128 (100)	102 (100)	300 (100)
5. Education				
Primary school	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.3)
Secondary	11 (15.7)	21 (16.4)	44 (43.1)	76 (25.3)
Technical College	21 (30.0)	44 (34.4)	39 (38.2)	104 (34.7)
University	38 (54.3)	62 (48.8)	19 (18.6)	119 (39.7)
6. Using Medicine regularly				
Yes	49 (70.0)	99 (77.3)	95 (93.1)	243 (81.0)
No	21 (30.0)	29 (22.7)	7 (6.9)	57 (19.0)
7. Number of regular Medicines				
0 Items	21 (30.0)	29 (22.7)	7 (6.9)	57 (19.0)
1-5 items	48 (68.6)	92 (71.9)	68 (66.7)	208 (69.3)
≥ 6 items	1 (1.4)	7 (5.5)	27 (26.5)	35 (11.7)

Medicine utilization

There were 93.1% of adults who were more than 60 years old (n= 95) had taken at least one prescribed medicine in the past 3 months. Moreover, 95 (94.0%) of those aged over 60 used at least one medicine regularly and 74.2% of these (n = 75) took more than one medicine. The prevalence of taking six or more medicines increased greatly with age, from 1.4% of those aged 18 to 30 to 26.5 % of those aged 61 and over (p<0.001).

For all participants, women (n= 144, 48.0%) were more likely than men to use prescribed medicine, but the difference was not significant. The prevalence of prescribed medicine use was also higher in more deprived areas: 100.0% of participants (n=78) in the Gillingham (high IMD) took at least one medicine, compared with 88.0% of participants (n=81) in Sevenoaks (low IMD) (p< 0.001). The number of medicines used by participant in each location is shown in Figure 7-1 Number of medicines used by location and age.

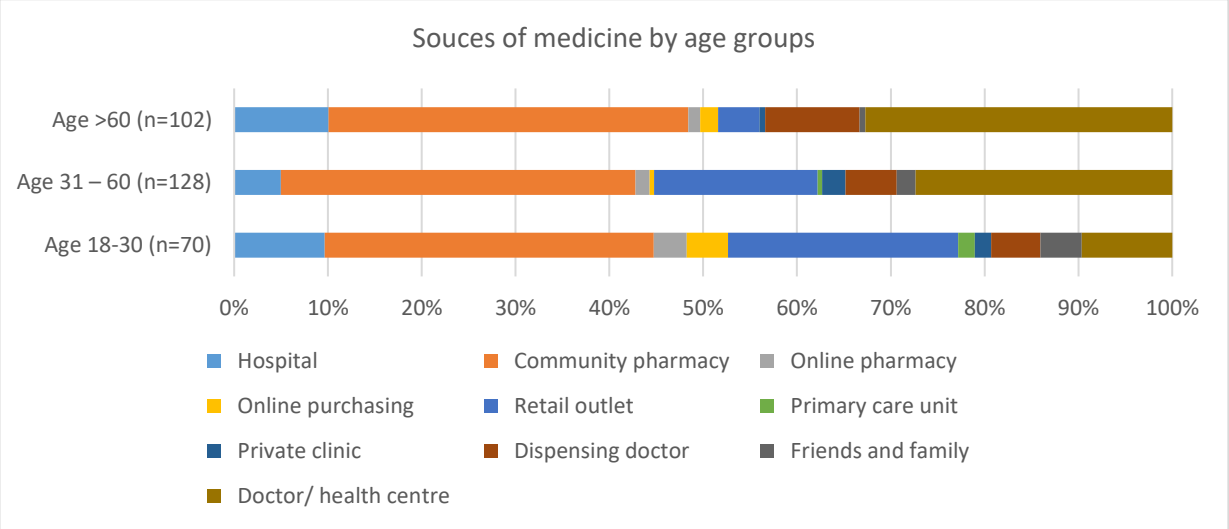
Figure 7-1 Number of medicines used by location and age



In the survey, all participants were asked to think about any medicines they had used in the past 3 months and interviewed about their views on these medicines. The total number of medicine sources cited was 474. As shown in Table 7-3 Sources and use of medicine in the past 3 months, the most common places where participants obtained medicines were community pharmacies (n=177, 59.0%) followed by the health centre/doctor (n=118, 39.3%). Retail outlet was the other main source of medicine for 18-30 and 31-60 age groups while the doctor/health centre was the

alternative source for 31-60 and over 60 age groups. Age group therefore had an influence on obtaining medicine from retail outlet and health centre/doctor ($p<0.001$). Participants with university degree obtained medicine from community pharmacy more than those with lower education ($p = 0.05$). The proportion of source of obtained medicines by age group is shown in Figure 7-2 Source of obtained medicines by age group.

Figure 7-2 Source of obtained medicines by age group



Just over half of participants obtained medicines from only one source (n=165, 55.0%) with a third using two sources (n= 102, 34.0%). The minority of participants obtained the medicines from more than two sources (n= 33, 11.0%).

These data also show that the majority of participants (n=218, 72.7%) received their medicines only from health professional sources e.g. hospitals, community pharmacies, health centres. The minority of participants (n=31, 10.3%) used only sources other than health professional (retail outlet, online purchase, friend and family) and there were 51 participants (17.0%) who obtained medicines from both types of sources. A summary of where participants had received medicines from and whether they had received information with their medicines in the past 3 months by age group is shown in Table 7-3 Sources and use of medicine in the past 3 months.

Table 7-3 Sources and use of medicine in the past 3 months

Obtaining medicines in the past 3 months	Number (%)			
	Age 18-30 (n=70)	Age 31 – 60 (n=128)	Age >60 (n=102)	Total (n=300)
1. Obtaining medicines from				
Hospital	11 (15.7)	10 (7.8)	16 (15.7)	37 (12.3)
Community pharmacy	40 (57.1)	76 (59.4)	61 (59.8)	177 (59.0)
Online pharmacy	4 (5.7)	3 (2.3)	2 (2.0)	9 (3.0)
Online purchasing	5 (7.1)	1 (0.8)	3 (2.9)	9 (3.0)
Retail outlet	28 (40.0)	35 (27.3)	7 (6.9)	70 (23.3)
Primary care unit	2 (2.9)	1 (0.8)	0 (0.0)	3 (1.0)
Private clinic	2 (2.9)	5 (3.9)	1 (1.0)	8 (2.7)
Dispensing doctor	6 (8.6)	11 (8.6)	16 (15.7)	33 (11.0)
Friends and family	5 (7.1)	4 (3.1)	1 (1.0)	10 (3.3)
Doctor/ health centre	11 (15.7)	55 (43.0)	52 (51.0)	118 (39.3)
2. Receiving any information about these medicines				
Yes	53 (75.7)	105 (82.0)	97 (95.1)	255 (85.0)
No	17 (24.3)	23 (18.0)	5 (4.9)	45 (15.0)

7.4.2 Sources of medicine information

Focusing on medicine information sources, the majority of the respondents (n=255, 85.0%) had obtained some information, while the remaining 45 (15.0%) indicated not receiving any information. The major sources of information regarding the medicines were written information (patient information leaflet/package insert, website, information on the medicine container) (n=197, 77.3%), followed by verbal information (from doctor, nurse, pharmacist) (n= 161, 63.1%), and few used other sources of information (TV, radio, newspaper, magazine, mobile app, social media, family member or friend, digital platform [e.g. Alexa, Siri]) (n=25, 9.8%).

Of the 255 participants who had obtained information, almost all (233; 92.5%) received either written information or verbal information from health professionals. There were 106 (41.6%) respondents who received a combination of written and verbal information. There were 20 (7.8%) participants who received both written information and who obtained additional information from other sources, such as friends and family, while 16 (6.3%) received information from health professionals and other sources. Only three (1.8%) participants only received information from additional sources. Therefore, in total, 48 (16%) participants did not receive any written and

verbal medicine information from usual sources. Age group was one factor affecting the source of medicine information received (p =<0.001), younger age group were least likely to have received verbal information and most likely to have used other sources. Those in Gillingham were more likely to get verbal information and less likely to get written information (p =<0.05). Types of medicine information obtained by participants are shown in Table 7-4 Types of medicine information obtained.

Table 7-4 Types of medicine information obtained

Types of information	Number (%)			
	Age 18-30 (n=53)	Age 31 – 60 (n=105)	Age >60 (n=97)	Total (n=255)
Written information	41 (77.4)	79 (75.2)	77 (79.4)	197 (77.3)
Verbal information	27 (50.9)	70 (66.7)	64 (66.0)	161 (63.1)
Others	11 (20.8)	12 (11.4)	2 (2.1)	25 (9.8)

Use of written information is the main focus of this study. The results of using written information are shown in Table 7-5. The survey reveals that leaflets (n =185, 93.9%) and medicine information on the medicine container (n =171, 86.8%) were the primary sources of written information. Most leaflets received were those included in the medicine package (n = 170, 86.3%), the remainder being provided by a health professional.

Use of written information on medicine containers included both that printed on a label by the person who dispensed the medicine (n=105, 53.3%) and printed on the container by the manufacturer (n=86, 43.7%). There were 23 participants (11.7%) who used both a label by the person who dispensed the medicine and printed on the container by the manufacturer. Furthermore, 159 (80.7%) participants read a combination of the leaflet and information on the container.

Fewer respondents (n =71, 36.0%) reported that they had used the website as a medicine information source. The majority of sites searched for information were Government organisation websites [NHS, NICE] (n=50, 70.4%), followed by patient organisation websites (n=13, 18.3%).

The participants who indicated they have used written information (n=197) were further asked about when and how they used the medicine information. The most frequent time when respondents read the information was when they were first given the medicine (n=178, 90.4%), followed by when they wanted to check whether the medicine was safe to take with another

medicine (n = 45, 22.8%). Just over half (n = 103, 53.9%) had looked at the information once only, the rest read it more than once. Almost all participants (n=90, 96.4%) claimed to have used the provided information. The most frequently cited reasons were for checking when to use the medicine (n=147, 77.4%), identifying possible side effects (n = 133, 70.0%), and checking whether the medicine was suitable for them (n=83, 43.7%).

Table 7-5 Types of written information accessed and how it was used.

	Number (%)			
	Age 18-30 (n=41)	Age 31 – 60 (n=79)	Age >60 (n=77)	Total (n=197)
1 What type of written information have you seen?				
a. A leaflet about your medicine	34 (82.9)	75 (94.9)	76 (98.7)	185 (93.9)
b. Information on the medicine container	34 (82.9)	71 (89.9)	66 (85.7)	171 (86.8)
c. Website	19 (46.3)	35 (44.3)	17 (22.1)	71 (36.0)
2 When/how did you get the leaflet?				
a. in medicine pack,	31 (91.2)	70 (93.3)	69 (90.8)	170 (91.9)
b. given by doctor or other health worker	3 (8.8)	5 (6.7)	7 (9.2)	15 (8.1)
3 What was the information on the container like?				
a. printed on a label by the person who dispensed the medicine	16 (47.1)	44 (62.0)	45 (68.2)	105 (61.4)
b. written on the medicine envelope by the person who dispensed the medicine	3 (8.8)	4 (5.6)	6 (9.1)	13 (7.6)
c. printed on the container by the manufacturer	22 (64.7)	36 (50.7)	28 (42.4)	86 (50.3)
4 Which website(s) have you looked at for information about your medicine?				
a. Government organisation website [NHS, NICE]	15 (78.9)	24 (68.6)	11 (64.7)	50 (70.4)
b. drug company website [GSK, Pfizer]	4 (21.1)	3 (8.6)	2 (11.7)	9 (12.7)
c. pharmacy website [Lloyds]	4 (21.1)	7 (20.0)	0 (0.0)	11 (15.5)
d. patient organisation website	3 (15.8)	9 (25.7)	1 (5.9)	13 (18.3)
e. hospital website [East Kent Hospital],	4 (21.1)	2 (5.7)	0 (0.0)	6 (8.5)
f. I can't remember	2 (10.5)	5 (14.3)	3 (17.6)	10 (14.1)
g. Others	4 (21.1)	4 (11.4)	2 (11.8)	10 (14.1)
5 When did you look at the information?				
a. when you were first given the medicine	36 (87.8)	72 (91.1)	70 (90.9)	178 (90.4)
b. when something unexpected happened	3 (7.3)	8 (10.1)	9 (11.7)	20 (10.2)

	Number (%)							
	Age 18-30 (n=41)		Age 31 – 60 (n=79)		Age >60 (n=77)		Total (n=197)	
c. when you wanted to find out whether you were able to drink or drive or use machinery	6	(14.6)	12	(15.2)	10	(13.0)	28	(14.2)
d. when you wanted to check if it was safe to take another medicine	11	(26.8)	16	(20.3)	18	(23.4)	45	(22.8)
e. I never looked at the information	2	(4.9)	4	(5.1)	1	(1.3)	7	(3.6)
f. Others	2	(4.9)	2	(2.5)	3	(3.9)	7	(3.6)
6 How often have you looked at the information? (once only, two or three times, more than three times)								
a. once only	17	(43.6)	46	(61.3)	40	(52.6)	103	(54.2)
b. two or three times	20	(51.3)	18	(24.0)	23	(30.3)	61	(32.1)
c. more than three times	2	(5.1)	11	(14.7)	13	(17.1)	26	(13.7)
7 How have you used the information?								
a. to check when to use the medicine	31	(79.5)	58	(77.3)	58	(76.3)	147	(77.4)
b. to check if the medicine was suitable for you	14	(35.9)	31	(41.3)	38	(50.0)	83	(43.7)
c. to make sure you avoided certain other medicines	10	(25.6)	25	(33.3)	25	(32.9)	60	(31.6)
d. to make sure you avoided certain foods or drinks	14	(35.9)	25	(33.3)	24	(31.6)	63	(33.2)
e. to identify possible side effects	28	(71.8)	50	(66.7)	55	(72.4)	133	(70.0)
f. to decide if it was safe to drink or drive or work with machinery	11	(28.2)	21	(28.0)	21	(27.6)	53	(27.9)
g. to find out what to do when I missed a dose	7	(17.9)	14	(18.7)	25	(32.9)	46	(24.2)
h. other way……	1	(2.6)	2	(2.7)	2	(2.6)	5	(2.6)

There were 55 (21.6%) respondents who claimed not to have received written information, but did receive verbal information about their medicines. The majority of these respondents had talked with their doctor (n=46, 83.6%) or pharmacists (n=23, 41.8%). They talked to their health professional when they were prescribed the medicine (n=46, 83.6%), and when they had a prescription dispensed (n=15%, 27.3). Use of verbal medicine information is shown in Table 7-6. The three participants who had used only other sources of verbal medicine information all received information from family and friends.

Table 7-6 Provision of verbal medicine information

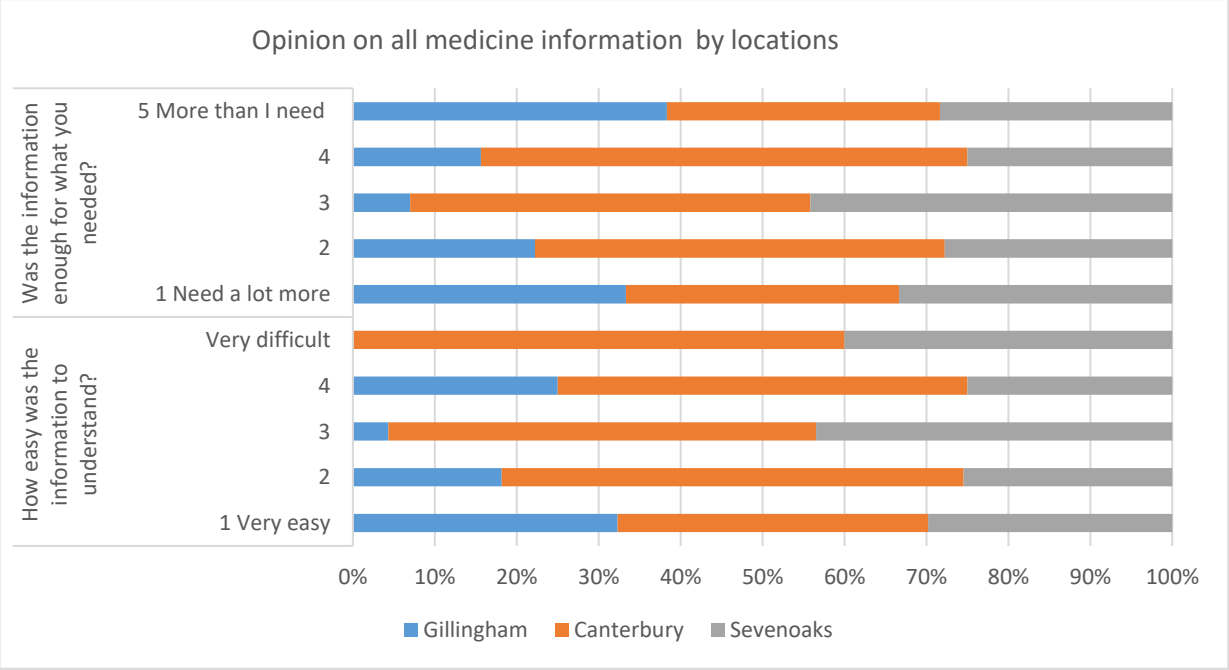
Verbal information	Number (%)			
	Age 18-30 (n=10)	Age 31 – 60 (n=25)	Age >60 (n=20)	Total (n=55)
1 Who talked to you about your medicine(s)?				
a. doctor	7 (70.0)	23 (92.0)	16 (80.0)	46 (83.6)
b. pharmacist	2 (20.0)	11 (44.0)	10 (50.0)	23 (41.8)
c. nurse	2 (20.0)	6 (24.0)	5 (25.0)	13 (23.6)
d. health worker	0 (0.0)	1 (4.0)	3 (15.0)	4 (7.3)
2 When did they talk to you?				
a. when you were prescribed the medicine	7 (70.0)	22 (88.0)	17 (85.0)	46 (83.6)
b. when you had a prescription dispensed for the first time or for refills	1 (10.0)	10 (40.0)	4 (20.0)	15 (27.3)
c. when you bought the medicine	4 (40.0)	1 (4.0)	1 (5.0)	6 (10.9)
d. when you asked them questions	2 (20.0)	2 (8.0)	3 (15.0)	7 (12.7)
e. when you had a review	0 (0.0)	3 (12.0)	4 (20.0)	7 (12.7)
f. Other time	1 (10.0)	0 (0.0)	2 (10.0)	3 (5.5)

The participants were asked their opinions in term of how easy the information was to understand and adequacy of all information. The large majority of the 248 who responded to this question considered that the information they received about their medicine was either very easy (n=161, 63.1%) or easy (n=55, 22.2%) to understand. Furthermore, all information about the medicine was judged to be more than they need by 120 (48.4%). In particular, a higher number of participants (n=103, 41.5%) in 31-60, and >60 age groups said that they received more medicine information than they need compared to younger participants (33.3%), but this difference was not significant. In addition, the proportion of participants recruited from the area of high IMD who indicated the amount of information they had received was more than they needed (46; 71.9%) was significantly higher than in those recruited from other areas (74; 40.2%) ($p<0.001$). Table 7-7 and Figure 7-3 Opinion on all medicine information by location show participants' opinion on the easy of understanding and sufficiency of medicine information received, and how these opinions differed by location.

Table 7-7 Opinion on all medicine information

	Number (%)							
	Age 18-30 (n=51)		Age 31 – 60 (n=101)		Age >60 (n=96)		Total (n=248)	
1 How easy was the information to understand?								
1 Very easy	30	(58.8)	65	(64.4)	66	(68.8)	161	(64.9)
2	16	(31.4)	22	(21.8)	17	(17.7)	55	(22.2)
3	3	(5.9)	9	(8.9)	11	(11.5)	23	(9.3)
4	0	(0.0)		(3.0)	1	(1.0)	4	(1.6)
Very difficult	2	(3.9)	2	(2.0)	1	(1.0)	5	(2.0)
2 Was the information enough for what you needed?								
1 Need a lot more	1	(2.0)	1	(1.0)	1	(1.0)	3	(1.2)
2	6	(11.8)	9	(8.9)	3	(3.1)	18	(7.3)
3	8	(15.7)	18	(17.8)	17	(17.7)	43	(17.3)
4	19	(37.3)	20	(19.8)	25	(26.0)	64	(25.8)
5 More than I need	17	(33.3)	53	(52.5)	50	(52.1)	120	(48.4)

Figure 7-3 Opinion on all medicine information by location



7.4.3 Perceptions on sources of medicine information

The participants were asked their views on different possible information sources: whether they would use each source and, if yes, whether they think it is easy to access, easy to understand, relevant to them and trustworthy. Overall, most people (n=275, 91.7%) preferred verbal information from health professional because it was trustworthy (n=233, 84.7%), relevant to them (n=180, 65.5%), easy to understand (n=179, 65.1%) but less than half considered such verbal information as easy to access (n=136, 49.5%).

These findings are supported by responses to an open question on the desirability of verbal information. Some participants preferred to receive only verbal information because verbal medicine information was thought to be easier to understand. They considered that HCPs avoided technical medical terms when they provided advice to their patients. Importantly, it provides both an opportunity to ask questions and information specific to their health conditions from someone they trusted.

"Verbal information helps clear up any misunderstandings when looking at new medicines, they help me understand what my medicine is for and how to take it. I learn better with spoken information then written info." (P157;Male, 26)

"I trust the word of my doctor, verbal info is something I understand more than written info. Having regular reviews with my doctor on my diabetes is useful and with my doctor knowing me so well, I trust the advice that comes from him regarding my medicine." (P160;Male, 60)

"Verbal info is less scarier than written, written info contains a lot of info that may not be relevant to me, my doctor gives me written info but highlights that some of the info in the leaflet is not relevant, I am more comfortable with verbally being told what side effects to look out for from the doctor than a leaflet"(P145; Male, 51)

"I have had verbal information from a pharmacist which I found very useful. They simply pointed out what side effects, how to use the medicine and what to do if I experienced any issues. I found them very easy to speak to and found them trustworthy to speak to." (P159; Male, 19)

Moreover, some participants had limited ability to read written information, for example following a stroke or found reading difficult because English was not their first language or because they were taking so many medicines.

"Verbal information I can understand better, my eyesight isn't very good to be able to read information on leaflets or websites. So I stick with my doctor" (P43; Male, 79)

"because I lost ability to read after stroke" (P285; Male, 67)

The second most frequent choice of medicine information source was a leaflet with medicine (n=211, 70.3%). A high number of people who selected the leaflet with the medicine thought it was easy to access (n=170, 80.6%), but fewer considered it easy to understand (n=143, 67.8%), relevant to them (n=122, 57.8%) and trustworthy (n=130, 61.6%). Again, this is supported by responses to open questions.

"I am not good English" (P 39; Male, 36)

"Hard to understand, want to ask something I don't understand" (P65; Female, 23)

"It is hard to read the leaflet in the box, my eyesight is not as it was before and the writing on the leaflet is very small. The leaflet contains too much information, things that are not relevant to me personally." (P152; Male 75)

Trust in the information was an important reason for preferring verbal information over the leaflet. They preferred to rely on their doctor. They believed that verbal information from the doctor provided them with more comprehensive information than the leaflet, which was also specific to them. Importantly, some respondents mentioned too much information, the font size used in the leaflet and distrust in manufacturers.

"I usually throw the leaflet away, I trust the word of my doctor or pharmacist. Leaflets are not visually appealing to me, they contain too much info and I don't consider them to be very important." (P157; Male, 26)

"Cannot reliable to manufacturer" (P92; Male, 51)

"I wouldn't bother to read it. Also instructions tend to be written in a tiny font size which just seems to discourage me to read" (P120; Male, 24)

Some participants thought that the leaflets seemed unnecessary in their opinion, not even opting to read them. The technical terms and side effects in the leaflet made them feel worried.

"Written info on leaflets have too much info, and I normally throw it away as too much info can worry me. The whole list of side effects on the leaflet scares me." (P159; Male, 19)

"Too much info on the leaflet, too wordy and very difficult words to read sometimes. I don't use it, I just throw it away. Not useful." (P160 ; Male, 60)

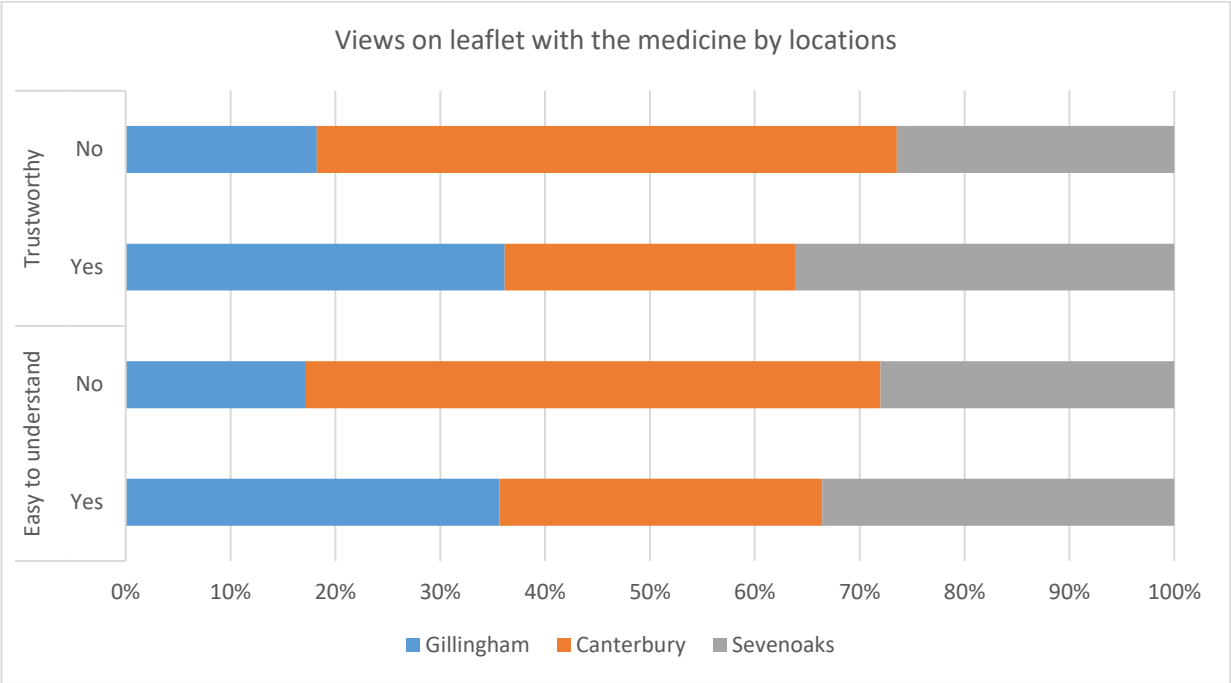
The characteristics of the 69 (32.5%) participants who selected leaflet with the medicine, but did not consider it easy to understand, were 18-60 age groups (n=50, 72.5%), female (n=46, 66.7%), and had either technical college (n=25, 36.2%) or university degree (n=29, 42.0%). Importantly, they (n=48, 69.6%) had used a medicine regularly in the past 3 months. In addition, there were 82 participants who preferred the leaflet with the medicine, but did not expect to trust them. These respondents were female (n=54, 65.9%), had either technical college (n=22 ,26.8%) or university degree(n=36, 43.9%). They (n=58, 70.7%) had also taken a medicine regularly in the past 3 months.

Among those participants who selected the leaflet with the medicine, participants who had used medicines regularly in the past three months (n=130, 61.6 %) were more likely to think that the leaflet was easy to understand ($p<0.001$). They (n=120, 56.9%) were more inclined to believe in the leaflet with the medicine ($p<0.001$). They also considered that the leaflet was relevant to them (n=113, 53.6%) and easy to access (n=151, 71.6) ($p<0.001$). Using medicines regularly was probably the key factor in influencing participants' views on the leaflet.

The participants (n=61, 28.8) who were in the 31-60 age group generally had a higher percentage of trustworthiness in the leaflet with the medicine ($p < 0.05$). Older people (n=58, 27.5%) considered leaflets more relevant to them than younger people ($p<.001$), and trustworthiness in leaflets also increased with age.

Ease of understanding, relevance and trust in a leaflet with the medicine was also affected by location, with participants recruited in Canterbury (moderate IMD) being less likely to view leaflets as understandable, relevant and trustworthy than those recruited in other locations ($p< 0.001$). In contrast, participants recruited in Gillingham (high IMD) were more likely to find leaflets easy to access ($p<0.05$), perhaps because a higher proportion were regular medicine users (Figure 7-4). Participants' gender, education, ethnicity and first language had no effect on views.

Figure 7-4 Views on PILs by location



Over half of participants agreed that they would use information on the dispensing label/ medicine envelope (n= 159, 53.0%), most of whom considered labels to be easy to access (n= 117, 73.6%). Government websites were also considered easy to access (n=157, 52.3%) and trustworthy (n=117, 74.5 %). Digital platforms (n= 19, 6.3%) were the least popular medicine information sources. The different views of participants on information sources are shown in Table 7-8. Figure 7-5 summarizes participants' opinions for each information source.

Table 7-8 Participant views on information sources

Source	Yes	% of 300	Easy to access	% of Yes	Easy to understand	% of Yes	Relevant to me	% of Yes	Trustworthy	% of Yes
Verbal from health professional	275	91.7	136	49.5	179	65.1	180	65.5	233	84.7
Drug company information on medicine container	135	45.0	88	65.2	66	48.9	53	39.3	53	39.3
Dispensing label/ medicine envelope	159	53.0	117	73.6	99	62.3	99	62.3	92	57.9
Leaflet with medicine	211	70.3	170	80.6	143	67.8	122	57.8	130	61.6
Leaflet from health workers	83	27.7	48	57.8	54	65.1	38	45.8	56	67.5
Government website	157	52.3	121	77.1	108	68.8	85	54.1	117	74.5
Manufacturer website	46	15.3	25	54.3	13	28.3	15	32.6	18	39.1
Patient support group website	73	24.3	49	67.1	47	64.4	42	57.5	38	52.1
Pharmacy website	61	20.3	43	70.5	33	54.1	20	32.8	29	47.5
Hospital website	44	14.7	26	59.1	20	45.5	12	27.3	27	61.4
Advertising on TV/radio/magazine	48	16.0	38	79.2	33	68.8	13	27.1	8	16.7
News reports	43	14.3	34	79.1	24	55.8	10	23.3	4	9.3
Mobile application	67	22.3	59	88.1	38	56.7	28	41.8	23	34.3
Social media/family and friends	112	37.3	85	75.9	73	65.2	65	58.0	63	56.3
Digital platform	19	6.3	14	73.7	6	31.6	4	21.1	2	10.5

Figure 7-5 Top five of the most preferred medicine information sources and perceptions of these

7.4.4 Medicine information needs

The respondents were asked about their needs for medicine information in future. The most desired information related to possible side effects (n=291, 97.0%), how to use the medicine (n=283, 94.3%), the name of the medicine (n=282, 94%), and what it is for (n=281, 93.7%). More than 85% of people preferred to receive the information when they were first given a medicine. Table 6-9 shows participants views on their needs for medicine information in future.

Table 7-9 Needs for medicine information in future

Medicine information	Yes	n/300	When first given	% of yes	Later after using for some time	% of yes
Name of medicine	282	94.0	279	98.9	10	3.5
What it's for	281	93.7	280	99.6	3	1.1
How to use it	283	94.3	282	99.6	4	1.4
Possible side effects	291	97.0	273	93.8	33	11.3
What you should avoid	265	88.3	243	91.7	33	12.5
Anything which means the medicine may not be right for you	248	82.7	230	92.7	27	10.9
How to store it	214	71.3	192	89.7	30	14.0
What to do if you miss a dose	230	76.7	201	87.4	42	18.3
How to get more information	175	58.3	148	84.6	36	20.6

7.4.5 Preferences for medicine information sources

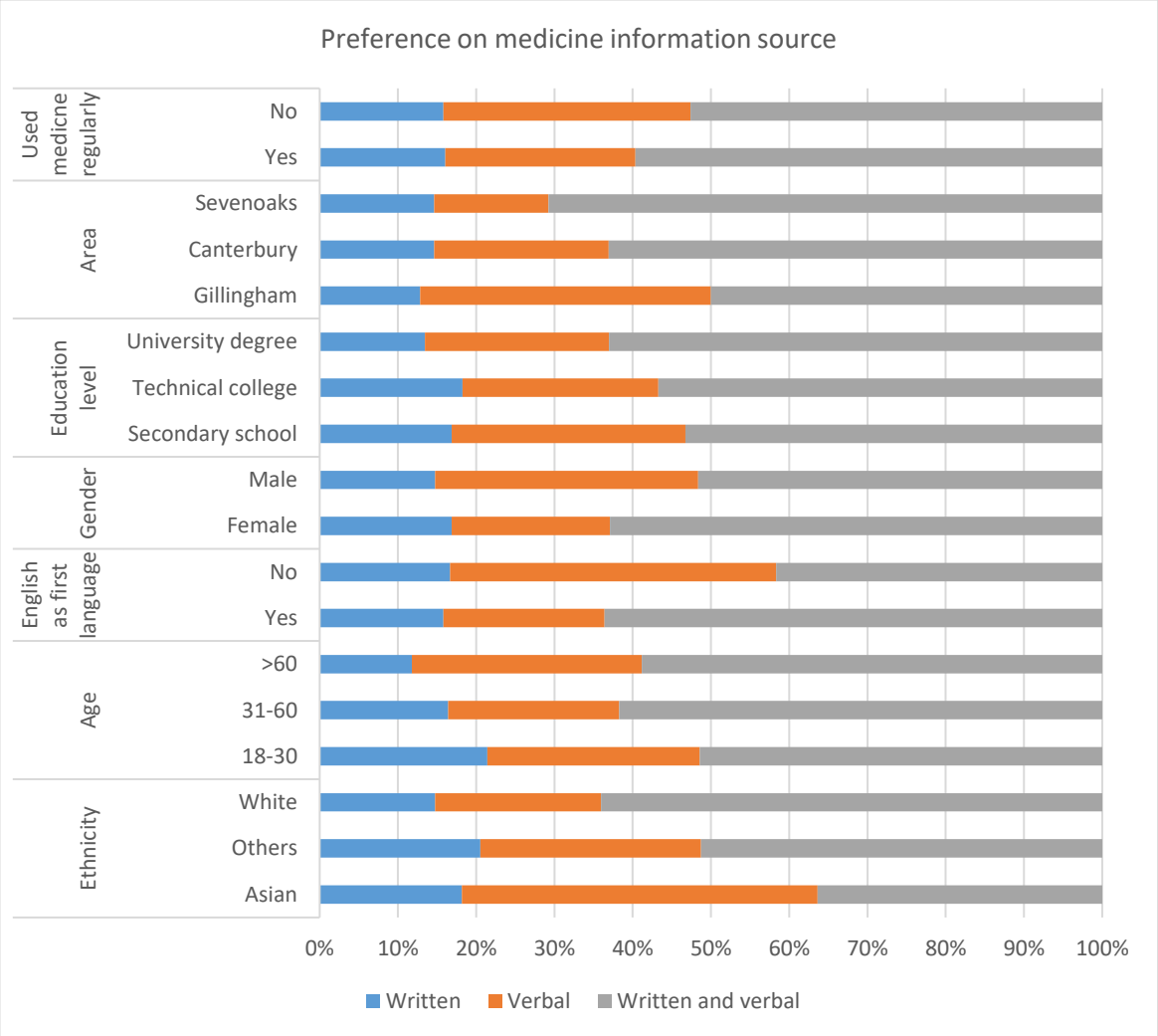
Overall, a higher number of participants in every age group (n=175, 58.3%) preferred both written and verbal information rather than either written or verbal information alone. Almost half of participants who preferred both written and verbal information were in the 31-60 age group (n=79, 45.1%).

A higher proportion of female respondents (n= 112, 62.9%) preferred to get medicine information in the form of both written and verbal information than males (62; 51.2%) ($p < 0.05$). There were also differences in the preferred way of getting information dependent on whether English was the first language. Respondents whose first language was not English (n=30, 41.7%) were more

likely to prefer verbal information only (p = 0.001), those whose first language was English preferred written and verbal medicine information.

Most respondents of white ethnicity (n=139, 64.1%) preferred both written and verbal medicine information, while most of Asian ethnicity (n=20, 45.5%) preferred verbal information from health care professionals (p<0.05). Education did not affect preferences. Figure 7-6 shows the preferences for medicine information sources by characteristic.

Figure 7-6 Preferences for future medicine information by characteristic



Participants described the advantage of having both written and verbal information as greater ease of understanding, and synergistic to each other. Verbal gives the opportunity to ask specific questions of health care providers so that particular concerns or issues can be addressed, whilst written provides an easy way to remember the medicine information or to refer back to something at a later point if necessary. It enables people to reflect on the information that they have received and helps to re-enforce key facts. It is particularly useful when reviewing the

administration guidelines for technical devices such as inhalers. Doctors and other HCPs were regarded as providing trustworthy information, which they could individualise for patients by highlighting certain paragraphs of relevance in the leaflets or recommending certain websites for more information.

"Written information is useful to refer to when I'm at work or at home, doctors advise me how to correctly use medicine, tell me the relevant info as written information is more generalised to everyone. So useful to have both with doctors involved in tailoring the leaflet to my needs. Pharmacists very helpful in tailoring this info to me" (P144; Female, 32)

"Written information has really helped me when I was put on inhalers, the pictures and diagrams helped me to understand how to use the inhalers. Verbal information from the pharmacist helped me to use the inhalers, with written info to refer to later on." (P153; Female, 38)

"Verbal information from doctors as they are trustworthy and give me the best advice, with it being accurate and reliable. Plus they can refer me to other useful information such as my leaflet" (P177; Male, 67)

"Written information so I can read at home, verbal information so the doctor can inform me how to take my medicines, most of the written info is irrelevant to me so my doctor highlights which part of the leaflet I should focus on" (P150; Male, 65)

"Verbal information has become very important to me recently, due to my pregnancy, nurses and doctors have been very attentive towards me in helping me through my pregnancy and answering any questions I have about my medicines. Written information from online websites on how to use my medicines correctly and ensure my baby is safe at the same time has been really helpful too. Especially with the websites being recommended by doctor and nurse." (P 171 ; Female, 36)

Written information was highlighted as being accessible to those with special needs such as those who were deaf or had hearing difficulties, although some aspects of the format of the leaflets, such as the font size, were identified as suboptimal. Whilst some participants thought that HCPs were easy to access others indicated that their experience differed. Participants recognized the time-pressure of standard patient consultations.

"If you are deaf you can read, leaflet font is too small." (P76; Male, 30)

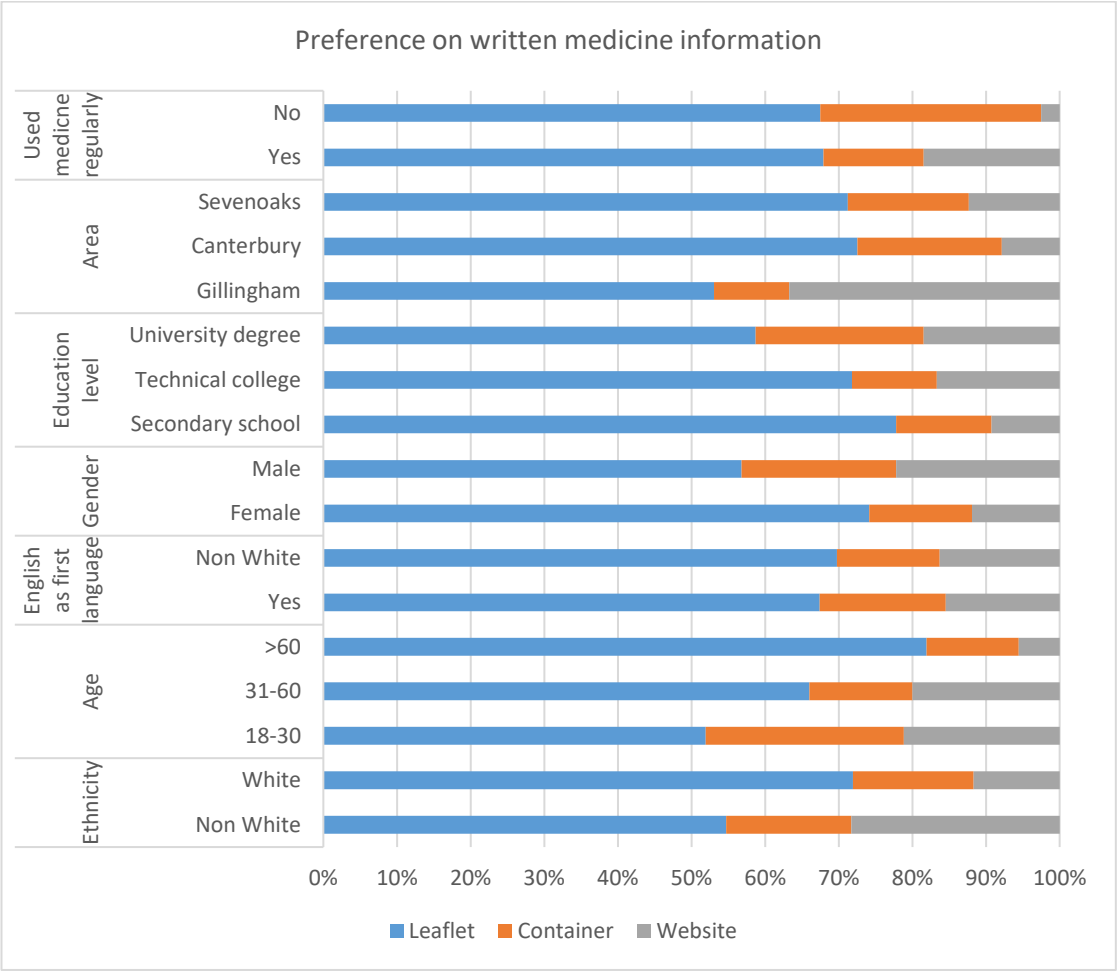
"Verbal info as doctors are accessible to me through my private clinics, follow what the doctors said since they know all about my condition and refer to leaflet in any special cases as easy to access" (P222; Female, 47)

“Verbal info so I can ask extra questions if I'm confused and written info is accessible and I can easily refer to it when needed. I couldn't have verbal info only as I could forget key info, doctors aren't fully accessible and they're rushing through consultations.” (P148; Female, 22)

Participants also considered that the health care professional knows their health conditions well and can provide suitable suggestions to them.

In particular, 224 participants (74.7% of the total) who preferred to have any written information indicated that leaflet with the medicine was their preferred written medicine information source (n= 152, 67.9%). The leaflet was the preferred source of written medicine information, irrespective of age and location. A higher proportion of female respondents (n = 106, n = 74.1%) selected leaflet with the medicine as their preferred source of written medicine information compared to males (46; 57.5%) ($p < 0.05$). Information on a website was the least preferred medicine information source for the over 60 age group (n=4, 5.6%) ($p<0.05$). The smallest number of participants (n= 5, 2.2%) who chose the information on the container as their written medicine information was found in Gillingham ($p < 0.001$). Figure 7-7 shows the preferences of participants for different written medicine information sources.

Figure 7-7 Preferences for written medicine information by characteristic



Data from open questions confirmed that many participants, particularly older participants, preferred leaflets over a website because they found the information easier to access, read and understand. Lacking computer hardware, a stable Internet connection or confidence in their own IT skills, required to access websites and on-line information, were often mentioned as reasons why PILs were preferred. That every medicine was packaged with a PIL was cited as an advantage in terms of accessibility. Furthermore, HCPs helped patients to individualise leaflets as they were described as directing the patient to specific points of information that were of relevance to them. Patients reported that they could refer to the leaflet at any time, and annotate it for themselves. In contrast to those who considered leaflets untrustworthy, because of being produced by manufacturers, some respondents regarded leaflets as being reliable in terms of the accuracy and validity of information they contained because they were reviewed or their content directed by a 'Government source'. These participants described the Internet as containing a lot of information some of which was biased and confusing.

"Leaflets are easier to read then websites online, I cannot access the Internet properly on my own so I just read the highlighted bits my doctor tells me to read" (P 177, Male, 67)

"Leaflet to look side effects, understand what is happening Website don't understand to use it" (P298; Female, 81)P183

"leaflets are government entailed, they are useful for the public to use, websites don't always have a lot of information and my doctor normally only refers me to leaflets" (P183; Female, 33)

"Older people may not have access to websites, websites give conflicting info" (P19; Female, 64)

"Leaflet is nice to be included with medicine, have all the info. Leaflets are concise and it's what government wants you to know, this info has been screened for suitability but websites can provide false info e.g. Wikipedia" (P148; Female, 22)

"Not trust with all websites. Forget where to find information online and may end up with something ridiculous" (P299 ; Female, 44)

"Information on a leaflet about my inhalers is all there, it's easy to access and I don't have to search any other info unless my doctor or pharmacist encourages me to look at a certain website. I feel more comfortable when I'm using a leaflet as a source of info. Websites can be tricky to use, in that the info may not be reliable or trustworthy and is it validated? It depends on the website." (P153; Female, 38)

"Websites can be tricky to rely on, it depends on if my doctor suggests I look at a certain website. I wouldn't check anything without checking with my doctor first. If my doctor or pharmacist sees my leaflet as a good source of info, I will use it."(P158; Male, 21)

However, a minority did prefer websites over PILs because websites provided additional information to the PIL, were easier to search for specific information, didn't need to be filed and then retrieved and were accessible at any time via a mobile phone. One participant suggested that medicine containers should contain a link directly to information about the medicine. Other reasons given for preferring a website included that information could be shared or discussed among friends, that the information was easier to read and up to date, and that the environment might be more protected by using websites. On-line support groups were also acknowledged as a resource that could be accessed via the Internet.

"Because it generally gives additional information and it would contain information that the leaflet might not have mentioned." (P134; Female, 19)

"Easier to access. Leaflets are verbose and hard to read through. Websites are easier for picking out info" (P41; Female, 86)

"Handy, easy to search, always lose the leaflet. Good for environment. Easy to share with people who have same disease" (P7; Female, 31)

"Because website info are always updated, always on my phone, sends you up to date info" (P143; Male, 55)

"Websites are easy to access on my phone, it comes with updated information so you know it's reliable. Leaflets contain too much information, some which may not be relevant to me." (P155 ; Male, 18)

"Websites are more up to date, I like the support groups online for pregnant mums, as we can all discuss together on how to use our medicines, and if I have any queries. It's very useful and accurate." (P171; Female, 36)

Previously mentioned negative aspects of leaflets with medicine were highlighted again, and contrasted with online information.

"Easier to access. Leaflets are verbose and hard to read through. Websites are easier for picking out info" (P41; Female, 86)

"Websites are easy to access and use, they are easier to read as well. Leaflets can have difficult words or phrases that I sometimes have to google, like complicated side effects in the leaflet. I usually throw away the leaflet as soon as I get my medicine." (P156 ; Male, 23)

"Websites are very informative, have different level of information and breaks down information simply then leaflets. leaflets have very difficult words, sometimes I don't understand" (P180; Male, 60)

"For factual evidence, drug companies may not be trustworthy" (P137; Male, 66)

In comparison between the source of medicine information that participants had received in the past 3 months and their preferred source, participants (n=124, 63.9) who received written medicine information preferred written together with verbal information. Those who had not received any information (n=26, 57.8) stated a preference for verbal. Half of the respondents (n=27, 49.1),who had received verbal information, agreed that this had met their needs. Focusing on written medicine information, most participants (n=152, 67.9%) needed written medicine

information in the form of a leaflet with the medicine. The comparison between the source of medicine information received in the past 3 months and preferences for format of medicine information and written information are shown in Table 7-10 and Table 7-11, respectively.

Table 7-10 Comparison between source of medicine information in the past 3 months and preference for medicine information

Preference on medicine information	Source of medicine information in the past 3 months (%)			
	Written Information (n=197)	Verbal Information (n=55)	Other (n=3)	Didn't receive (n=55)
Written	36 (18.3)	4 (7.3)	0 (0.0)	8 (17.8)
Verbal	37 (18.8)	27 (49.1)	2 (66.7)	11 (24.4)
Written and verbal	124 (63.9)	24 (43.6)	1 (33.3)	26 (57.8)

Table 7-11 Comparison between the source of medicine information in the past 3 months and preference on written information.

Preference on written medicine information	Source of medicine information in the past 3 months			
	Written Information (n=161)	Verbal Information (n = 28)	Other (n=1)	Didn't receive (n=34)
Leaflet	118 (73.3)	14 (50.0)	1 (100.0)	19 (55.9)
Information on the medicine container	23 (14.3)	10 (35.7)	0 (0.0)	4 (11.8)
Website	20 (12.4)	4 (14.3)	0 (0.0)	11 (32.4)

Despite differing views on leaflets versus online information, most people agreed that both the PIL and information about all medicines on a government website were extremely important to provide to every patient (Table 7-12). Over half of every age group (176 of 300 (58.7%)) believed that a leaflet was an extremely important medicine information source which must be provided with all medicines, while there were 96 (32.0%) and 70 (23.3%) who considered that providing medicine information on a Government website was extremely important and somewhat important, respectively. Focusing on age group, a higher percentage of participants aged 18-30

(n=33, 47.1%) and 31-60 (n = 45, 35.2%) thought that it was extremely important to provide medicine information on a government website, whereas more participants who were more than 60 years old judged it to be not at all important (n=35, 34.3%) (p<0.001).

Table 7-12 Opinions on how important participants perceived the availability of information either in a leaflet provided with their medicines or on a government website

	Number (%)			
	Age 18-30 (n=70)	Age 31 – 60 (n=128)	Age >60 (n=102)	Total (n=300)
1. How important is it to you that a leaflet for patients is given with all medicines?				
Extremely important	37 (52.9)	73 (57.0)	66 (64.7)	176 (58.7)
Very important	20 (28.6)	23 (18.0)	20 (19.6)	63 (21.0)
Somewhat important	8 (11.4)	12 (9.4)	7 (6.9)	27 (9.0)
Not so important	5 (7.1)	11 (8.6)	5 (4.9)	21 (7.0)
Not at all important	0 (0.0)	9 7.0()	4 (3.9)	13 (4.3)
2. How important is it to you that information about all medicines is available on a government website?				
Extremely important	33 (47.1)	45 (35.2)	18 (17.6)	96 (32.0)
Very important	21 (30.0)	31 (24.2)	10 (9.8)	62 (20.7)
Somewhat important	12 (17.1)	33 (25.8)	25 (24.5)	70 (23.3)
Not so important	2 (2.9)	12 (9.4)	14 (13.7)	28 (9.3)
Not at all important	2 (2.9)	7 (5.5)	35 (34.3)	44 (14.7)

7.5 Discussion

7.5.1 Use of medicines by the general public

This study involved the general public while previous studies in the UK aimed to investigate views in specific groups of patients with asthma, learning disability, cancer, and other conditions.[77,78,248]

Whilst quota sampling was attempted, difficulty was experienced in recruiting participants, particularly in the area of low IMD, resulting in a higher than average representation of females

in the study compared to average for the Kent and Medway area. Furthermore fewer people of white ethnic origin, compared to population data from the Kent and Medway area, were included.[285]

Many studies found that women were more interested in, and actively seek, health-related information than men. According to employment data, the female employment rate reached an all-time high of 72.4 percent in October-December 2019. The male labour force participation rate was 80.6 percent. Part-time employment was held by 40% of working women versus 13% of men. On weekdays, men may be more likely than women to go to work. These findings may explain why women were more likely than men to participate in this health-related survey. [287–289, 290]

In this survey 80% of participants used medicines regularly in the past 3 months (on most days). This proportion was higher than a previous study that found that only 50% used a regular medicine[113] because of the broader definition used in this study of using medicine regularly. This study did not focus only on using medicine in chronic diseases, but also included participants as regular medicine users if they had used medicines on most days with in the past 3 months for any reason.

Considering age and gender, it was found that using medicine increased with age, 19% of young adults aged 16 to 24 had taken one or more medicines in the last week, and this increased to more than 90% of those aged 75 and over. Also women were more likely than men to use prescribed medicine and those from an area of high deprivation were more likely to be using regular medicines than those from areas of lower deprivation. This reflected NHS data in 2016 which revealed that prescribed medicine use increased with age, that women used more prescribed medicine than men and the prevalence of prescribed medicine use was higher in the more deprived areas. [291]

Community pharmacies and doctors in health centres were the major source of obtaining medicines for the general public. Within the health care system in the UK, most medicines, particularly if they are taken on a regular basis, are prescribed by the patients' General Practitioner (GP), and then dispensed by a community pharmacist, therefore it is not surprising that community pharmacy and doctor in health care centre were the major source of medicines. From NHS data in 2017/18, the proportion of prescriptions dispensed by community pharmacy, dispensing GPs and appliance contractors was 91.6%, 7.6% and 0.8%, respectively.[292]

Retail outlets such as Boots and Wilko are also places where the general public can purchase over-the-counter medicines for mild illnesses. This may explain why the retail outlet was the most frequently used in the 18-30 and 31-60 age groups, who were less likely to be suffering from chronic disease than the over 60 age group, more of whom received medicines from their doctor.

7.5.2 Using medicine information in general public

The sources of medicine information used by the general public, focused on in this study, included written information (leaflets, information on the containers, websites), verbal information, and others (family and friends, digital media). Previous studies in the UK have also shown that the most common medicine information sources were patient information leaflets, verbal information, and information on the Internet.[91,106] In contrast, other studies have shown that written information was not the most frequently used and that verbal information from health workers was the primary source of medicine information for prescription drugs. In these studies, conducted in Saudi Arabia, Armenia, Pakistan, and Singapore, written information was viewed as complementary to the verbal instructions of doctors and pharmacists.[10,91,95,97]

Age group was an important factor affecting the source of medicine information received. Younger respondents were least likely to have received verbal information and most likely to have used other sources. This was possibly associated with where they obtained their medicine from which was the retail outlet where verbal information from a health care professional was not available. An alternative explanation is that they did not expect to receive verbal information in retail-outlet.

The majority of the participants received information about the medicines they had used. A much higher proportion of participants usually received written information in comparison with verbal and other sources of information. Most of them who received medicine information chose to read information written on the leaflet (72.5%) and information on the medicine container (76.0%) as their first choice of medicine information sources. This is similar to studies which found that 67-75% of people in England read the PILs.[113,120,293]

Apart from in the UK, studies from Saudi Arabia, Palestine, and Nigeria have revealed that the percentage of the public reading the patient information leaflet ranged from 45%-90.6%.[918684]

It is compulsory by law among EU countries that manufacturers must provide a leaflet with the medicine together with written information on the medicine container so that this can be the easiest accessible information, which patients can read on any occasion. The information on the

container, the so-called label, can be another source of medicine information. The items required on the label are shorter than in the leaflet and include the name of the medicine, expression of strength (where relevant), route of administration, posology, and warnings. [294] However for dispensed medicine, there is also a requirement for the pharmacist to attach a dispensing label to the container, providing a third source of written medicine information. This must include the name of the medicine, strength, dose for the particular patient, and any important additional administration instructions and warnings.[295]

The majority of the general public stated that they normally read the information when they were first given the medicine, followed by when they wanted to check whether the medicine was safe to take with another medicine. These findings support former studies in Egypt, Palestine, Saudi Arabia, Armenia, and the UK that found that most patients read the information when first-time of using a medicine.[76,83,86,91,95,97]

The participants also used the provided information for checking when to use the medicine, identifying the possible side effects, and checking whether the medicine was suitable for them. The findings reveal that most participants usually read the sections relating to the method of administration, adverse effects, and contraindications. The results were similar to the previous studies in Armenia, Singapore, Korea, Saudi Arabia, Nigeria, Egypt, and the UK that found that the information viewed as most important and needed by patients/ the general public were adverse effects, dosage, indications, and method of administration, duration of treatment, expiry date, and contraindications [10,83,84,91,97,106,120]

Verbal was the second most frequent source of medicine information with the majority receiving this from their doctor, followed by their pharmacist. They talked to their health professional when they have been prescribed the medicine, and when they had a prescription dispensed. Other studies in Armenia, Pakistan, Singapore, South Africa, Thailand, and the UK have similarly found that physicians and pharmacists were the most commonly used source of information about prescribed medicines.[10,70,77,78,95,97,98,113,123]

Other sources of information such as family and friends, or digital media were perceived as less important amongst the general public. This is in contrast to previous research in Iran and Australia which has found that relatives or friends were common sources for non-prescription medicines.[70,103] Friends and family were infrequently used, but one study in Sri Lanka suggested that family and friends may be important sources for people who have no Internet access.[296]

7.5.3 Perceptions of the general public on different medicine information sources

This survey found that the large majority of people would prefer to obtain information about their medicine verbally from a health worker and the leaflet with the medicine. Verbal information was assessed as the most trustworthy and leaflets as the most accessible sources. Both sources have been reported as preferred information sources previously, both in England and other countries.[293,296]

With regard to verbal information, the reasons to support verbal information which was the most important source and be repeatedly mentioned by general public were that this type of information is provided from someone whom they trust, is easier to understand, provides an opportunity to ask questions, and is specific to a patient's health conditions. Earlier studies in Armenia, Australia, Sri Lanka, and the UK have shown similar results. Within these studies most patients stated that medicine information from the staff of community pharmacies was judged to be important for patients and the majority of them trusted the information received. Receiving information from a doctor significantly improved their knowledge about their medicines. [78,97,104,297]

However, verbal information was judged to be much less accessible than written information. This has been found in previous studies.[293,296,298] Although verbal information was much less accessible the ability to tailor information to the individual, through having all relevant medical information about that individual was thought to be of greater importance than accessibility. [293,298]

In term of the leaflet, there were both positive and negative points of view. The leaflet with the medicine is general public's knowledge source. This supports previous research conducted in Palestine and the UK that some people thought that the leaflet could generate new knowledge and may have a positive impact on behaviour.[76,86,114,119] The information was easier to access, read and understand.

The results also showed that participants who have regularly used a medicine in the past three months had more likely thought that the leaflet with the medicine was easy to understand. They were also more likely to trust the leaflet. Ease of understanding and trust in a leaflet with the medicine was also affected by location of living. This may be because people who live in in high IMD area had higher prevalence of prescribed medicine use than those in lower deprived area[291] and therefore could be assumed to have more experience with and familiarity in using a medicine leaflet. Participants recruited from an area of high IMD were however also more likely to have

received verbal information as well as written information and their more positive views on overall ease of understanding of information they received, perhaps surprising given the likelihood of lower educational levels in areas of high IMD, may be related to this.

The participants also assumed that leaflets could be counted on in terms of the accuracy and validity of information which was reviewed and conducted by a government body. Importantly, some expressed distrust in manufacturers. Previous work in the same geographical area found similar views in relation to PILs, with most considering them easy to access, but fewer considering them trustworthy and easy to understand and also that verbal information from health workers was the most trustworthy information source.[293]

Nevertheless, the PIL were that the leaflets were easily lost, often difficult to read with small font and text size, and contained information that was outdated, basic and directed at the general population rather than specific to individual conditions. Respondents also reported problems in term of language used, medical terms which were difficult to understand. Some recognized that they were written by manufacturers which raised doubts about their trustworthiness. The information written with technical terms in the leaflet made some feel worried.

These findings support a large number of studies which found that people in many countries were dissatisfied with poor format and language used in medicine leaflets. They had some difficulty in comprehension or understanding related to the language used, technical terms, and the small font size used. They felt that PILs raised fears and concerns.[79,84,87,91,95,107,248]

In term of written medicine information on websites, strengths and weaknesses were defined. In general, the websites seem to be accepted that it is the centre of knowledge. The participants preferred websites because websites provided additional information to the leaflet. It is also easier to search for specific information, can accessible at any time via information technology devices e.g. mobile phone, laptop. The information and experiences could be shared or discussed among group of people with the same conditions. The information was also easier to read and up to date.

A prior study found that the Internet plays an important role as an easily accessible medicine information source. A literature review and some studies conducting in the UK, and also found the Internet to be cited as the most frequently used source of health information.[10,296]

This study supported the results that information from, in particular, the government website was easy to find and understandable. However, another research study revealed that it was difficult to find reliable information on the Internet. They perceived it difficult to find reliable

information on the Internet as well.[10] This current study also found that the Internet was described as containing a lot of information some of which was biased and confusing.

Overall, ease of access was considered as a key characteristic which may explain the frequent use of PILs as an information source. This was a similar result that strongly supports a previous study which investigated in using information sources regarding medicine side effects among the general population.[293] Sources such as leaflet and the Internet, although viewed as trustworthy by fewer people, were probably most likely to be used as a complementary source to seeking information from a health professional.[296]

7.5.4 Preferences for medicine information sources

The general public anticipates and is entitled to receive good quality information about their medicines, whether they are prescribed or bought over the counter. Good information can encourage patients to participate fully and be confident in decision making about the medicines they are prescribed.[1] It may also increase their adherence.[105]

The most important finding from this study is that verbal together with written information (leaflet with the medicine) is the most preferred way to receive medicine information. General public needs medicine information in the way that they can have face-to-face communication, opportunity to ask questions, specialized information to individual conditions, trustworthiness, easy to understand, easy to access information. However, they also need written information to refer to when they want to check for specific details. A previous study from Ghana found that more people read leaflets if told to do so by a pharmacist.[80] Therefore, pharmacists should provide verbally information while encouraging the patient to read the leaflet together.

The preferred way of getting information depended on whether English was the first language. Participants whose first language was not English were more likely to prefer verbal information only than the remaining respondents. This was also found in previous studies which investigated patient's information needs and preferences. Studies in Palestine and Pakistan revealed that patients need medicine information in their own languages.[86,96] Gender and ethnicity were also factors affecting the preferred way of getting medicine information. Women are more active information seekers than men.[287–289] In term of ethnicity, this is a category of people who identify with each other, usually on the basis of presumed similarities such as a common language, culture, social treatment, or behaviour. As a result, these characteristics can affect the preferred way of getting medicine information one way or another.

As mentioned previously, preferences for a leaflet with the medicine was influenced by location, gender, and having experience of using medicine regularly. The leaflet was also assessed as easiest to access and one of the easiest to understand sources of medicine information.

Providing a leaflet with the medicine to every patient was seen as an extremely important issue for most participants. However, age group influenced the opinion of government websites, with older age groups less likely to consider this as important than younger age groups. Younger respondents had more need for medicine information on the government website than older respondents. This finding was similar to prior studies showing that age group only affected potential use of the Internet and receiving information on some specific topics. [97,293]

7.6 Strengths and limitations

This study used a quota sampling technique which sought to maximise diversity and ensure a representative sample of demographic factors of participants particularly their gender, age and location. The questionnaire was designed and developed to include every aspect of receiving medicine information.

In the sample size calculation, some statistical indicators, including p-values and confidence intervals, were used to help determine that the results observed did not arise by chance. Any significant error in the sample size calculation will have an impact on the power and value of a study. This study calculated the sample size based on assumption from an earlier study that, in 2013, 75% of patients in England read the PILs. This study was conducted in National Health Service (NHS) hospitals in North West England involving 1,218 in-patients. If this assumption has changed, the study may be underpowered to detect the desired difference and the truth.[299]

Despite the adoption of quota sampling the actual sample recruited included a higher proportion of females, and fewer people of white ethnic origin compared to population data from the Kent and Medway area. In addition, the sample included a high proportion of respondents with higher educational levels than the UK average. Surveying in the winter months was not conducive to data collection as participants were reluctant to stand out in the cold whilst completing the survey. The length of questionnaire may also have reduced participation.

7.7 Recommendations and future work

There were similar findings to other studies that medicine information leaflets did not currently meet the needs of patients. Individualized information was also valued and medicine leaflets were generally seen as less helpful than face-to-face advice because they couldn't deliver this.

Using medicines regularly was the key factor in considering using leaflet. This study showed strong evidence that people who used medicine regularly had the potential to read the leaflet with the medicine in the future because they considered the leaflet as easy to understand, trustworthy, accessible, and relevant to them, significantly. Their experiences should be valued. Therefore, this supports the prior study that patients with long experience of using medicines should be involved in the development of medicine information leaflets.[78]

The most favourable characteristic of verbal information is the ability to tailor information to the individual. This characteristic may be of greater importance than other sources.[298] All of these results reveal the importance of verbal together with the leaflet with the medicine as the most desired medicine information source.

Therefore, the healthcare professionals should pay attention to patients as individuals when providing information, to ensure that it meets their needs. There is a need for healthcare professionals to evaluate patient comprehension and need for drug information. This is also the suggestion for pharmacists, in particular, which need to be aware of a patient's desire for personalised medicines information and seek to maximise communication with their patients about their individual information needs during consultations.[75]

The leaflet with the medicine was also defined as the preferred way to get written medicine information. However, the study findings supports those of prior studies in that even though the leaflet was the most preferred way to receive medicine information and is developed with due regard to international standards, it still did not fully meet the general public's needs.[249] Finding out what patients and public needs are and ensuring they are met within the leaflet is essential, before applying into the practice.

Moreover, previous research has found that their participants appreciated the concept of tailored information, desiring shorter and more relevant information. Information tailored to their condition or disease was most sought-after, followed by tailoring by age or gender. [75,78,86,96]

The language used was a critical factor, for participants supporting prior studies that the leaflet must be written in a local language, [75,84,86] but also terminology needs to be considered. The information on the government website must be tailored as well.

More studies to investigate and explore how information on the leaflet and government website could be tailored to fit with patient needs should be carried out. The provision of targeted patient information could facilitate a dialogue about a patient's medicine information needs.

Chapter 8 Sources of medicine information in the Thailand: A public perspective

8.1 Introduction

Previous studies have explored the views of patients in Thailand on medicine information[98,273] and recently, a new survey has sought the views of the general public.[100] However it was considered valuable to compare directly the use of medicine information sources and opinions on these between the UK, where medicine information systems are well established, and countries such as Thailand, where the system is developing. Therefore, in addition to the survey carried out in the UK, a parallel study was carried out in Thailand. The present study was conducted in Songkhla province which is located in the southern part of Thailand. The same protocol was used for these two surveys. The questionnaire was translated into Thai so that the results can be equally compared. However, there is a difference in routine dispensing practice. In Thailand, medicines have been supplied with either strip of the medicine in an envelope dispensed, or in the original pack, Contrastingly, in the UK, the medicines have been dispensed with the original packaging with labels on the package. Therefore, the questionnaire had to be changed slightly in order to accommodate this difference.

8.2 Aim and objectives

The aim of the study was to identify medicine information sources used, and views on different sources and perceived needs for medicine information among the general public in Songkhla Thailand with experience of using medicines.

8.2.1 Objectives

1. To identify medicine information sources used by general public
2. To describe how general public use the medicine information
3. To find out the perceptions of the general public on different medicine information sources
4. To determine preferences for the content and format of medicine information among the general public

8.3 Method

This study was a cross-sectional questionnaire-based survey study, carried out between January and February 2020 in Songkhla province. The study surveyed the general population in term of their medicine information source, and their preferences on each source.

8.3.1 Instrument development

1. Questionnaire translation

   Back-translation technique was used to validate the questionnaire. A native Thai speaker (the principal researcher) translated the English language of the questionnaire into Thai. A native Thai speaker who is proficient in the English language re-translated the Thai language of the questionnaire into English version. Then, the back-translation and the original document were compared by a native English speaker (the co- researcher) to find out for discrepancy. Then, the inconsistencies were corrected. The translation was considered equivalent if no disagreement was found.

2. Pilot testing

   The Thai questionnaire was piloted prior to use in a sample up to 30 members of the public. This was conducted by two Thai research students. As same in the UK, this process was conducted to ensure that the Thai research students developed interviewing skills as well as validating appropriateness of the translated questionnaire. Participants were provided with a participant information sheet (Appendix 7). Verbal informed consent was obtained from every participant prior to interview. All comments were used to improve and amend the Thai questionnaire.

8.3.2 Participant inclusion and exclusion criteria

The adult population in Songkhla province were used as a sampling frame. As well as in the UK, quota sampling approach was used to cope with diversity and reflected the demographic factors including gender, age and socioeconomic status.

c. Inclusion Criteria
   1. Participants were older than 18 years old.
   2. Participants were able to communicate in Thai
   3. Participants currently used at least one regular medicine, or have used a medicine in previous 3 months.

d. Exclusion criteria

1. Participants who had no experience of using a medicine themselves in the previous 3 months.
2. Participants who were unable to communicate in Thai.
3. People who did not want to take part in the study.
4. Participants who were health professional or training in health care sciences.

8.3.3 Main survey - General method

1. The survey was a collaboration between the principal researcher and two Thai undergraduate pharmacy students. The survey was conducted in general public places in Songkhla province. The survey procedure was similar to that carried out in the UK.
2. Before the survey, the two fieldwork interviewers completed on-line Good Clinical Practice: ICH-GCP training. Interviewing training and mock data collection were also carried out.
3. Where permission was necessary, a formal request for access to places was issued. The data collection could only be started in these places when permission was obtained.
4. To conduct the survey, each step of surveying Thailand; approaching the participants, screening, informing consent, and interviewing was followed by the procedure carried out in the UK.

8.3.4 Sample size calculation

The sample size calculation used for this study was the same as in Chapter 7,. The following formula was used:

$n = N*X / (X + N - 1)$, where,

$X = Z_{\alpha/2}^2 * p*(1-p) / MOE^2$,

and $Z\alpha/^2$ is the critical value of the normal distribution at $\alpha/2$ (for a confidence level of 95%, α is 0.05 and the critical value is 1.96), MOE is the margin of error, p is the sample proportion, and N is the population size.

Adult population size in Songkhla province were 1,417,440 persons.[300] For the sample proportion, one study found that 28% of people in Thailand read the PIL (p=28%).[225] Therefore, assuming that taking a confidence level of 95%, α was 0.05 and the critical value was 1.96, MOE is 5%, minimum sample size computed was 310. However, the sample size was adjusted to 350 respondents.

In order to ensure variation in deprivation: high, medium and low, areas were selected for quota sampling, while the possibility for travel and safety were taken into consideration. In each area, the population was classified according to gender, age. In order to ensure sufficient participant numbers were included in each quota, subsequent sampling units were selected. Three sub-districts of Songkhla province, Thailand were selected: Hatyai, Namom, and Khlong Hoi Khong. These areas were chosen by their tax revenue; high, medium, and low, respectively. Numbers of participants were based on population size in each area.

8.3.5 Participant recruitment procedures

The researchers worked at various selected public places, with frequent numbers of passers-by. Individual passers-by were approached by one researcher, and invited to participate by completing the face-to-face interview. Again, as same as in the UK, the study was briefly communicated and some screening questions were asked. If a person qualified for inclusion and accepts to be a participant, he/she has been recruited.

8.3.6 Ethical issue and informed consent

This study was approved by the Prince of Songkla University Ethic Committee (Appendix 8). Participants were given a participant data sheet (Appendix 6) which contains information of researchers' contact if they have concerns about the study and how they are concerned about the purpose of the study, the risks and benefits of participating, and the use of these anonymous data. The participants were also asked to express their verbal consent, an integral part of this questionnaire.

8.3.7 Data analysis

The data analysis was analysed using the statistical programme SPSS. Data from the Surveymonkey programme was exported directly into SPSS, then, as with the UK survey, cleaning data was conducted, following by recoding and managing of any missing data. Descriptive statistics were used. Frequency distributions and means were used to describe categorical and continuous variables, respectively. The hypotheses that sources of medicine information used, views on different medicine information sources, and preferred ways of getting this information were different depending on age, gender, and education were tested. The chi-squared test or Fisher's exact test were used to determine whether there were any significant differences between sub-groups.

8.4 Results

Initially, there were minor differences between the original and back-translated versions of the questionnaire. The inconsistencies were then corrected until there was no longer any disagreement. Furthermore, the pilot study results were used to improve and modify the Thai questionnaire. Minor changes were made to accommodate the Thai public's cultural and contextual acceptability.

8.4.1 General information

A total of 352 participants were included; 23 in Khlong Hoi Khong, 20 in Namom, and 309 in Hatyai. The target numbers, and participants recruited in each area is shown in Table 8-1.

Table 8-1 The target numbers, and participants recruited in each area.

		18-30		31-60		>60		
		Male	Female	Male	Female	Male	Female	Total
Low income (Khlong Hoi Khong)	Target	4	3	6	6	2	2	23
	Achievement	3	4	6	6	2	2	23
	Difference	-1	+1	0	0	0	0	
Medium income (Namom)	Target	2	2	5	6	2	2	19
	Achievement	1	3	4	6	3	3	20
	Difference	-1	+1	-1	0	+1	+1	
High income (Hatyai)	Target	42	43	78	95	22	29	309
	Achievement	49	59	65	99	16	21	309
	Difference	+7	+16	-13	+4	-6	-8	

Table 8-1 shows the difference between the target and number of recruited participants. The major differences were in Hatyai. The target sample in each group was not achieved because of time restrictions. People over 60 years old were not willing to stop and be included into the survey. Men were less cooperative than women in taking the surveys.

A total of 352 patients were included in the survey. All of them were of Thai ethnicity. The majority of the respondents were female (n=203, 57.7%). This compares to a population of 51.2% females (2016) in Songkhla. The percentage of females was slightly higher than average number of females in Songkhla.

Thai language was the first language for most of them (n=346, 98.3%). Five and one participant spoke Malay and Chinese language as their mother tongue language, respectively. Most participants (n=282, 80.1%) were able to read English; however: their level of English was not tested.

Most respondents had a university degree (n=219, 62.2%). The percentage of participants who have higher education was much higher than the percentage of people who have higher education in the Songkhla province. Data from the Songkhla labour population survey shows there were 24.4% with primary education, 47.6% with secondary education, and 19.9% with a technical college education, or university degree.[300]

The majority of participants (n=273, 77.6%) did not use any medicines regularly. However, some (n=79, 22.4%) had used medicines regularly (on most days) in the past 3 months, and stated that they (n= 60, 17.0%) had regularly used 1-2 medicines. The general characteristics of participants are shown in Table 8-2.

Table 8-2 Summary of demographic characteristics of participants

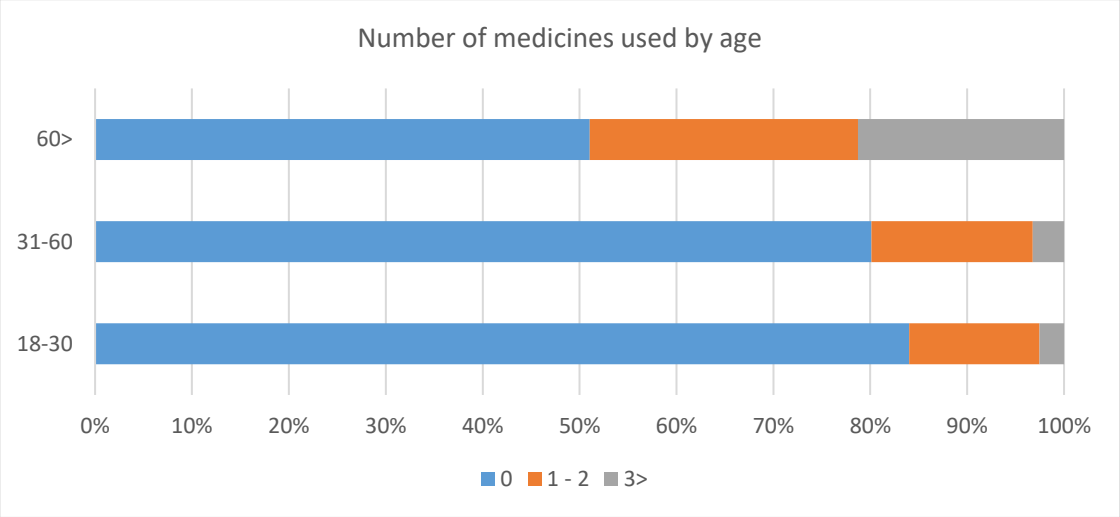
Demographic	Number (%)			
	Age 18-30 (n=119)	Age 31 – 60 (n=186)	Age >60 (n=47)	Total (n=352)
1. Gender				
Male	51 (42.9)	73 (39.2)	20 (42.6)	144 (40.9)
Female	66 (55.5)	111 (59.7)	26 (55.3)	203 (57.7)
Gender diverse	2 (1.7)	2 (1.1)	0 (0.0)	4 (1.1)
Prefer not to say	0 (0.0)	0 (0.0)	1 (2.1)	1 (0.3)
2. Ethnicity				
Thai	119 (100.0)	186 (100.0)	47 (100.0)	352 (100.0)
3. First language				
Thai	115 (96.6)	184 (98.9)	47 (100.0)	346 (98.3)
Others	4 (3.4)	2 (1.1)	0 (0.0)	6 (1.7)
4. Read English				
Yes	107 (89.9)	152 (81.7)	23 (48.9)	282 (80.1)
No	12 (10.1)	34 (18.3)	24 (51.1)	70 (19.9)
5. Read Thai				
Yes	119 (100.0)	186 (100.0)	47 (100.0)	352 (100.0)
5. Education				
Primary school	0 (0.0)	7 (3.8)	12 (25.5)	19 (5.4)
Secondary	32 (26.9)	28 (15.1)	9 (19.1)	69 (19.6)
Technical College	9 (7.6)	26 (14.0)	10 (21.3)	45 (12.8)
University	78 (65.5)	125 (67.2)	16 (34.0)	219 (62.2)
6. Using Medicine regularly				
Yes	19 (16.0)	37 (19.9)	23 (48.9)	79 (22.4)
No	100 (84.0)	149 (80.1)	24 (51.1)	273 (77.6)
7. Number of regular Medicines				
0 Items	100 (84.0)	149 (80.1)	24 (51.1)	273 (77.6)
1-2 items	16 (13.4)	31 (16.7)	13 (27.7)	60 (17.0)
≥ 3 Items	3 (2.5)	6 (3.2)	10 (21.3)	19 (5.4)

8.4.2 Medicine utilization

There were 23 of 47 (48.9%) of adults who were more than 60 years old and had regularly taken at least one prescribed medicine in the past 3 months. The prevalence of taking medicines increased greatly with age, from 16.0% of those aged 18 to 30 to 48.9 % of those aged over 60

(p<0.001). The percentage of those taking 1-2 medicines regularly increased greatly with age, from 13.4 % of those aged 18 to 30 to 27.7 % of those aged over 60, and taking at least three medicines from 2.5% of those aged 18 to 30 to 21.3 % of those aged more than 60. (p<0.001). For all participants, women (n= 47, 13.4%) were more likely than men (n=32, 9.1%) to use medicines regularly. The number of medicines used by age is shown in Figure 8-1.

Figure 8-1 Number of medicines used by age



In the survey, all participants were asked to think about any medicines they had used in the past 3 months and interviewed about their views on these medicines.

The total number of medicine sources cited was 594. As shown in Table 8-3, the most common places where participants obtained medicines were community pharmacies (n=230, 65.3%) followed by the hospital (n=202, 57.4%). While hospital was the most frequent source of obtaining medicine in older adults (> 60 years old), community pharmacy was the most frequent choice for younger adults aged 18-30 years old (n=83, 69.7%) and 31-60 years old (n=127, 68.3%). Retail outlets (n=23, 19.3%) and friends and family (n= 14, 11.8%) were the other main sources of medicine for the 18-30 year old age group. Age group influenced on obtaining medicine from community pharmacy (p<0.05), Retail outlet (p < 0.001), friend and family (p < 0.001). A private clinic was the alternative source of medicines for 18-30 year olds (n=32, 26.9 %) and also the over 60 age groups (n=12, 25.5%). The proportion of source of obtained medicines by age group is shown in Figure 8-2. Participants with university degree obtained medicine from a private clinic more than those with lower education (p = 0.05).

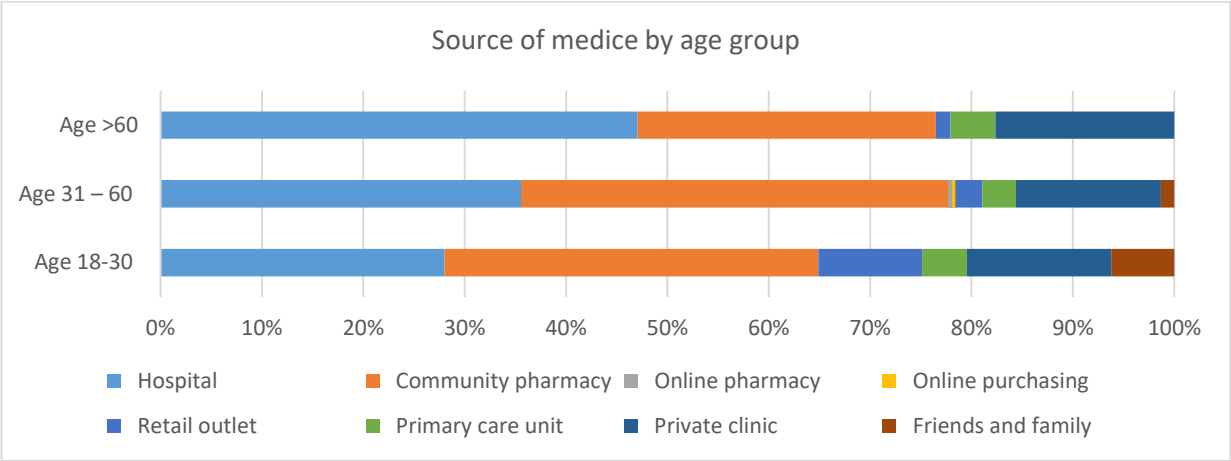
Just over half of participants obtained medicines from only one source (n=192, 54.5%) with nearly one third using two sources (n= 100, 28.4%). A minority of participants obtained the medicines from more than two sources (n= 60, 17.0%).

These data also show that the majority of participants (n=344, 97.7%) received the medicines only from health professional sources e.g. hospitals, community pharmacies, health centres, and private clinics. A very small minority of participants (n=8, 2.3%) used only sources other than health care professionals (retail outlet, online purchase, friend and family). There were 40 participants (11.4%) who obtained medicines from both types of sources. A summary of where participants had obtained medicines from and whether they had received information with their medicines in the past 3 months by age group is shown in Table 8-3.

Table 8-3 Using medicine in the past 3 months

Obtaining medicines in the past 3 months	Number (%)			
	Age 18-30 (n=119)	Age 31 – 60 (n=186)	Age >60 (n=47)	Total (n=352)
1. Obtaining medicines from				
Hospital	63 (52.9)	107 (57.5)	32 (68.1)	202 (57.4)
Community pharmacy	83 (69.7)	127 (68.3)	20 (42.6)	230 (65.3)
Online pharmacy	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.3)
Online purchasing	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.3)
Primary care unit	10 (8.4)	10 (5.4)	3 (6.4)	23 (6.5)
Private clinic	32 (26.9)	43 (23.1)	12 (25.5)	87 (24.7)
Retail outlet	23 (19.3)	8 (4.3)	1 (2.1)	32 (9.1)
Friends and family	14 (11.8)	4 (2.2)	0 (0.0)	18 (5.1)
2. Receiving any information about these medicines				
Yes	117 (98.3)	182 (97.8)	45 (95.7)	344 (97.7)
No	2 (1.7)	4 (2.2)	2 (4.3)	8 (2.3)

Figure 8-2 Source of obtained medicines by age group



8.4.3 Sources of medicine information

Focusing on medicine information sources, the majority of the respondents (n=344, 97.7%) stated that they had obtained some information about their medicine, while the remaining eight participants (2.3%) indicated not receiving any information.

The major sources of information regarding the medicines were verbal from health care professional (n=314, 91.3%), followed by written information (n= 224, 65.1%), and few used other sources of information (TV, radio, newspaper, magazine, mobile app, social media, family member or friend, digital platform [e.g. Alexa, Siri]) (n=49, 14.2%).

Of the 344 participants who had obtained information, almost all (n=341, 99.1%) received either written information or verbal information from health professionals. There were 197 (56.0%) respondents who received a combination of written and verbal information.

There were 44 (12.5%) participants who received written information and also obtained additional information from other sources, such as friends and family, while 43 (12.2%) received both verbal information from health professionals and other sources.

Only three (0.8%) participants only received information from other sources. Therefore, in total, only 11 (3.1%) participants did not receive any written and verbal medicine information from reliable sources. Types of medicine information obtained by participants are shown in Table 8-4.

Table 8-4 Types of medicine information obtained

Types of information	Number (%)			
	Age 18-30 (n=117)	Age 31 – 60 (n= 182)	Age >60 (n=45)	Total (n=344)
Written information	78 (66.7)	120 (65.9)	26 (57.8)	224 (65.1)
Verbal information	105 (89.7)	167 (91.8)	42 (93.3)	314 (91.3)
Others	17 (14.5)	28 (15.4)	4 (8.9)	49 (14.2)

Use of written information is the main focus of this study. The survey reveals that leaflets (n =192, 85.7%) and information on the medicine container (n =209, 92.9%) were the primary sources of written information. Most leaflets received were those included in the medicine container (n = 164, 85.4%), which in Thailand could be a PIL or a PI, the remainder being provided by a health professional (n=28, 14.6%).

Only three of 19 respondents (15.8%) who had educational level in primary school had received a leaflet about their medicine, while 127 (58.8%) of the 219 participants who graduated with university degree received a leaflet ($p < 0.05$).

Use of written information on medicine containers included information written on the medicine envelope by the person who dispensed the medicine (n=135, 64.6%), and information printed on a label by the person who dispensed the medicine (n=107, 51.2%), or information printed on the container by the manufacturer (n=107, 51.2%). The majority (n=177, 79.0%) of participants who used written information stated that they read a combination of the leaflet and information on the container.

Fewer respondents (n =153, 68.3%) reported that they had used a website as a medicine information source. The majority of sites searched for information were a government organisation website [Thai Food and Drug Administration (FDA)] (n=91, 59.5%), followed by a drug company website (n=25, 16.3%).

The participants who indicated they have used written information (n=224) were further asked about when they looked at it. The most frequent time was when they were first given the medicine (n=128, 57.1%), followed by when they wanted to check information when something unexpected happened (n = 85, 37.9%), or to check whether it was safe to take another medicine 57 (25.4%). Nearly half (n = 76, 40.0%) had looked at the information they received two or three times.

There were 190 participants (84.8%) who claimed to have used the provided information. The most frequently cited reasons were to check if the medicine was suitable for them (n=137, 72.1%), to check when to use the medicine (n = 124, 65.3%), and to identify possible side effects (n=100, 52.6%). The results of using written information are shown in Table 8-5.

Table 8-5 Type of written information accessed and how it was used.

	Number (%)			
	Age 18-30 (n=78)	Age 31 – 60 (n=120)	Age >60 (n=26)	Total (n=224)
1 What type of written information have you seen?				
a. A leaflet about your medicine	68 (87.2)	105 (87.5)	19 (73.1)	192 (85.7)
b. Information on the medicine container	69 (88.5)	115 (95.8)	24 (92.3)	209 (93.3)
c. Website	52 (66.7)	87 (72.5)	14 (53.8)	153 (68.3)
2 When/how did you get the leaflet?				
a. in medicine pack,	54 (79.4)	95 (90.5)	15 (78.9)	164 (85.4)
b. given by doctor or other health worker	14 (20.6)	10 (9.5)	4 (21.1)	28 (14.6)
3 What was the information on the container like? (Total n=209)				
a. printed on a label by the person who dispensed the medicine	34 (49.3)	61 (52.6)	12 (50.0)	107 (51.2)
b. written on the medicine envelope by the person who dispensed the medicine	48 (69.6)	77 (66.4)	10 (41.7)	135 (64.6)
c. printed on the container by the manufacturer	37 (53.6)	59 (50.9)	11 (45.8)	107 (51.2)
4 Which website(s) have you looked at for information about your medicine? (n= Total 153)				
a. Government organisation website	33 (63.5)	51 (58.6)	7 (50.0)	91 (59.5)
b. drug company website	9 (17.3)	15 (17.2)	1 (7.1)	25 (16.3)
c. pharmacy website	8 (15.4)	14 (16.1)	0 (0.0)	22 (14.4)
d. patient organisation website	2 (3.8)	9 (10.3)	0 (0.0)	11 (7.2)
e. hospital website	8 (15.4)	13 (14.9)	3 (21.4)	24 (15.7)
f. I can't remember	11 (21.2)	13 (14.9)	4 (28.6)	28 (18.3)
g. Others	4 (7.7)	3 (3.4)	1 (7.1)	8 (5.2)
5 When did you look at the information?				
a. when you were first given the medicine	46 (59.0)	68 (56.7)	14 (53.8)	128 (57.1)
b. when something unexpected happened	27 (34.6)	51 (42.5)	7 (26.9)	85 (37.9)
c. when you wanted to find out whether you were able to drink or drive or use machinery	17 (21.8)	13 (10.8)	1 (3.8)	31 (13.8)

	Number (%)							
	Age 18-30 (n=78)		Age 31 – 60 (n=120)		Age >60 (n=26)		Total (n=224)	
d. when you wanted to check if it was safe to take another medicine	26	(33.3)	24	(20.0)	7	(26.9)	57	(25.4)
e. I never looked at the information	9	(11.5)	21	(17.5)	4	(15.4)	34	(15.2)
f. Others	3	(3.8)	4	(3.3)	0	(0.0)	7	(3.1)
6 How often have you looked at the information? (once only, two or three times, more than three times) (n=190)								
a. once only	15	(21.7)	39	(39.4)	8	(36.4)	62	(32.6)
b. two or three times	34	(49.3)	37	(37.4)	5	(22.7)	76	(40.0)
c. more than three times	20	(29.0)	23	(23.2)	9	(40.9)	52	(27.4)
7 How have you used the information? (Total n = 190)								
a. to check when to use the medicine	51	(73.9)	56	(56.6)	17	(77.3)	124	(65.3)
b. to check if the medicine was suitable for you	56	(81.2)	65	(65.7)	16	(72.7)	137	(72.1)
c. to make sure you avoided certain other medicines	22	(31.9)	26	(26.3)	6	(27.3)	54	(28.4)
d. to make sure you avoided certain foods or drinks	26	(37.7)	29	(29.3)	8	(36.4)	63	(33.2)
e. to identify possible side effects	39	(56.5)	53	(53.5)	8	(36.4)	100	(52.6)
f. to decide if it was safe to drink or drive or work with machinery	14	(20.3)	19	(19.2)	2	(9.1)	35	(18.4)
g. to find out what to do when I missed a dose	14	(20.3)	15	(15.2)	2	(9.1)	31	(16.3)
h. other way……	0	(0.0)	1	(1.0)	0	(0.0)	1	(0.5)

The majority of medicine information was provided verbally with most participants (n=314, 91.3%) receiving verbal information from health care professionals. There were 117 (33.2%) respondents who claimed not to have received written information, but did receive verbal information about their medicines.

The majority of these respondents had talked with their pharmacist (n=93, 79.5%) or doctor (n=30, 25.6%). They talked to their health professional when they obtained a medicine for the first time or for refills (n=57, 48.7%), and when they bought the medicine (n=49, 41.9%). Use of verbal medicine information is shown in Table 8-6. The three participants who had used only other sources of verbal medicine information received information from family and friends (n=2) and television (n=1).

Table 8-6 source of verbal information

Verbal information	Number (%)			
	Age 18-30 (n=37)	Age 31 – 60 (n=61)	Age >60 (n=19)	Total (n=117)
1 Who talked to you about your medicine(s)?				
a. doctor	9 (24.3)	16 (26.2)	5 (26.3)	30 (25.6)
b. pharmacist	31 (83.8)	48 (78.7)	14 (73.7)	93 (79.5)
c. nurse	3 (8.1)	1 (1.6)	3 (15.8)	7 (6.0)
d. health worker	4 (10.8)	0 (0.0)	1 (5.3)	5 (4.3)
2 When did they talk to you?				
a. when you were prescribed the medicine	3 (8.1)	2 (3.3)	1 (5.3)	6 (5.1)
b. when you had a prescription dispensed for the first time or for refills	20 (54.1)	25 (41.0)	12 (63.2)	57 (48.7)
c. when you bought the medicine	14 (37.8)	28 (45.9)	7 (36.8)	49 (41.9)
d. when you asked them questions	3 (8.1)	3 (4.9)	2 (10.5)	8 (6.8)
e. when you had a review	4 (10.8)	11 (18.0)	3 (15.8)	18 (15.4)

The participants were asked their opinions in term of how easy all the information they obtained was to understand and whether it was sufficient. A third of the 310 participants who responded to this question gave a neutral opinion (n=101, 32.6%) neither difficult or easy to understand, while 162 (52.3%) considered it easy/very easy to understand (n=96, 31.0%) and 47 (15.2%) difficult/very difficult. Furthermore, the majority considered the information received about their medicines was sufficient for their needs (n=171; 55.2%). There were 106 (34.2%) participants who thought that they had received more information than they needed, but only 33 (10.6%) who felt they needed more. Table 8-7 shows proportion of the opinion about all medicine information in different age groups.

Table 8-7 Opinion on all medicine information

	Number (%)							
	Age 18-30 (n=108)		Age 31 – 60 (n=161)		Age >60 (n=41)		Total (n=310)	
1 How easy was the information to understand?								
1 Very easy	14	(13.0)	40	(24.8)	12	(29.3)	66	(21.3)
2	38	(35.2)	43	(26.7)	15	(36.6)	96	(31.0)
3	30	(27.8)	59	(36.6)	12	(29.3)	101	(32.6)
4	23	(21.3)	16	(9.9)	1	(2.4)	40	(12.9)
Very difficult	3	(2.8)	3	(1.9)	1	(2.4)	7	(2.3)
2 Was the information enough for what you needed?								
1 Need a lot more	1	(0.9)	3	(1.9)	0	(0.0)	4	(1.3)
2	14	(13.0)	14	(8.7)	1	(2.4)	29	(9.4)
3	55	(50.9)	88	(54.7)	28	(68.3)	171	(55.2)
4	37	(34.3)	50	(31.1)	12	(29.3)	99	(31.9)
5 More than I need	1	(0.9)	6	(3.7)	0	(0.0)	7	(2.3)

8.4.4 Perceptions of sources of medicine information

All participants were interviewed about their opinions on different possible information sources: whether they would use each source and, if yes, whether they thought that it would be easy to access, easy to understand, relevant to them and trustworthy.

Overall, most people (n=348, 98.9%) preferred verbal information from health professional, many of whom thought this source was trustworthy (n=258, 74.1%) and easy to understand (n=257, 73.9%), but few thought it was easy to access (n=65, 18.7%), and relevant to them (n=62, 17.8%).

These findings are supported by responses to an open question on the desirability of verbal information. Participants described that verbal medicine information from health care professionals was easier to understand. They preferred face-to-face information as this communication provided them an opportunity to ask questions, discuss, as well as get more detailed information. They thought that receiving information verbally gave the doctor the opportunity to emphasize the information that they need to know. The information received in this way was easier to remember.

"It is easy to understand, doctor can emphasize information that I need to know" (P159; Male, 40)

Trustworthiness and confidence were issues that participants gave as reasons for preferring verbal medicine information over written information. They believed that their doctors were the person who knew their specific health and medicines needs. Also the fact that health professionals have been highly trained was mentioned.

"Trust the doctor and would like to take medicine under doctor's advice" (P26; Female, 63)

"I trust verbal information and I am confident to take medicine along with their suggestions" (P114; Female, 21)

"Verbal come from health professionals who are trained specifically." (P254; Female, 43)

"It is easy to understand, trustworthy. I can ask questions. Doctors can emphasize the information I need to know" (P314; Female,41)

The second most frequent choice of medicine information source was the dispensing label/ medicine envelope (n=317, 90.1%). A high number of people who selected the dispensing label/medicine envelope thought it was easy to understand (n=188, 59.3%), but fewer thought it was easy to access (n=123, 38.8%), trustworthy (n=89, 28.1%), and relevant to them (n=59, 18.6%). The third most frequent option for a medicine information source was the manufacturer's information on the medicine container (n=298, 84.7%). More people considered this as a source which was easy to access (n= 146, 49.0%) and trustworthy (n=115, 38.6%), but fewer thought it was easy to understand (n=141, 47.3%) and relevant to them (n=37, 12.4%).

The leaflet provided with the medicines, which in Thailand could be a PIL or a PI, was ranked as the fourth most preferred written information source (n=287, 81.5%). However only around half considered they would use a leaflet because it was easy to understand (n=151, 52.6%), and less than half that it was easy to access (n=127, 44.3%), trustworthy (n=96, 33.4%), and relevant to them (n=39, 13.6%).

The characteristics of the 136 (47.4%) participants who selected leaflet with the medicine who did not consider it easy to understand, were younger than 60 (n=71, 52.2%), female (n=80, 58.8%), and had a university degree (n=98, 72.1%).

There were 191 participants who preferred the leaflet with the medicine, but did not expect to trust them. These respondents were mostly female (n=119, 62.3%), had university degree

(n=123, 64.4%). However few of them (n=42, 22.0%) had taken a medicine regularly in the past 3 months.

Generally, participants who had a university degree (n=187, 53.1%) would be more likely to use the leaflet with the medicine ($p<0.001$) than participants who had a technical and primary education. Younger adults with 18- 30 (n=101, 84.9%) and 31-60 (n=154, 82.8%) were more likely to prefer the leaflet than adults aged 60 or over(n=32, 68.1%) ($p<0.05$).

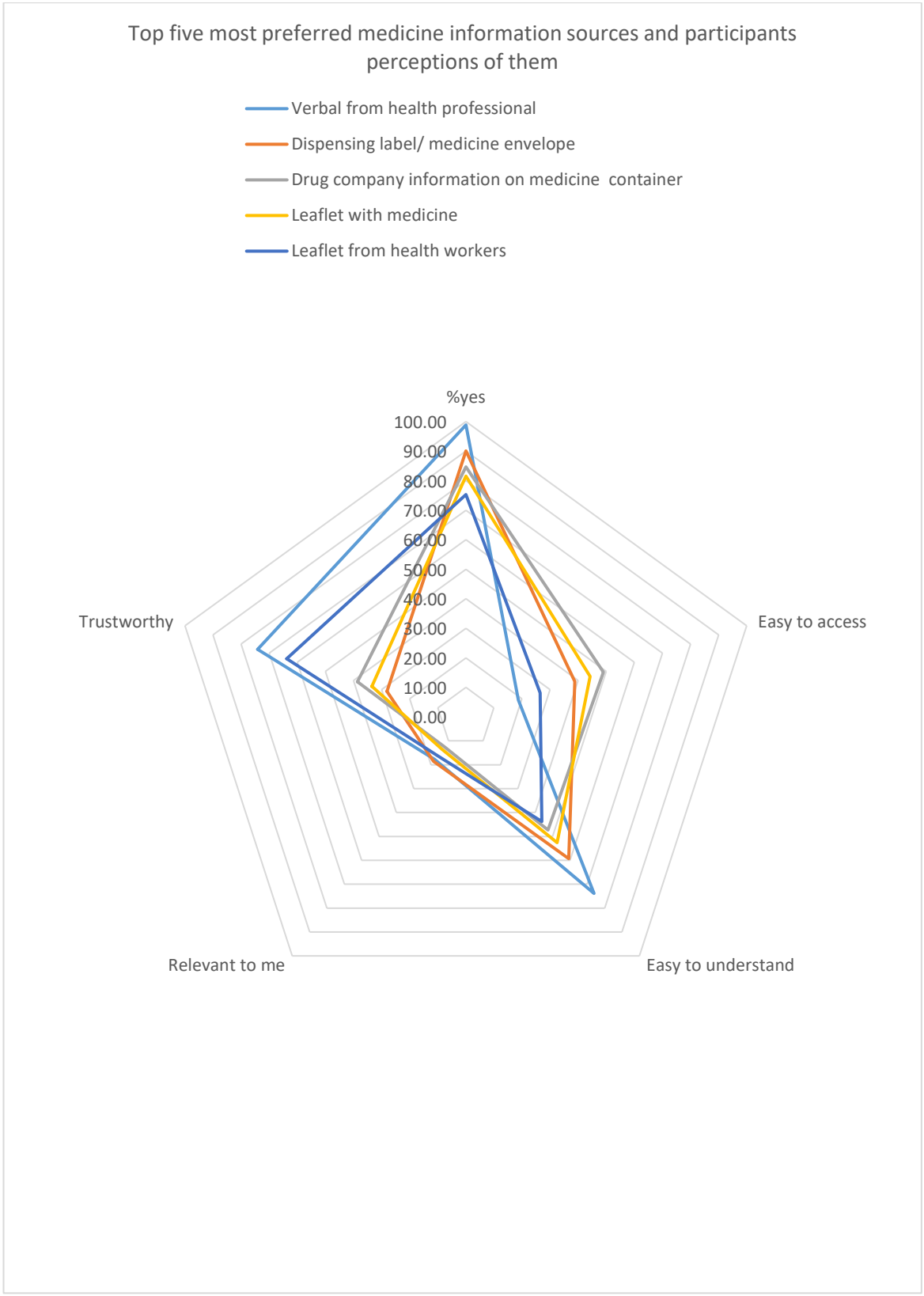
Trust in a leaflet with the medicine was also affected by gender, with males (n=51, 53.1%) being more likely to view them as trustworthy than females (n=43; 44.8%). ($p< 0.05$).

Over half of participants agreed that they would use information on government websites (n= 109, 54.5%), The websites were considered easy to access (n=109, 56.8%) and trustworthy (n=89, 46.4%). Digital platforms (n= 99, 28.1%) were the least popular medicine information sources. The different views of participants on information sources are shown in Table 8-8 and Figure 8-3summarizes participants' opinions for each information source.

Table 8-8 Participant views on information sources

Source	Yes	% of 300	Easy to access	% of Yes	Easy to understand	% of Yes	Relevant to me	% of Yes	Trustworthy	% of Yes
Verbal from health professional	348	98.9	65	18.7	257	73.9	62	17.8	258	74.1
Drug company information on medicine container	298	84.7	146	49.0	141	47.3	37	12.4	115	38.6
Dispensing label/ medicine envelope	317	90.1	123	38.8	188	59.3	59	18.6	89	28.1
Leaflet with medicine	287	81.5	127	44.3	151	52.6	39	13.6	96	33.4
Leaflet from health workers	265	75.3	70	26.4	116	43.8	43	16.2	169	63.8
Government website	192	54.5	109	56.8	48	25.0	19	9.9	89	46.4
Manufacturer website	174	49.4	93	53.4	55	31.6	16	9.2	70	40.2
Patient support group website	157	44.6	76	48.4	55	35.0	14	8.9	58	36.9
Pharmacy website	162	46.0	87	53.7	54	33.3	21	13.0	48	29.6
Hospital website	188	53.4	95	50.5	61	32.4	18	9.6	95	50.5
Advertising on TV/radio/magazine	178	50.6	113	63.5	82	46.1	11	6.2	29	16.3
News reports	186	52.8	126	67.7	73	39.2	17	9.1	30	16.1
Mobile application	184	52.3	130	70.7	72	39.1	27	14.7	21	11.4
Social media/family and friends	183	52.0	119	65.0	73	39.9	39	21.3	16	8.7
Digital platform (e.g. Alexa, Siri)	99	28.1	72	72.7	31	31.3	9	9.1	12	12.1

Figure 8-3 Top five of the most preferred and perception on medicine information sources



8.4.5 Medicine information needs

The respondents were asked about their needs for medicine information in the future. The most desired information related to what it's for (n=350, 99.4%), how to use the medicine (n=348, 98.9%), the name of the medicine (n=44, 97.7%), and possible side effect (n=340, 96.6%). More than 86% of people preferred to receive the information when they were first given a medicine. Table 8-9 shows participants views on their future medicine information needs.

Table 8-9 Needs for medicine information in future

Medicine information	Yes	n/300	When first given	% of yes	Later after using for some time	% of yes
Name of medicine	344	97.7	337	98.0	18	5.2
What it's for	350	99.4	350	100.0	12	3.4
How to use it	348	98.9	347	99.7	11	3.2
Possible side effects	340	96.6	295	86.8	60	17.6
What you should avoid	313	88.9	293	93.6	31	9.9
Anything which means the medicine may not be right for you	296	84.1	247	83.4	61	20.6
How to store it	317	90.1	287	90.5	43	13.6
What to do if you miss a dose	302	85.8	252	83.4	63	20.9
How to get more information	250	71.0	200	80.0	59	23.6

8.4.6 Preferences for medicine information sources

Overall, a higher proportion of participants (n=165, 46.9%) preferred both written and verbal information rather than either written or verbal information alone, with no differences dependent on age or gender.

Although only 19 respondents had primary level education, none of this preferred written information, compared to 13-16% of those with higher educational levels. More also want verbal only as opposed to verbal and written medicine information.

Responses to open questions explained participants' preferences for both written and verbal information as being easy to understand, and they can get complete and correct information. Verbal provision provided the opportunity to ask questions to their health care providers so that

they could receive more clear information, and could get the detail that they want to know. They also needed information that was specific information to their condition, and only key information which verbal information can be tailored. Specifically, verbal information seemed to be ready to use, they had no need to read by themselves.

"Verbal is clear and can ask questions can read leaflet at any times when needed" (P31; Female, 54)

"Verbal is clear and straight to the point, specific for me. A leaflet is easy to access" (P201; Female, 52)

"Verbal information, I can get correct information, prevent misunderstanding. I can read leaflet later, it is just for reminding me later" (P212; Female, 40)

Verbal information can also give health-care professionals the opportunity to show patients how to use some medicines clearly and correctly, in particular, with inhaled medicines. Written information was considered to be suitable for caregivers as a means of ensuring that the caregiver, who was also able to understand the information, had access to it.

"Written information is suited for a patient who has caregiver because their caregiver can understand the same information" (P280; Male, 49)

"It is too much information, do not understand" (P19; Male, 46)

"I am not confident whether the leaflet is suitable for my disease." (P297, Male, 55)

"Reading cannot show you how to use an inhaler. Only reading might make me misunderstand and cannot use inhaler correctly. It had small texts" (P316, Female, 45)

Participants perceived verbal and written information provided by health care professionals to be trustworthy. Participants anticipated that the health care professional knew their health conditions well and could provide tailored suggestions and advice for them. Some participants also trusted the information provided by manufacturer. Many participants stated that written information was useful as it could be referred to at any time.

"For verbal, I can be taught from the Doctor directly. The leaflet is for reminding me." (P277, Female, 30)
"Need clear information from doctor at the first time and, the leaflet is for reminding" (P129; Male, 20)

"I would like a confirmation from a doctor. Trust information from drug company." (P118; Female, 29)
"Verbal is easy to understand and clearer, Keep leaflet for reference" (P294, Male, 41)

Participants who preferred both verbal and written information felt more confident and safe when they took their medicines.

"Both verbal information and the leaflet make me feel confident and safe" (P284; Female, 51)

There were 130 (36.9%) participants who preferred verbal information as their medicine information source. A minority of participants (n = 52, 14.8%) stated that they would like to use only written medicine information.

When considering the type of written information, 149 (68.7%) participants indicated that information on the medicine container was their preferred source, while the leaflet with the medicine was the preference for fewer (n=66, 30.4%). Only two respondents preferred to obtain medicine information from website.

The leaflet was preferred over the website because it was considered to be easier to understand. It was also recognized that the leaflet provided complete information about a medicine, which was specific to that medicine. In contrast the information on the website was perceived as too complicated and lengthy for some participants.

"Sometimes, the doctor can't tells me all the details. The leaflet is trustworthy. The website has too much information." (P349;male, 44)

The leaflet was also perceived as easier to access because it was packed together with the medicine. It was also more convenient to use compared with the website where individuals had to find information by themselves.

"I can read [the leaflet at] any time, it is clear. The website is complicated." (P29; Female, 40)
"A leaflet is easy to access, I don't want to find information by myself." (P201; Female, 52)
"I can keep and read it anytime when I want to take the medication." (P250; Male, 39)

Some participants trusted the leaflet because it was provided by their doctor. Participants also believed that the leaflet was produced by the pharmaceutical company who knew the medicine well. Furthermore, it was approved by the Thai FDA and it was specific to the medicine. They also thought that there was much information on the Internet , which might not be specific to their

medicines. It was recognized that the information on the Internet was not as trustworthy as that in the leaflet. Participants suggested that information on the website may actually be advertisements.

"Leaflet is made from drug company who know the medicine well and is approved by the Thai FDA" (P226; Female, 50)

"Because it might be an advertisement on the website" (P17; Male, 34)

"There is so much information on the website. They provided different information which cannot be trust" (P63; Male, 21)

However, disadvantages of the leaflet were also recognised. Most frequently participants expressed concern that they might misunderstand the information when they read it. For some the leaflets seemed not to be necessary. The font size, language used, and the information provided were not attractive to read. The information provided was too much, and was too difficult to understand. More importantly, even the information that was provided may not cover what they want to know. Technical language in the leaflet made them feel worried and confused. One participant thought that the information on the leaflet sometimes was an advertisement. Concerns were also raised relating to whether the leaflet was suitable for their disease. Leaflets were also identified as being a waste of paper; over time the print could fade.

"The information I want to know is not showed." (P72;Female,18)

"Don't understand technical terms" (P92; Male,19)

"I think that it does not cover what I want to know" (P149;Female,36)

"Small text, I might misunderstand because I have to read by myself." (P159;Male,40)

"I am an elderly person. I cannot read clearly." (P204;Male,78)

"Information might be an advertisement." (P254;Female,43)

"it [the text/ print] might be faded and disappear" (P282; Female, 55)

"It is small text, too much information, and difficult. It uses complicated language, I feel confused" (P337;Male, 72)

"I am not confident whether the leaflet is suitable for my disease." (P297; Male, 55)

There were only two participants who preferred a website over a leaflet. They appreciated receiving information in different formats and wanted more information, so that they could compare facts and advice from different sources for themselves. Information on the Internet was also recognized as being more convenient to access.

"I can get more information, compare information from different sources so that I am sure." (P312,Female,48)

In comparison between the source of medicine information experienced in the past 3 months and the preferred source, almost half of those participants (n=106, 47.3%) who had received written medicine information stated a preference for written together with verbal information as their medicine information source. Nearly half of the respondents (n=54, 46.2%) who had received verbal information stated that they would prefer written and verbal information. Even those (n = 98) who had received verbal together with written information were preferred by 49.7%. Furthermore half of the respondents (n=4, 50.0%) who responded that they had not received any medicine information, would prefer written with verbal information.

With regards to written medicine information, most participants (n=94, 64.4%) who had received written information preferred the information on the medicine container as their source of medicine information. The comparison between the source of medicine information received in the past 3 months and preferences for format of medicine information and written information are shown in Table 8-10 and Table 8-11, respectively.

Table 8-10 Comparison between source of medicine information in the past 3 months and preference on medicine information

Preference on medicine information	Source of medicine information in the past 3 months (%)									
	Written Information (n=224)		Verbal Information (n=117)		Written and verbal (n=197)		Other (n=3)		Didn't receive (n=8)	
Written	40	(17.9)	9	(7.7)	28	(14.2)	1	(33.3)	2	(25.0)
Verbal	76	(33.9)	51	(43.6)	70	(35.5)	1	(33.3)	2	(25.0)
Written and verbal	106	(47.3)	54	(46.2)	98	(49.7)	1	(33.3)	4	(50.0)
Other source	2	(0.9)	3	(2.6)	1	(0.5)	0	(33.3)	0	(0.0)

Table 8-11 Comparison between the source of medicine information in the past 3 months and preference for written information.

Preference on written medicine information	Source of medicine information in the past 3 months							
	Written Information (n=146)		Verbal Information (n = 63)		Other (n=2)		Didn't receive (n=6)	
Leaflet	51	(34.9)	13	(20.6)	1	(50.0)	1	(16.7)
Information on the medicine container	94	(64.4)	49	(77.8)	1	(50.0)	5	(83.3)
Website	1	(0.7)	1	(1.6)	0	(0.0)	0	(0.0)

Despite differing views on leaflets versus information on the Internet , most people agreed that both the PIL and information about all medicines on a government website were extremely important to provide to every patient (Table 8-12). Over half of every age group (n=250, 71.0%) believed that a leaflet was an extremely important medicine information source which must be provided with all medicines, while nearly half of participants (n= 170, 48.4%) considered that providing medicine information on a government website was extremely important. Almost half of participants who had a university degree (n=165, 46.9%) thought that it was extremely important to provide leaflet with the medicine to patient ($p<0.001$. In term of information on the Internet, a high percentage of participants aged 18-30 (n=61, 51.3%) and 31-60 (n = 92, 49.7%) thought that it was extremely important to provide medicine information on a government website, whereas more participants who were aged 60 or more judged it to be less or not at all important (n=17; 36.2%).

Table 8-12 Opinion on how important of providing leaflet and information on a government website

	Number (%)							
	Age 18-30 (n=119)		Age 31 – 60 (n=186)		Age >60 (n=47)		Total (n=352)	
1. How important is it to you that a leaflet for patients is given with all medicines?								
Extremely important	88	(73.9)	135	(72.6)	27	(57.4)	250	(71.0)
Very important	20	(16.8)	37	(19.9)	10	(21.3)	67	(19.0)
Somewhat important	10	(8.4)	10	(5.4)	7	(14.9)	27	(7.7)
Not so important	1	(0.8)	4	(2.2)	2	(4.3)	7	(2.0)
Not at all important	0	(0.0)	0	(0.0)	1	(2.1)	1	(0.3)
2. How important is it to you that information about all medicines is available on a government website?								
Extremely important	61	(51.3)	92	(49.7)	17	(36.2)	170	(48.4)
Very important	24	(20.2)	47	(25.4)	10	(21.3)	81	(23.1)
Somewhat important	24	(20.2)	27	(14.6)	3	(6.4)	54	(15.4)
Not so important	6	(5.0)	7	(3.8)	10	(21.3)	23	(6.6)
Not at all important	4	(3.4)	12	(6.5)	7	(14.9)	23	(6.6)

8.5 Discussion

The study was carried out in the general public and focussed on participant's experiences of receiving information about their medicines in general, while most previous studies in Thailand have aimed to investigate medicine information needs of people taking a certain medicine, with drug allergy, those who are blind or whom have low literate skills.[68,100,191,273,301,302] Only one previous study has sought views of the general public.[100]

The quota sampling was conducted, recruiting participants in an area of high tax income was difficult, resulting in a slightly higher than average representation of females and the younger adults in the study compared to average for Songkhla province. The percentage of participants who have higher education was much higher than the average percentage of people who have higher education in the Songkhla province.[300] This may affect the results.

Generally, there are 1-2 cities with the highest tax revenue in a province in Thailand. These cities are economic and educational centres of the province; therefore the proportion of the population with high education levels in this kind of city is normally much higher than in small tax income cities.[300,303,304]

Many studies in the past have found that women are more interested in seeking of health-related information than men. These findings may explain why women tended to be more active in

answering this health-related survey.[287–289] As well as this, two co-researchers were students at the university, and recruitment of participants of the same age was easier than recruiting older respondents and they were easier to approach.

8.5.1 Using medicine in general public

In this survey, a high number of participants had not used medicines regularly in the past 3 months (on most days). When considering with age, it was found that using medicine increased by age and that a higher percentage of women regularly take medication than men. This reflected Thai data in 2016, in which a pain killer was used as representing medicine use behaviour in Thai people. The prevalence of taking a painkiller increased with age, and a higher percentage of women took painkiller medication than men.[305]

Community pharmacies, hospitals, and private clinics were the major source of obtaining medicines for the general public. Within the health care system of Thailand, patients can obtain medicines from many sources. They can meet their doctor with or without an appointment, and they are dispensed the medicine at pharmacy unit in the hospital. For this source, health expenditure is paid upon patients' health insurance scheme. They can also meet the doctor with or without an appointment, then be dispensed the medicine within the private clinic. But most of them have to pay the expenditure by themselves. In community pharmacy, most of medicines can be dispensed by a pharmacist without any prescription.

In some cases, individuals who were under National Health Insurance scheme, must have been seen by a doctor and have been prescribed the medicine before for the pharmacist to continue with the supply. However, this was a pilot project under National Health Insurance Office and is not standard practice throughout Thailand. Therefore, this pilot project is the most convenient and favourite option for obtaining the medicine. Again, the expenditure must be paid by patient.

Retail outlets (convenience store), are also places where the general public can purchase over-the-counter medicines for mild illnesses. They can also obtain medicines or simply seek advice from friends and family. This may explain why the retail outlet was the most frequently used in the 18-30 age groups, who were less likely to be suffering from chronic disease than the over 60 age group more of whom received medicines from their doctor.

From non-communicable diseases surveillance Thai National Health Examination Survey, most of the people who take painkillers obtained medicine from pharmacies (27.4%), followed by health care centres (26.8%), hospitals 19.7% and from retail outlet (17.3%). The national survey covered all areas in Thailand.[305] However, in urban areas (high tax income area), obtaining the

medicine in pharmacies or hospital is easier to access than in rural area, where there are few such facilities.

Participants with university degrees obtained medicine from private clinics more than those with lower education. This is because this group in general has a high income with private health insurance, so they can afford their health expenditure.

8.5.2 Using medicine information in general public

The sources of medicine information used by the general public in this study included written information (leaflet, information on the container, website), verbal information, and others (family and friends, digital media). The majority of the participants advised that they had received information about the medicines they had used. Responses from participants showed that the most common medicine information sources were verbal information from health care professionals, follow by written information, and other sources.

Verbal was the most frequent source of medicine information with the majority receiving this from their pharmacist, followed by their doctor. They talked to their health professional when they had a prescription dispensed, and they bought the medicine. This finding correlates with other studies in some countries (UK, South Africa, Armenia, Palestine, and Singapore) which have shown that verbal information from health workers was the primary source of medicine. Physicians and pharmacists were the most commonly used source of information about prescribed medicines.[10,70,77,78,95,97,113,123] With some studies in Saudi Arabia, Armenia, Pakistan, and Singapore, written information was not frequently used, and was viewed as supplementary to the verbal instructions of doctor and pharmacist. [10,91,95,97]

While the findings are in line with an earlier study involving hospital out-patients in Thailand, which showed that physicians and pharmacists were the major sources of medicine information, they are in contrast to a more recent study which found that the most frequently used sources of information regarding medication were PIs, followed by pharmacists, doctors, or the Internet.[100,273]

Even if the main source of information was verbal information from health workers, a very high proportion of participants also responded that they used written information. Most of them chose to read written information on the medicine container as their first choice of medicine information source, followed by the leaflet with the medicine. The most frequent use of written information on the medicine container was the information written on the medicine envelope by the person who dispensed the medicine. In general practice, medicines are mostly dispensed

in pharmacies. The medicines usually are dispensed in small quantities (1 or 2 blister strips, or 10 – 20 tablets from bottles), they are then packed in a small zip-lock plastic bag (so-called envelope). Pharmacists will write or print some short important information on the envelope before dispensing to the patient together with verbal information.[191]

With regards to the patient information leaflet, all drugs must be registered with the Thai Food and Drug Administration (Thai FDA). Thai regulations require that medicine leaflets should be prepared by pharmaceutical companies, include basic details plus warnings, and be written in Thai language. Submission of a Summary of Product Characteristics or Package Insert with or without a PIL is a prerequisite for drug registration process with the Thai FDA.

Although in theory, there is a requirement for provision of a PIL with medicines and guidelines for preparing PILs were introduced in Thailand in 2013,[26] in practice, PILs are still voluntarily produced and supplied by pharmaceutical companies, and there is a very limited number of available PILs for medicinal products supplied in Thailand.[273] In many countries, including Thailand, the leaflet provided with medicines is a package insert, designed for use by health professionals, rather than a PIL, designed specifically for use by patients.[191]

To illustrate this point, a study in Thailand reported that of all ten NSAIDs in their survey, only 4% of different products had proper patient-oriented leaflets and a sufficient amount of these for distribution.[25] Therefore, in this current study, some participants might have thought of package inserts instead of PILs when discussing and giving their responses to the survey questions.

Some participants in this study did state that they had used the leaflet supplied with the medicine. This is similar to a study conducting in Saudi Arabia, Palestine, Thailand, and Nigeria which revealed that the percentage of the public reading the patient information leaflet ranged from 45%-90.6%.[84,86,91,273] and 67-75% of people in England read the PILs.[113,120,293]

Educational level was a factor affecting receiving the leaflet with the medicine. Respondents with higher levels of education were more likely to receive a leaflet with the medicine than other participants with lower levels of education. This may be related to their health literacy and health insurance. An earlier study found that higher health literacy was associated with more thorough reading of drug labels, which was in turn associated with better perceived medication adherence.[76] People who had limited health literacy, had poor awareness of information source, lack of health knowledge and that stigma contributed to a lack of information seeking practice.[80]

The majority of the general public stated that they normally read the information when they were first given the medicine, followed by when something unexpected happened. These findings support former studies in the UK, Egypt, Palestine, Saudi Arabia, Thailand and Armenia that found that most of patient read when first-time of using a medicine. [76,83,86,91,95,97,273]

The participants also used the provided information for checking when to use the medicine, checking whether the medicine was suitable for them and identifying the possible side effects. Moreover, the most desired information related to what it's for, how to use the medicine, the name of the medicine, and possible side effects. The findings reveal that most participants usually read the sections relating to the method of administration, adverse effects, and contraindications sections. The results were similar to previous studies in the UK, Armenia, Singapore, Korea, Saudi Arabia, Nigeria, Thailand and Egypt that found that the sections viewed as most important information were adverse effects, dosage, indications, and method of administration, duration of treatment, expiry date, and contraindications [10,83,84,91,97,106,120,273]

The opinion on all medicine information in terms of how easy the information and its adequacy showed that the large majority of opinion was somewhat neutral both in its ease and sufficiency. They might not express their real view. It might mean that they just got used to the information they had received in the past, but they had no experience, or no idea with the ideal medicine information they must receive. This is a vital room for improvement in providing medicine information in Thailand.

8.5.3 Perceptions of the general public on different medicine information sources

Verbal information from health professional is the most desirable source of medicine information because it was trustworthy, easy to understand, easy to access, and relevant to them. Verbal information are considered as being easy to understand and people believe that using this source they can access complete and correct information. They also see receiving verbal information as an opportunity to ask questions to their health care providers. More importantly, responses to open questions revealed that verbal information was a way of obtaining individualised information, where only key messages were provided.

Many studies showed that medicine information from the pharmacist was judged to be important for patients and the majority of them trusted the information received. Receiving information from a doctor has been also shown to significantly improve patient's knowledge about their medicines.[78,97,104,297] However, verbal information was judged to be much less accessible than written information even in Thailand. This has been found in previous studies.[293,296,298] Although

verbal information was much less accessible, the ability to tailor information was thought to be more important than accessibility. [293,298]

The second and the third most frequent source of medicine information was the dispensing label/ medicine envelope, and drug company information on medicine container, respectively. A high number of people who selected the dispensing label/ medicine envelope thought it was easy to understand, and easy to access. This is also the traditional way to get medicine information within Thailand where people are familiar with this source.

Focusing on the leaflet with the medicine, it was ranked as the fourth. It would be used because it was easy to understand, east to access. Among participants, those who had a university degree would more likely use the leaflet with the medicine. Younger adults also had more potential to use the leaflet than older adults. In term of the leaflet again, there were both positive and negative points of view. The leaflet with the medicine is general public's knowledge resource. This supports previous research that some people thought that the leaflet could generate new knowledge and may have a positive impact on behaviour. [86,76,114,119] The information was easy to access, read and understand, source of accuracy and validity of information which was approved by a government body.

On the contrary, fear of misunderstanding was the most frequent reason, so they did not want to read. The font size, language use, the information provided were not easy to read. The information provided was overwhelming, and difficult to understand. More importantly, even if much information was provided, it did not cover what people want to know. The information written with technical terms in the leaflet made them feel worried and confused. The leaflet was also considered to be waste paper, which could fade and disappeared eventually. Some also expressed the view that the leaflet was a part of the advertisement for the medicine which cannot be trusted.

These findings support a large number of studies which found that people in many countries were dissatisfied with poor format and language used in medicine leaflets. They had some difficulty in comprehension or understanding related to the language used, technical terms, and the small font size used. They also felt that PILs raised fears and concerns.[79,84,87,91,95,107]

With regards to medicine information needs, the most desired information related to what it is for, how to use the medicine, the name of the medicine, and possible side effects. Almost all preferred to receive the information when they were first given a medicine. This supports a

previous study in Thailand about what and when people want from their medicine information.[100,273]

8.5.4 Preference on medicine information sources

The most important finding from this study is that verbal together with written information (information on the medicine container) was the most preferred way to receive medicine information irrespective of participants' previous experience. Participants considered that this would provide easy to understand, complete and correct information.

Providing a leaflet with the medicine to every patient was seen as an extremely important issue for most participants. Participants who had a university degree thought that it was extremely important to provide leaflet with the medicine to patients. Even though they stated that the leaflet they had experienced was complicated, they can keep it as a reference, and can read it when need. Studies show that the leaflets most frequently seen by both patients and the general public in Thailand are in fact PIs, not PILs. Despite the possible lack of experience of PILs, the result was consistent with previous studies conducted in Thailand that patients accepted PILs as having an important role in providing medicine information. They reported a strong need to use PILs in order to gain more knowledge about the medicines.[273]

However, the age group influenced the opinion of the government website. The older judged to vary in its importance, while it seemed extremely important in younger groups. This finding was similar to cited studies showing that age group only affected potential use of the Internet. [97,293]

8.6 Strengths and limitations

This study used a quota sampling technique which can ensure the diversity of sample. The questionnaire was designed and developed to include every aspect of receiving medicine information. However, despite the adoption of quota sampling the actual sample recruited included a higher proportion of females, with participants who had a higher education.

In the sample size calculation, some statistical indicators, including p-values and confidence intervals, were used to help determine that the results observed did not arise by chance. Any significant error in the sample size calculation will have an impact on the power and value of a study. This study calculated the sample size based on an assumption from only one study that, in 2019, 28% of people in Thailand read the PIL in 2019. If this assumption has changed, the study may be underpowered to detect the desired difference and the truth.

The length of questionnaire. it took participants a long time to answer, might also be the obstacle to this survey. This could be disturbing participants' concentration. It was possible that participants would be confused between PILs and PIs because PILs were not widely used in Thailand.[299]

8.7 Recommendations and future work

Results from this study showed that verbal together with written information is the preferred approach to get medicine information among the Thai general public.

There was consistency with previous studies that have indicated the importance of verbal explanations by healthcare professionals together with written information. Both are important ways that patients receive medicine information enabling them to receive complete and correct information. Written information can be complementary to verbal information from healthcare workers.

Although participants preferred medicine information on the medicine container, providing a leaflet with the medicine was seen as an extremely important issue for most participants. However, the PILs which are specifically designed for patients are provided with a very limited number of available PILs for medicinal products dispensed in Thailand.

Therefore, the healthcare professionals should pay attention to patients as individuals when providing information, to ensure that it meets their needs. More importantly, provision of PILs should be vitally and urgently endorsed as a compulsory regulation together with conducting further studies about how to improve PILs to meet patient's needs.

Chapter 9 Sources of medicine information in the United Kingdom and Thailand: A comparative study

9.1 Introduction

The health-care system in Thailand has a multilevel of services. Hospitals are the major source of obtained medicine for Thais. There are various 'levels' of hospitals that provide health care services within each administrative district; provincial, district and sub-district levels. There is at least one health centre in each sub-district, one "community hospital" general hospital" at the provincial level. There are also some general hospitals which are upgraded to become regional hospitals ("central hospital") for referrals in particular geographical regions. At the top level of the system, there are 11 medical school hospitals which provide general and specialist health care services. Private hospitals are a part of health care service in Thailand. All hospitals are the major source of medicine for Thais. All medicines can be prescribed by a doctor and dispensed by pharmacist at a pharmacy unit in the hospitals. Apart from hospitals, medicines are available in private pharmacies operated by a registered pharmacist. The so-called "dangerous" (similar to prescribed medicines in the UK) e.g. antibiotics can be dispensed in pharmacy without prescription. Other health personnel such as nurses, dentists and physical therapists can dispense a number of medicines, especially in certain health centres. Thai traditional medical services and Thai traditional medicine (TTM) are also a part of healthcare services in Thailand. All these can be a source of medicines and medicine information in Thailand.[306]

In comparison, most healthcare in England is provided by the National health service (NHS) England. NHS system work through General Practitioners (GPs) to provide primary health care, and provide referrals to other services as needed. More specialised services, such as psychiatric diseases, direct access to emergency departments, are then further provided in hospitals, known as secondary care. As in Thailand, some centres provide highly specialised services, known as tertiary care. Community pharmacies are privately owned but have contracts with the relevant health service to supply prescription drugs and medical advice. The majority of medicines are dispensed in community pharmacies with a prescription.[307] Hospital pharmacies provide medicines for their in-and out-patients.

Health care services in Thailand and the UK are different. As a result, there is a distinction between the sources of received medicines and the sources of medicine information.

Importantly, Thailand's PILs provisions have been in place for less than a decade, compared to the UK's regulations, which have been in place for about half a century.

In the initial stage of PILs provision in Thailand, by comparing the survey results with the UK, it is possible to gain a further comprehension of the similarities and differences between the two countries. The outcomes could be beneficial to the Thai system in terms of identifying and filling gaps.

9.2 Aim and objectives

The study aimed at comparing the sources of medicine information used and views on different sources and perceived medicine information needs among the general public between the UK and Thailand.

9.2.1 Objectives

1. To compare medicine information sources used by general public between the UK and Thailand.
2. To describe the difference in the use of medicine information by the general public from the UK to Thailand.
3. To compare the perceptions of the general public on different medicine information sources.
4. To find out the difference of the preferences for the content and format of medicine information among the general public.

9.3 Methods for data analysis

The data were analysed using the statistical programme SPSS. Cleaned data from two datasets, UK and Thailand was exported directly into SPSS, and combined into the same database.

The data were analysed by using descriptive statistics. Frequency distributions and means were used to describe categorical and continuous variables, respectively. The hypotheses that sources of medicine information used, views on different medicine information sources, and preferred ways of getting this information were different depending on age, gender, and education were tested. The chi-squared test or Fisher's exact test were used to determine whether there were any significant differences between sub-groups.

9.4 Results

9.4.1 Demographic Data

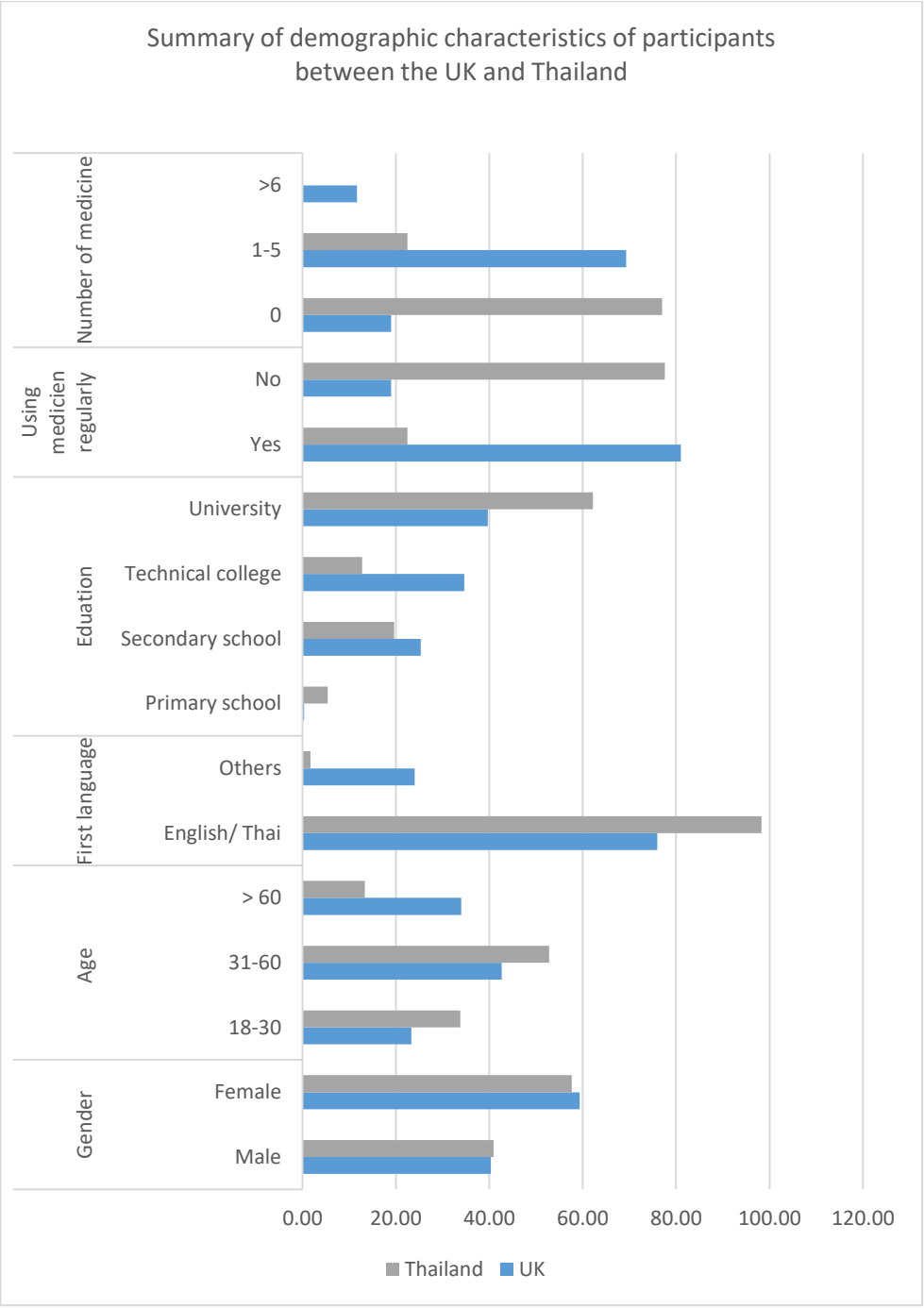
The survey was conducted in two countries with the same protocol. In the UK, the locations were chosen by their index of multiple deprivation (IMD) high, medium and low, while they were selected by tax revenue; high, medium and low in Thailand.

The majority of the respondents in both countries were female, in similar proportions (UK n = 178, 59.3%, Thailand n = 203, 57.7%) Most spoke their native language, and most of them were of local ethnicity. Most of the participants in the UK were of white ethnicity (n= 217, 72.3%) whose first language was English (n=228 ,76.0%), while all of the respondents in Thailand were of Thai ethnicity (n= 352, 100%), and for the large majority their first language was Thai (n= 346, 98.3%).

In the UK, a greater number of participants were more than 60 years old (UK, n= 102, 34.0% vs. Thailand, n= 47, 13.4%), whereas in Thailand more younger people participated (UK, n= 70 ,23.3% vs. Thailand, n= 119,33.8%) and these differences in the age of the two cohorts were significant ($p<0.001$). Even though a larger proportion of participants had a university degree in Thailand (UK; n=119, 39.7%, Thailand; n= 219, 62.2%), there were also more participants from Thailand with a primary school qualification as their highest education award (n=19 ,5.4% vs. n=1 ,0.3%, Thailand vs UK, respectively). In the UK, more participants had completed a technical college education (n=104 ,343.7%) than in Thailand (n=45 , 12.8%) ($p<0.001$).

More participants in the UK (n=243, 81.0%) had used any medicines regularly (on most days) in the past 3 months, and most stated that they (n=208, 69.3%) had regularly used 1-5 medicines. This is in sharp contrast to the Thai cohort where the majority of participants (n=273, 77.6%) did not use any medicines regularly ($p<0.001$). Some (n=79, 22.4%) had used medicines regularly (on most days) in the past 3 months but most of these participants stated that they (n= 60, 17.0%) had only regularly used 1-2 medicines ($p<0.001$). The summary of demographic characteristics of participants for the UK and Thailand is shown in Figure 9-1.

Figure 9-1 Comparison of demographic characteristics of participants between the UK and Thailand

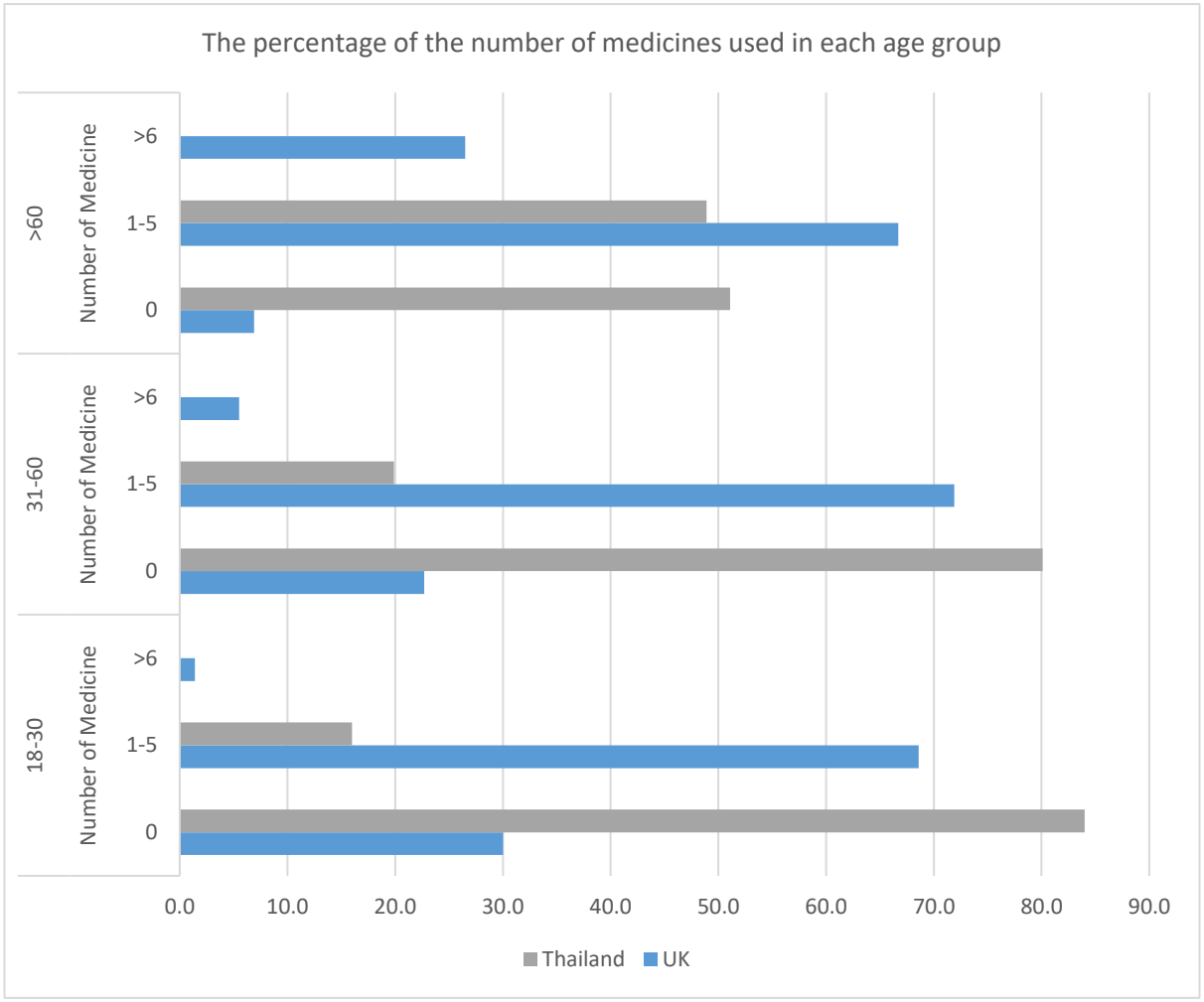


9.4.2 Medicine utilization

The number of participants who used medicines regularly in the UK were much greater than those in Thailand in every age group ($p<0.001$). The prevalence of taking medicines increased greatly with age in both countries. In the UK, 95 (93.1%) of those aged 60 or over used at least one medicine regularly, while in Thailand, there were only 23 (48.9%) adults who were more than 60 years old and had regularly taken at least one prescribed medicine in the past 3 months

(p<0.001). The percentage of the number of medicines used in each age group is shown in Figure 9-2.

Figure 9-2 the percentage of the number of medicines used in each age group

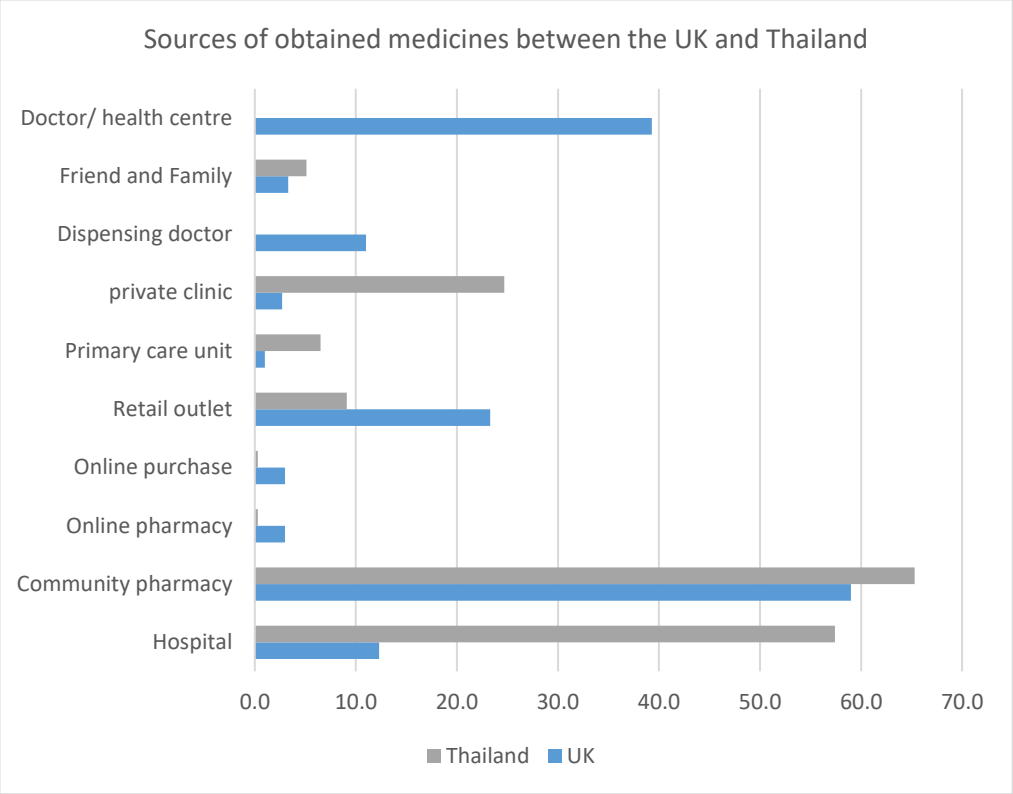


In the UK, the most common places where participants obtained medicines were community pharmacies (n=177, 59.0%) followed by the health centre/ doctor (n=118, 39.3%). In Thailand, community pharmacies were also the most common source of medicines (n=230, 65.3%), closely followed by hospitals (n=202, 57.4 %). The percentage of medicines obtained from retail outlets (n=70,23.3%) in the UK was greater than in Thailand (n=32, 9.1%), whereas hospitals (n=202, 57.4%) and private clinics (n=87, 24.7%) were more frequently used to obtain medicines in Thailand than in the UK (Hospital, n=37, 12.3%, private clinic; n= 8, 2.7%). The source of medicines for both the UK and Thailand cohorts are shown in figure 3.

These data also show that the majority of Thai participants (n=344, 97.7%) compared with the UK participants (n=218, 72.7%) received their medicines only from health professional sources e.g. hospitals, community pharmacies, health centres, and private clinics. A small minority of Thai

participants (n=8, 2.3%) used sources other than health care professionals (retail outlet, online purchase, friend and family), whereas these latter sources were more common in the UK (n=31, 10.3%). There were 40 Thai participants (11.4%), and 51 UK participants (17.0%) who obtained medicines from both types of sources. These data are shown in Figure 9-3.

Figure 9-3 Sources of medicines for participants from the UK and Thailand



9.4.3 Medicine information sources

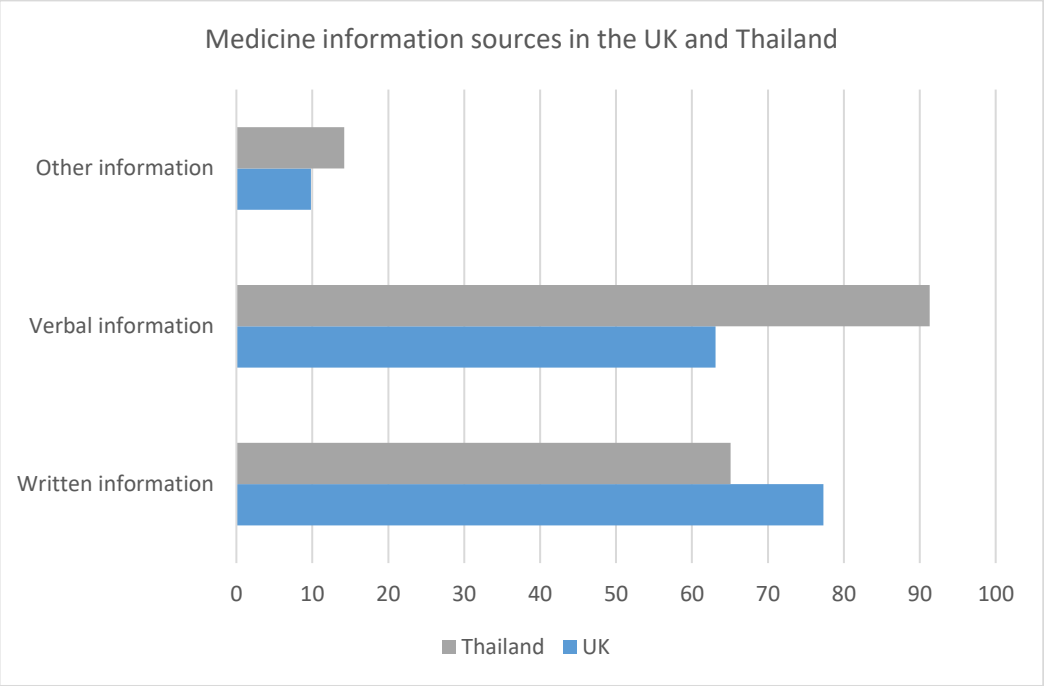
The majority of the UK respondents (n=255, 85.0%) reported having received some information with their medicines whilst in Thailand almost everyone (n=344, 97.7%) had received some information with their medicines, (p<0001).

In the UK, the major type of information provided was written which included the PILs, PIs, website, or information on the medicine container (n=197, 77.3%). The percentage (n= 224, 65.1%) of participants receiving WMI among Thai participants was significantly less than in the UK (p=0.001). WMI was the second most common type of information in Thailand, after verbal from health care professionals, (n=314, 91.3%) whereas verbal was the second most frequent form of information obtained in the UK (n= 161, 63.1%) (p<0.001).

Few other sources of information (TV, radio, newspaper, magazine, mobile app, social media, family member or friend, digital platform [e.g. Alexa, Siri]) were used in either country (UK; n=25,

9.8%), (Thailand; n=49, 14.2%). A comparison of medicine information sources used in the UK and Thailand is shown in Figure 9-4.

Figure 9-4 Medicine information sources used in the UK and Thailand



In terms of written medicine information, the most frequently received source among the UK participants (n=185, 93.9%) was a leaflet provided with the medicine, while the information on the medicine container was the most common source for Thai respondents (n=209, 93.9%). The percentage of those searching for information via the website among Thai participants (n=153, 68.3%) was much higher than those within the UK (n=71, 36.0%).

The information written on the medicine envelope by the person who dispensed the medicine was the most frequently used by Thai respondents (n=135, 64.6%). This proportion is similar to the UK where 105 participants (61.4%) read the information which was printed on a label by the person who dispensed the medicine. There was also a quite similar proportion who used information printed on the container by the manufacturer in Thailand (n=107, 51.2%) and the UK (n=86, 50.3%). The medicine information on a government website was the most popular Internet source among Thai (n=91, 59.5%) and UK (n=50, 70.4%) participants, compared to other websites. Most of them had shared the same interest in looking at the medicine information when they were first given the medicine (UK; n=178, 90.4%, Thailand; n=128, 57.1%), but a higher proportion of Thai respondents looked at it when something unexpected happened. Over half of the UK participants (n=103, 54.2%) claimed to read the medicine information once only, while a higher proportion of Thai respondents (n=128, 67.4%) read the medicine information more than once.

One of the most common reasons for using the information among British participants (n=147, 77.4 %) was to check when to use the medicine. This was different from the Thai participants as most of them (n=137, 72.1 %) used it to check whether the medicine was suitable for them. When to use the medicine (n=124, 65.3%) was the second most common reason given by Thai respondents. Participants from both countries (UK; n=133, 70.0 %) (Thailand; n=100, 52.6 %) were interested in looking at the information to identify possible side effects. The type of written information accessed and how it was used is shown in Table 9-1.

Table 9-1 Type of written information accessed and how it was used

	UK (n=197)		Thailand (n=224)	
1 What type of written information have you seen?				
a. A leaflet about your medicine	185	(93.9)	192	(85.7)
b. Information on the medicine container	171	(86.8)	209	(93.3)
c. Website	71	(36.0)	153	(68.3)
2 When/how did you get the leaflet?				
a. in medicine pack,	170	(91.9)	164	(85.4)
b. given by doctor or other health worker	15	(8.1)	28	(14.6)
3 What was the information on the container like?				
a. printed on a label by the person who dispensed the medicine	105	(61.4)	107	(51.2)
b. written on the medicine envelope by the person who dispensed the medicine	13	(7.6)	135	(64.6)
c. printed on the container by the manufacturer	86	(50.3)	107	(51.2)
4 Which website(s) have you looked at for information about your medicine?				
a. Government organisation website	50	(70.4)	91	(59.5)
b. drug company website	9	(12.7)	25	(16.3)
c. pharmacy website	11	(15.5)	22	(14.4)
d. patient organisation website	13	(18.3)	11	(7.2)
e. hospital website	6	(8.5)	24	(15.7)
f. I can't remember	10	(14.1)	28	(18.3)
g. Others	10	(14.1)	8	(5.2)
5 When did you look at the information?				
a. when you were first given the medicine	178	(90.4)	128	(57.1)
b. when something unexpected happened	20	(10.2)	85	(37.9)
c. when you wanted to find out whether you were able to drink or drive or use machinery	28	(14.2)	31	(13.8)
d. when you wanted to check if it was safe to take another medicine	45	(22.8)	57	(25.4)
e. I never looked at the information	7	(3.6)	34	(15.2)
f. Others	7	(3.6)	7	(3.1)
6 How often have you looked at the information? (once only, two or three times, more than three times)				
a. once only	103	(54.2)	62	(32.6)
b. two or three times	61	(32.1)	76	(40.0)
c. more than three times	26	(13.7)	52	(27.4)
7 How have you used the information?				
a. to check when to use the medicine	147	(77.4)	124	(65.3)
b. to check if the medicine was suitable for you	83	(43.7)	137	(72.1)
c. to make sure you avoided certain other medicines	60	(31.6)	54	(28.4)
d. to make sure you avoided certain foods or drinks	63	(33.2)	63	(33.2)
e. to identify possible side effects	133	(70.0)	100	(52.6)
f. to decide if it was safe to drink or drive or work with machinery	53	(27.9)	35	(18.4)
g. to find out what to do when I missed a dose	46	(24.2)	31	(16.3)
h. other way……	5	(2.6)	1	(0.5)

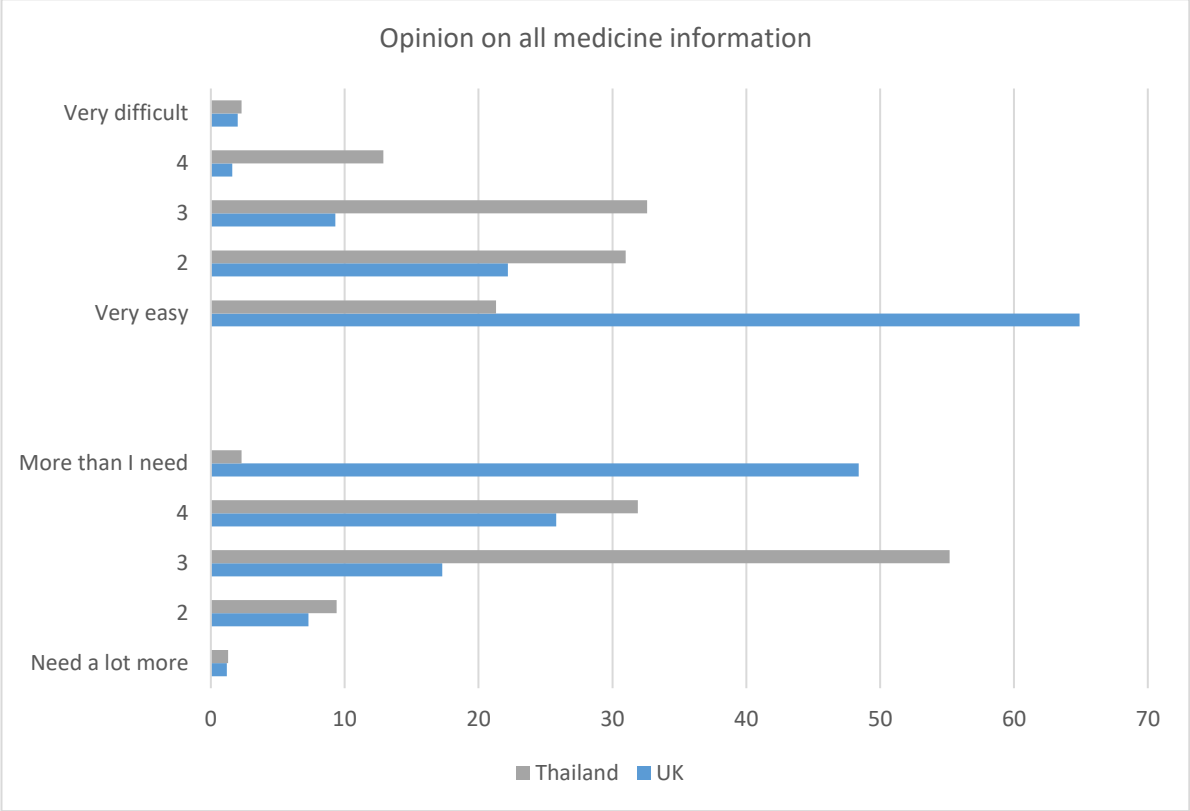
There were 55 (21.6%) UK and 117 (33.2%) Thai respondents who claimed not to have received written information, although they did receive verbal information about their medicines. Overall the percentage of receiving verbal information among Thai was higher than participants in the UK. The majority of Thai respondents had talked with their pharmacists (n=93, 79.5%), whereas the doctor was the most frequently cited source of verbal medicine information among the UK participants (n=46, 83.6%). In the UK, most people talked to their health professional when they were prescribed the medicine (n=46, 83.6%), while most Thai participants talked to their health care workers not only when they had a prescription dispensed for the first time or for refills (n=57, 48.7%), but also when they bought the medicine (n=49, 41.9%). A summary of the results relating to the provision of verbal medicine information is shown in Table 9-2. The three UK and three Thai participants who had used only received information from other sources.

Table 9-2 Provision of verbal medicine information

	UK (n=55)		Thailand (n=117)	
1 Who talked to you about your medicine(s)?				
a. doctor	46	(83.6)	30	(25.6)
b. pharmacist	23	(41.8)	93	(79.5)
c. nurse	13	(23.6)	7	(6.0)
d. health worker	4	(7.3)	5	(4.3)
2 When did they talk to you?				
a. when you were prescribed the medicine	46	(83.6)	6	(5.1)
b. when you had a prescription dispensed for the first time or for refills	15	(27.3)	57	(48.7)
c. when you bought the medicine	6	(10.9)	49	(41.9)
d. when you asked them questions	7	(12.7)	8	(6.8)
e. when you had a review	7	(12.7)	18	(15.4)
f. Other time	3	(5.5)	0	(0.0)

Overall, the UK participants were more likely satisfied with the medicine information they had received than Thai participants in terms of both ease of understanding and adequacy of medicine information ($p<0.001$). Their comparative opinions are shown in Figure 9-5.

Figure 9-5 Opinion on all medicine information



9.4.4 Perception on medicine information

The participants were asked their views on different possible information sources: whether they would use each source and, if yes, whether they think it is easy to access, easy to understand, relevant to them and trustworthy.

The most preferred source of medicine information that both participants from the two countries would like to use was verbal information from health care professionals (UK; n=275, 91.7%, Thailand; n=348, 98.9 %) because they perceived it as being easy to understand and trustworthy. Most of the UK participants also thought that it was relevant to them.

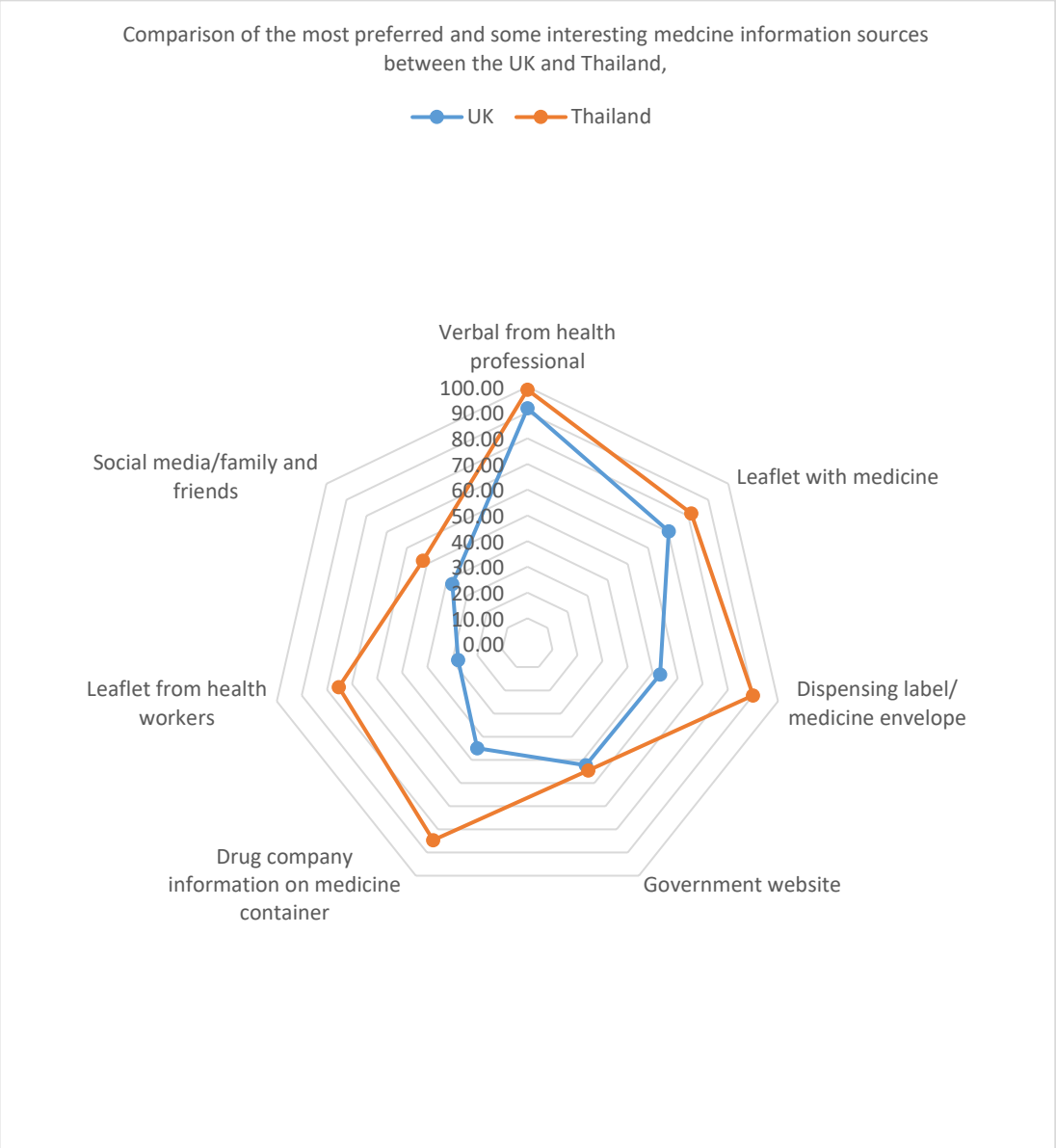
The leaflet provided with the medicine was the second option for reading medicine information among the UK participants (n= 212, 70.7%). This was different from Thailand. Thai respondents (n=317, 90.1%) liked to read medicine information on the dispensing label/ medicine envelope because they thought that it was easy to understand.

In terms of the websites, both cohorts had the same percentage in the interest of looking for information on the government website (UK; n=157,52.3 %, Thailand; n= 192, 54.5 %). This was

straightforward that most participants accepted it as an easy to access source of medicine information. Family and friends were less preferred but still important sources of medicine information among participants in both countries (UK; n=112, 37.3%, Thailand; n=183, 52.0%).

Comparison of preferred medicine information sources in the UK and Thailand is shown in Figure 9-6.

Figure 9-6 Comparison of the most preferred and some interesting medicine information sources between the UK and Thailand.



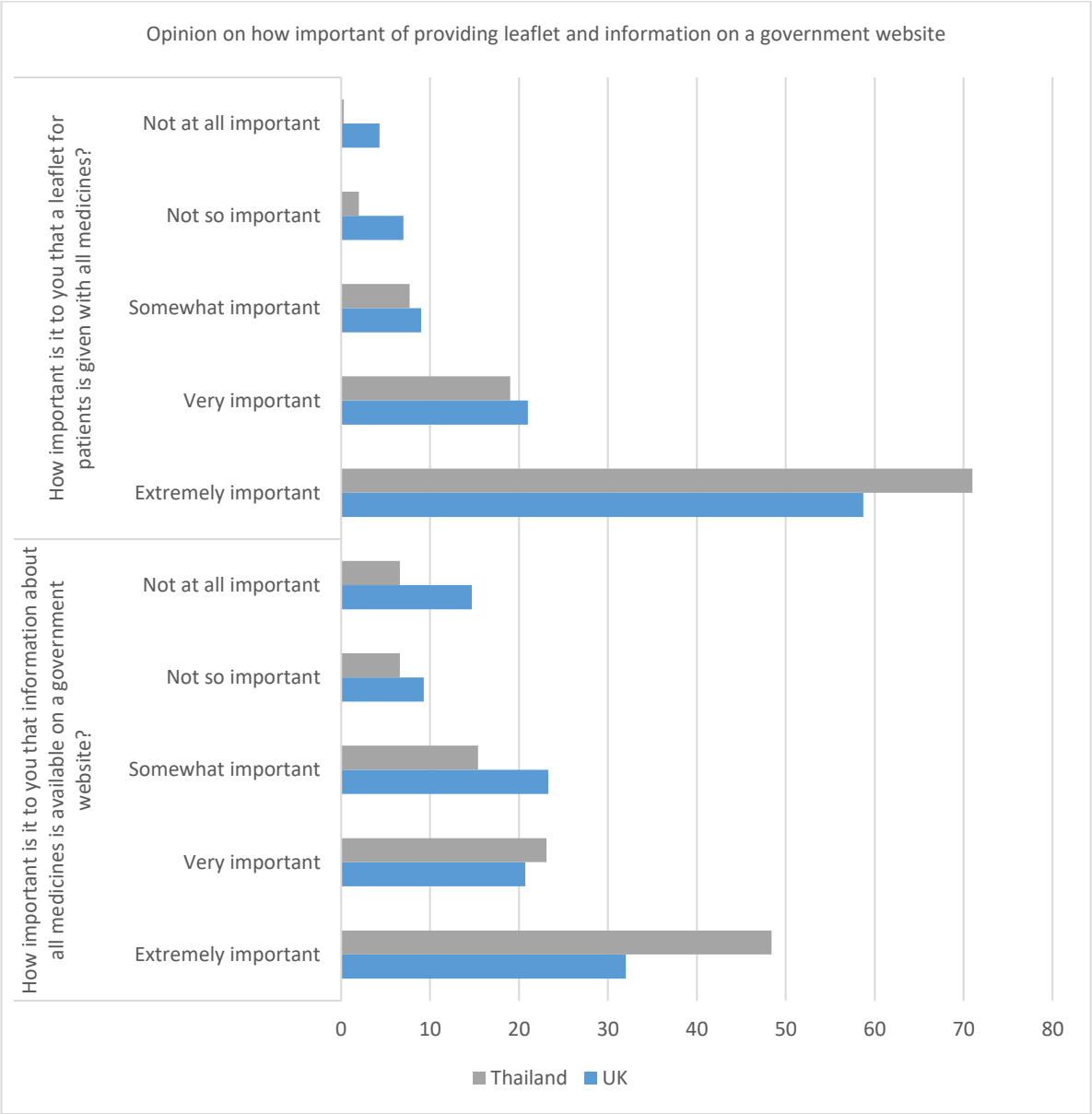
9.4.5 Preference on medicine information

Overall, a high proportion of participants in both countries preferred receiving both verbal and written information. However, Thai participants were significantly more likely to prefer verbal medicine information alone compared to the UK participants ($p=0.001$).

With regards to the written medicine information, there was a difference between these two countries. The most preferred way in receiving written information among the UK participants was the leaflet with the medicine, whereas for Thai participants this was information on the medicine container ($p<0.001$).

Despite differing views on leaflets versus online information, most Thai and UK participants agreed that both PILs and the availability of information on a government website were extremely important to provide to every patient, although of these sources PILs were judged important by more respondents. Opinion on the perceived importance of providing leaflets and information on a government website is shown in Figure 9-7.

Figure 9-7 Opinion on how important of providing leaflet and information on a government website



9.5 Discussion

This study was carried out in general public in the UK and Thailand with the same protocol and questionnaire. The questionnaire was piloted with a small number of people in both countries prior to recruitment to ensure that cultural and language differences did not affect understanding.

The majority of the respondents in both countries were female. This finding confirmed the previous studies that women tended to be more cooperative in answering the health-related survey.[287–289] In comparison, the UK participants were older, more culturally diverse in terms of

their main ethnic group, but less diverse in terms of their education than Thai participants. In England, there is a multicultural society with a diverse population in comparison with Thailand, which has a predominantly Asian population. In Thailand, the overall main ethnicity is Asian, but the population can be divided into three main subgroups. Estimates claim that of the total population, 75% were Ethnic Thai, 14% were Thai Chinese, and 3% were ethnically Malay. The remainder of the population falls into small minority groups including hill tribes, Khmers and Mons (data represent population by nationality).[308]

While in the UK, according to the 2011 Census, the total population of England and Wales was 56.1 million, and 86.0% of the population was White. People from Asian ethnic groups made up the second largest percentage of the population (at 7.5%), followed by Black ethnic groups (at 3.3%), Mixed/Multiple ethnic groups (at 2.2%) and Other ethnic groups (at 1.0%).[309] The more diverse in ethnicity the country is, the more diverse in cultures, language uses, and behaviours the country becomes. This may affect preferences and use of medicine information.

9.5.1 Using medicine in general public

In the UK, the number of participants who had used any medicines regularly (on most days) in the past 3 months were much higher than Thai participants. The prevalence of taking medicines increased greatly with age in both countries. The percentages of elderly people in the UK (18.8%) were more than in Thailand (12.9%)[310], and people also have more long-term conditions in the UK which they normally needed more medicines routinely.[311] Therefore the proportion of people who participated in this survey and had used any medicines regularly was greater in the UK.

Community pharmacies and doctors/health centres were the major sources of obtaining medicines for the general public in the UK. Within the health care system in the UK, most medicines, particularly if they are taken on a regular basis, are prescribed by the patients' General Practitioner (GP), and then dispensed by a community pharmacist therefore it is not surprising that community pharmacy and doctors/health centres were the major source of medicines. From NHS data in 2017/18, the proportion of prescriptions dispensed by community pharmacy, dispensing GPs and appliance contractors was 91.6%, 7.6% and 0.8%, respectively.[292] Retail outlets are also a place where the general public can purchase over-the-counter medicines for mild illnesses.

Overall, community pharmacies, hospitals, and private clinics were the major sources of obtaining medicines for the general public in Thailand. In Thailand, patients can obtain medicines from more sources, sometimes, without any prescription from a doctor. They can

also meet a doctor with or without an appointment in the hospital, or private clinic, then any medicines needed are dispensed at the hospital pharmacy or clinic. For community pharmacy, most medicines can be dispensed by a pharmacist without prescription; therefore, community pharmacy is the most convenient and favourite option for obtaining the medicine. Retail outlets (convenience store) are also places where the general public can purchase over-the-counter medicines for mild illnesses. For comparison, the revenue value of OTC sales is over three times higher in the UK ($2403m) than in Thailand ($747m).[312]

9.5.2 Source of medicine information

In the UK, the major source of medicine information was written, which included the patient information leaflet, website, or information on the medicine container. The number of participants receiving written medicine information among Thai participants was significantly less than in the UK. Written medicine information was the second most common source of medicine information in Thailand, after verbal from health care professionals, whereas verbal was the second most frequent form of information obtained in the UK.

PILs with medicines has been regulated in the United Kingdom since 1977.[1] Over the years this regulation has developed. PILs are prepared and provided by the medicine manufacturer following a standardised template which must consist of the same information. All medicines must be provided with PILs in the UK and almost all medicines are supplied as original packs. Therefore, the UK participants are used to being given a leaflet with their medicine and this reflects the higher proportion of respondents who identified the leaflet as their main source of medicine information.

In Thailand, submission of a SmPC or PIs with or without a PIL is a prerequisite for drug registration with the Thai FDA. Although in theory, there is a recommendation for provision of a PIL with medicines and guidelines for preparing PILs were introduced in Thailand in 2013,[26] as this is optional in practice, PILs are still voluntarily produced and supplied by pharmaceutical companies, and there is a very limited number of available PILs for medicinal products in Thailand.[25] Therefore, the amount of PILs distributed to patients is in this study was less than in the EU countries where PILs are widely provided to patients.[273] In contrast, PIs are compulsory and all medicines must be provided with PIs in Thai language. Therefore in Thailand, the leaflet provided with medicines is often a PI, designed for use by health professionals, rather than a PIL, designed specifically for use by patients.[25] However, PIs are not necessarily supplied to every patient during the dispensing process, due to the common practice of supplying strips rather than original packs of medicines.

The difficulty of understanding PIs, and limitations in the availability of PILs are the main challenges to the provision of written information in Thailand. Therefore, it is not surprising that written information was less preferred among Thai respondents as they are less likely to have experienced this format in the past. This is particularly the case given that the majority of Thai participants in this survey were not regular medicine users.

For using the Internet , the Thai cohort was more likely to search on the Internet / on websites for information. This may be related to their higher educational backgrounds. This may also be the fact that the information that they were initially provided was inadequate, and therefore if they need to know more, then they have to look on-line.

Majority of the general public in both countries stated that they normally read the information when they were first given the medicine. These findings support former studies in the UK, Egypt, Palestine, Saudi Arabia, Thailand and Armenia that found that most patients read when first-time of using a medicine. [76,83,86,91,95,97,273] While the UK cohort wanted to check whether the medicine was safe to take with another medicine, more of the Thai cohort used the leaflet when something unexpected happened. This reflected the greater use of medicines generally in the UK. The UK patients are more likely to be taking multiple medicines so need to check if it's safe to use them together. Again, this difference probably also reflects the more limited experience with PILs in the Thai cohort.

The participants in both countries had similar interests in checking when to use the medicine, and identifying the possible side effects, and checking whether the medicine was suitable for them. The results were similar to previous studies in the UK, Armenia, Singapore, Korea, Saudi Arabia, Nigeria, Thailand and Egypt that found that the viewed as most important information were adverse effects, dosage, indications, and method of administration, and contraindications [10,83,84,91,97,106,120,273]

There were a greater number of Thai respondents who received verbal medicine information with their medicines than participants in the UK. The major source of verbal information was the pharmacist. This may be because the majority of participants from Thailand obtained their medicines from a community pharmacy. Most Thai pharmacies, the main source of medicines for participants, are privately owned. Patients receive a more consumer focussed experience, than if they receive their medicine from a government sponsored facility, and the expectation is that as part of this service they will be given verbal advice as to how to take their medicine. However, some illegal practice has been reported, there was no pharmacist present all the time in some

pharmacies. Medicines were dispensed by somebody other than a pharmacist. This is illegal, and as well the information which was provided to the patients may be incorrect.[313,314]

In comparison, in the UK, participants reported that they received verbal information from their doctor. This could be because the pharmacy staff in the UK do not have as much time to spend with each patient because they have to dispense so many items compared to Thai pharmacy staff. There is some evidence that community pharmacists' workload has increased since the introduction of the new contracts in England and Wales, especially around the core activity of dispensing prescriptions and medicines use reviews.[315]

9.5.3 Perceptions of the general public on different medicine information sources

This survey found that, irrespective of the differences in healthcare practices, the large majority of people in both countries would prefer to obtain information about their medicine verbally from a health worker because the medicine information is provided from health professional whom they trust, is easier to understand, provides an opportunity to ask questions, and is specific to a patient's health conditions. Earlier studies in Armenia, Australia, Sri Lanka, and the UK have shown similar results which medicine information from the staff of community pharmacies was judged to be important for patients and the majority of them trusted the information received. Receiving information from a doctor significantly improved their knowledge about their medicines. [78,97,104,297]

In terms of written information, the leaflet with the medicine was the most preferred source among the UK cohort, whereas the Thai respondents would like to read medicine information on the dispensing label/ medicine envelope because they thought that it was easy to understand. Using medicines regularly was probably the key factor in influencing participants' views on the leaflet. The survey in the UK showed that participants who have regularly used a medicine in the past three months were more likely to think that the leaflet with the medicine was easy to understand, trustworthy, relevant to them and easy to access. In contrast there were a minority of Thai participants who had regularly used a medicine in the past three months. Therefore, this probably affected preferences on the leaflet with the medicine amongst the Thai cohort.

From responses to open questions, feedback on the written information leaflets from participants in both countries demonstrated similar findings. The leaflets were often reported as being often difficult to read with small font and text size, and contained information that was outdated, basic and directed at the general population rather than specific to individual conditions. They also

were problematic in terms of the language used, including the use of medical terms which were difficult to understand. The information written with technical terms in the leaflet made some feel worried.

With regards to websites, both cohorts had the similar percentage in their preference for the government website. Most participants viewed that it as an easy to access the source of medicine information.

In term of preferred way to receive medicine information, there was some clear difference between the two countries. It would appear that the Thai cohort wanted to receive more of every type of information in comparison with the UK. In Thailand, the majority are simply told the information on the container – most probably the dosage instructions when they are given the medicine. Furthermore, this can be linked to participants' satisfaction about their medicine information. Participants in the UK were more likely to be satisfied with the medicine information they had received than Thai participants in terms of both ease of access and adequacy of medicine information. However, a substantial proportion in the UK also said they had too much information. These findings may relate to the historical provision of information which has been high in the UK for many years compared to the relative paucity in Thailand. Therefore, there is a huge amount of medicine information available in the UK and it may have seemed too much detail for some people. Overall, the surveys both suggest that medicine information is still needed, but does not meet people's needs, either in terms of the quality of the information or the sources of the information. The UK information may need to be reduced in quantity, whereas in Thailand greater quantity is needed, but for both greater simplicity is needed.

9.5.4 Preferences for medicine information sources

A greater number of participants in both countries preferred receiving both verbal and written information. However, Thai participants were significantly more likely to prefer verbal medicine information alone compared to the UK participants. The most preferred way of receiving written information among the UK participants was a leaflet with the medicine, whereas Thai participants preferred information on the medicine container as their written medicine information.

As previously mentioned, there is a limitation of PILs for medicinal products dispensed in Thailand.[273] The Thai participants have less experience of reading PILs as well as there were the difficulty and complexity of PIs. Therefore, the short and concise information on the medicine container is the choice for their medicine information. However, the information on the medicine

container generally contained inadequate medicine information. This is the key issue so providing patients with effective PILs would be beneficial, and is therefore essential.

Even in the UK, PILs are prepared and provided by the medicine manufacturer by following a standardised template which must consist of the same information. However, despite substantial regulatory efforts to improve readability and comprehensibility, the leaflets are still suboptimal and do not meet patients' needs.[249]

9.6 The need for changes

Most participants in both countries preferred receiving both verbal and written information. The outstanding characteristic of verbal information was the opportunity to tailor this to the individual patient. Therefore, the healthcare professionals should pay attention to patients as individuals when providing information, to ensure that it meets their needs.[316] There is a need for healthcare professionals to evaluate patient comprehension and need for drug information. This is also the suggestion for pharmacists, in particular, which need to be aware of a patient's desire for personalised medicines information and seek to maximise communication with their patients about their individual information needs during consultations.[75] From NHS Community Pharmacy Contractual Framework Essential Service – Support for self-care, service description is the provision of advice and support by pharmacy staff to enable people to derive maximum benefit from caring for themselves or their families. One of the services outlined indicates that pharmacy staff will advise on the appropriate use of the wide range of non-prescription medicines which can be used in the self-care of minor illness and long-term conditions.[317] The results from this study could suggest that pharmacists should also ensure they provide verbal information with prescription medicines, not only when patients ask for advice. The pharmacists may need to be more proactive in determining what information patients need.

With regard to the leaflet, the recent study findings supports those of prior studies in that even though the leaflet was the most preferred way to receive medicine information and is developed with due regard to international standards, it still did not fully meet the general public's needs.[249]

For the PILs provision, the PILs still need to be established and improved practically both in Thailand and in the UK to achieve patient's needs. The provision and regulation must be developed taking account of the patient-oriented aspect. It would be better to ensure PILs suit patient needs in the individual countries rather than verbatim reproduce or imitate those in other countries, but much can be learnt from international research (Chapters 5 and 6). User-testing, widely practised in the EU, has been shown to be feasible in Thailand. The PILs should also be

made simpler to increase patient understanding of medicines, such as those produced by the Thai FDA (Chapter 8).[273,318] Furthermore, a single leaflet designed for patients must be packed into the box. It is not appropriate to include both PILs and PIs with a medicine, as this may lead to patient misunderstanding, and may mean that patients throw them away eventually. An ideal leaflet for patients should not include all information about the medicine which is needed for prescribers. Health professionals can basically find information by themselves as their fundamental skill, and they are not the people who actually use the medicines, so they are not getting the leaflet even it's in the box. More importantly, the health professionals must encourage their patient to read leaflet routinely.

In research and development process, using medicines regularly was the key factor in considering using leaflet. This means that if patients have experience in reading the PILs, they will have the potential to consider that leaflet is easy to understand, trustworthy, accessible, and relevant to them. Their experiences should be valued. Therefore, they should be a part of PILs development process. Finding out what patients and the public need to ensuring their needs are met within the leaflet before applying into the practice is also essential in the UK. Moreover, previous research has found that their participants appreciated the concept of tailored information, desiring shorter and more relevant information. Information tailored to their condition or disease was most sought-after, followed by tailoring by age or gender. [75,78,86,96]

In Thailand, there are a very limited number of available PILs. Participants had no experience or no idea of the ideal medicine information written on the PILs they would like to receive. Therefore, most participants preferred medicine information on the medicine container instead of PILs. Moreover, the study in Thailand found that patients who had never heard of PILs were expecting to gain knowledge from PILs. Thai patients perceived the importance of PILs which can enhance the appropriate medicine use. This is a vital room for improvement in providing PILs in Thailand.[273] However, even if PILs were widely available in Thailand, people would still need information from HCPs. This is clearly the case in the UK – PILs are widely available, but respondents still wanted verbal information as their first choice. Therefore, PILs are important but so is talking to patients.[225]

Chapter 10 Exploring medicine information needs for people taking regular medicines: A qualitative study

10.1 Introduction

In quantitative survey research, this can take the form of multiple scales or indices focusing on the same construct. In a qualitative study, this can be reflected from multiple comparison groups to increase confidence in the data.[319] In-depth face-to-face interviews with open-ended questions are a qualitative approach to deeply explore the respondent's feelings and perspectives on a topic.[41,43]

A triangulation approach is one method to integrating data. The triangulation uses multiple techniques within a given method to collect and interpret data. Blending and integrating various data and methods can be cross-checking for internal consistency or reliability and the degree of external validity.[319]

According to the survey conducted in the United Kingdom (Chapter 7), there was a further need to explore more depth of the views of the public on what information about their medicines they want or need, how they use PILs, how they feel or react to the information within the PIL. Furthermore, using medicines on a regular basis was the most important factor in considering leaflets to be easy to understand, trustworthy, accessible, and relevant to them. Their experiences should be valued. However, the participants had to recall their previous experiences which were various among the participants. To explore participant's specific opinions, needs and suggestions about PILs in a more standardised way therefore a sample PIL, shared with all participants, could be used as a medium to focus the discussion. In-depth face-to-face interviews could be used as a part of the triangulation approach to cross-check and confirm the results from the survey, and to find out more information.

Therefore, to capture a more complete, holistic, and contextual portrayal of participant views on PILs, this study was proposed to conduct a qualitative study to explore more findings from the survey (Chapter 7) in greater depth.

10.2 Aim and objectives

To explore in depth views of the public on PILs and how they use them.

10.2.1 Objectives

1. To interview members of the general public who have recent or current experience of using prescribed or purchased medicines.
2. To explore their views on the importance of receiving or being able to access written medicine information and to determine the information that they consider most important to be shared.
3. From their experience to explore how they use medicine information (PILs).
4. To explore their views on an exemplar PIL (ibuprofen) in terms of quality of the design and readability, comprehensibility and trustworthiness of the leaflet.
5. To explore their views on how important it is that verbal information is available alongside written information and their ideas for how this support could be provided by healthcare professionals.

10.3 Method

10.3.1 Study Design

This study was a qualitative study involving members of the public in England, which utilised on-line interviews with participants through either Zoom, or Teams, according to the preferences of the participant.

10.3.2 Instrument

The topic guide (Appendix 11) was developed by the research team, based on analysis of the main findings from the 2019/2020 survey. It covered opinion on current experience of using prescribed or purchased medicines, views on the importance of receiving WMI, experience in using PILs, views on an exemplar PIL (ibuprofen) in terms of quality of the design and readability, comprehensibility and trustworthiness of the leaflet, views on how important of verbal information alongside written information.

10.3.3 Participant inclusion/exclusion criteria

Participants were members of the general public.

Inclusion criteria were:

- aged 18 or over
- currently using one or more medicines regularly OR have used a medicine purchased or prescribed in the previous three months
- able to understand, read and converse in English

Exclusion criteria were:

- age under 18
- not using any medicines (prescribed or purchased) regularly.
- a health professional or training to become one
- unable to converse in English or an appropriate local language

10.3.4 Interviewer training

Three undergraduate students were trained to carry out on-line semi structured interviews by the principal researcher and study supervisor. This was to ensure that the undergraduates were confident in their interviewing skills and could perform the interviews effectively. Three mock interviews were also conducted with members of the general public. All participants were interviewed by one of three undergraduate students. The PhD researcher arranged, attended and observed all interviews.

10.3.5 Recruitment

A purposive sample of people ensuring diversity in age, and number of regular medicines were recruited. Participants were recruited by using on-line forums and social media to promote the study. Potential participants were provided with an information leaflet (Appendix 9) and signed a consent form (Appendix 10) before being interviewed by a researcher. Prior to the interview they were asked whether they have any questions and to confirm that they consent to take part and for their data to be used as described in the participant information leaflet.

10.3.6 Procedures

A mutually convenient date and time for the interview was arranged with eligible participants by the Ph.D. researcher Prior to the interview, participants were asked whether they had any

questions and to confirm that they consent to take part and for their data to be used as described in the participant information leaflet. Participants completed a short form, which included a record of their demographic details such as their age and the number of medicines that they took on a regular basis, before the interview (Appendix 12). The participants name was not recorded on this form, but the form was coded to ensure that the demographic form and interview transcript were matched. The interviews were arranged through on-line platform such as Zoom and Teams, dependent upon the participant's preference. It was digitally recorded (sound only). Interviews were anticipated to last no more than 30 minutes. As this was a qualitative study the sample size could not be specified. The final number of participants interviewed was based on obtaining data saturation.

10.3.7 Data Analysis

Interviews were transcribed verbatim. The transcriptions were made immediately after each interview. The transcripts were extracted from the Microsoft stream, then the undergraduate students checked the transcript against the recording to correct any transcription errors. Participants were given a pseudonym at transcription so that the participant was not identifiable from the written transcript. Framework analysis was carried out in NVIVO 12, using a framework developed from the literature, results of the survey data (Chapter 7), the pre-determined themes connected to the interview schedule and analysis of the first interview by the research team.

Further analysis of interviews was done concurrently with data collection to ensure any issues missed out from previous interviews were captured. The research team each analysed the transcripts individually. However, issues and identified themes were discussed at weekly research meetings which were led by the project supervisor. This process ensured the reliability and validity of the analysis.

10.3.8 Ethical approval

This study was approved by Medway School of Pharmacy Ethics committee (Appendix 13).

10.4 Results

10.4.1 General information

There were 18 participants who expressed their interest in the study. However, three of them were not eligible as one wasn't currently using medicine, one participant was living in Scotland, and one had IT issues.

The 15 interviews were conducted between November and December 2020 using Microsoft Teams or Zoom applications. There were no interruptions during any interviews. The total recorded duration of interviews was 462 minutes, with individual interviews ranging from 14 to 56 minutes. The median duration was 30 minutes.

Eight of the 15 participants were male. The majority (n=8) of them were over 60 years old, while three and four were aged 18-30 and 31-60, respectively. Only two people were of Asian ethnicity with Persian or Farsi as their first language. The rest were white British with English as their first language. All of the participants were proficient in reading English. Nine of the fifteen had graduated with a university degree, while the rest had either a technical college (n=3) or secondary level (n=3) education. All of the participants used medicines regularly with a median of 3.0 medicines (range 1-11). Table 10-1 shows participants' demographic data.

Table 10-1 Demographic data

	Date of Interview	Gender	Age	Ethnicity	First Language	English readability	Education	Used regular medicine	Number of medicines	Duration of interview (minute)
01	12-Nov-20	Male	63	White	English	Yes	University	Yes	11	47
02	12-Nov-20	Male	33	Asian	Persian	Yes	University	Yes	2	31
03	19-Nov-20	Female	29	Asian	Farsi	Yes	University	Yes	2	14
04	20-Nov-20	Male	30	White	English	Yes	University	Yes	2	20
05	21-Nov-20	Male	77	White	English	Yes	Technical college	Yes	6	33
06	25-Nov-20	Male	25	White	English	Yes	University	Yes	2	19
07	02-Dec-20	Female	61	White	English	Yes	Secondary level	Yes	4	56
08	25-Nov-20	Female	71	White	English	Yes	Secondary level	Yes	6	30
09	03-Dec-20	Female	45	White	English	Yes	Technical college	Yes	1	23
10	07-Dec-20	Male	63	White	English	Yes	University	Yes	5	27
11	08-Dec-20	Male	62	White	English	Yes	University	Yes	1	30
12	08-Dec-20	Male	53	White	English	Yes	University	Yes	3	51
13	11-Dec-20	Female	63	White	English	Yes	University	Yes	10	19
14	10-Dec-20	Female	58	White	English	Yes	Technical college	Yes	3	25
15	14-Dec-20	Female	77	White	English	Yes	Secondary level	Yes	2	37

10.4.2 Themes

The three following major themes emerged from study objectives and analysis of interview data: sources of medicine information (past experiences); opinion on sample PILs and preferences to receive medicine information.

The source of medicine information (past experiences) theme will describe participants' past experiences in seeking their medicine information. The sources of obtaining medicine information include verbal medicine information, the Internet, and patient information leaflet (PILs). Focusing on the PILs, the theme will also show participants' views on the importance of receiving and being able to access PILs, how often they read them, which information they read, how they used the medicine information, and whether they trust PILs as an information source. Positive and negative views on PILs will be expressed.

The second theme, opinion on sample PIL focuses upon the content, layout and design of the example PILs. The final theme is their preferences for both the content of PILs and their preferred way to receive medicine information. This will show participants' preference for verbal information and written medicine information. This will also explore in the information that was considered as the most important to be written in PILs. The features, and design for improving the PILs will also described.

The supporting and correlating quotes will be presented with participant details (participants ID; gender, age) at the end of each quote.

10.4.2.1 Theme 1: Source of medicine information (past experiences)

Verbal medicine information

Verbal medicine information was the most frequent source of medicine information that all participants talked about. Most participants informed that at first they had been diagnosed by their GPs, then some of them were referred to a specialist. During these consultations, they received advice about their health and medicines. Some had a physical check-up, blood testing, or a review. After the medicine had been prescribed, other healthcare professionals including the GP, pharmacist or nurses gave advice about their health care and correct use of medicines. These interactions gave the participants opportunity to have a verbal discussion with the health care professional. The participants stated that they had the opportunity to ask questions and discuss about their particular problems.

“I was given a little bit of advice prior to getting the medication from the respiratory clinic. Then when I went to the GP, she gave me some further information, so she made sure that I was aware of how to how to administer the medication, how to how to use inhaler correctly, and what dosage to take as well.” (P04; Male, 30)

“oh Yes, yes it was very thorough if I remember…mind you this is 40 odd years ago originally, but I can remember them being very thorough and respectful and um. yes, giving me lots of opportunities to discuss,” (P08; Female, 71)

However, some of the participants were not satisfied with the services they had received. Particularly they described situations where they were not asked about their individual history or circumstances, for example whether they had any allergies to medicines, or given advice about a medicine when it was first prescribed.

“For example, they never asked me about anything else. I have an allergy. They never asked me.,” (P02; Male, 33)

’’ I do have an annual review of all with the pharmacist Um…like they do. They do it with everybody, um? That's a chance to actually talk to them about it, but it is generally going through. How are you?, What.. what are you doing? And things like that? But it's when you get a new medication, nobody sits down with you to go through it and the doctors just prescribe something” (P13; Female, 63)

Most participants mentioned that it was difficult to access verbal information from their GP. From their point of view, GP seemed unavailable and busy. Their health care professionals could not spend much time with them. The HCP sometimes only provided general information, while patients might expect more discussion.

“ So I think that's the easiest way. I mean, trying to get advice from a doctor now it's very difficult, not their fault, but because now you have to book telephone appointments and it's just you're not going to ring a doctor and pester them just to ask information about a drug. So pharmacists are the answer. The trouble is some of them are very busy at the moment and some of them are closing, so it's getting more difficult to find a pharmacist now..” (P10; Male, 63)

“Funnily enough, over the years I've become less trusting of the doctor and the pharmacist, giving me the medication. Because as I said before, they tend to just prescribe it. It then gets given and……. and I've notice that over the years because they used to do that, your doctor used to talk to you about your medication and then the pharmacist would always make sure that you

understood what the medication was for. But I find that now, everybody keeps saying they're too busy there…. too busy. and that's the that's the problem you know" (P13; Female, 63)

The participant mentioned that they could also consult about their medicines with pharmacists instead of their GP. Some of them have a good relationship with their pharmacists as well. Getting service with a good care health service could impress them especially service from pharmacy unit. However, some pharmacists didn't always provide such good service. Some of participants experienced poor pharmacy services.

"But also I find that I have a good relationship with my pharmacist because obviously being diabetic I'm there every month. At least so over the years I've built up a good [relationship] and I'm more than happy to go in his little room and have a chat and he You know he's actually very knowledgeable and very, very helpful in my estimation of pharmacist." (P01; Male, 63)

"I just wish that If you got new medication that they would actually take you into the little room and discuss it with you." (P13; Female, 63)

When participants obtained the medicine, they were aware that the medication normally came with a patient information leaflet. However, HCPs did not encourage or remind them to read the PILs.

"I kinda know there always in there but she (GP) didn't say that it would. But yes, I was aware it came with it." (P09; Female, 45)

The Internet

The Internet was the one source of medicine information that some participants mentioned. The participants revealed that they search for their needed information via Google. Some of them chose trustworthy websites such as those from the National Health Service (NHS) or the British National Formulary websites. The advantages of the Internet were its accessibility, and that it contains a lot of information. However, those participants who sought information on the Internet described their reluctance to act on it without confirmation from a HCP that the action would be appropriate for them to undertake.

" I have, I have Googled medication. I have looked into it to see what else it may or may not say about medications and the reasons for them. ….. I'm not that confident of using that information to actually act on it, the, the action would be from a pharmacist or a professional medic like a nurse or doctor." (P01; Male, 63)

" I feel reasonably I'm normally found what I need, so yeah, I'm reasonably confident in doing it, but if I wasn't totally sure or you know there was just a mild question, I would go back to the doctor just to make sure." (P09; Female, 45)

Patient information leaflet

All participants perceived the importance of PILs as a medicine information source. They were thought to provide correct and comprehensive information. Participants experienced that PILs contained medicine information in terms of instruction, dosage, side effects, the interaction between drug-drug, and food and drink. They informed that PILs could increase their knowledge about their medicines and therefore the medicine's effectiveness and safety.

***"** I think it's incredibly important that people know what they're taking, what the side effects are, what to know when things are going right, and want to know when things are going wrong, and what to do in those situations. When either one occurs.**"** (P08; Female, 71)*

Participants kept the leaflets as their basic information source so that they could remind themselves of something, or could check at any time and confirm some information that they might forget. Participants with multiple medicines got used to reading the PILs. PILs were easy to access because they are packed together with the medicine. They were also convenient to use. Some of the participants also mentioned the good layout of PILs which was clear and like a map making information easy to find.

"when I see a quick scan through, you know, like say the thing opens up and it's this huge, almost like a map…. but know that it's accessible when you look there, so you can kind of quickly scan through." (P04; Male, 30)

***"**But occasionally when I get home. I may wish to know a bit more, so I will get the leaflet out and have a look at it. ….. So sometimes I will scan. I will scan read it ..**"** (P11; Male, 62)*

With regard to usability and utility, some of the participants normally read the PILs for the first time they obtained their medicines. Most participants scanned and skimmed only the important information, while some of them also read the whole information carefully.

"Um, whenever I get a new medication, I always read the leaflet because let's face it, the doctors are quite busy and there are not going to explain every little thing that you should know so. I always tend to try my best to read it, cover to cover before I start taking it." (P06; Male, 25)

“I think like a lot of information now we just get information overload. So if it's a regular drug that I've taken before, even if the packet was different and sometimes simvastatin I've had different brands. I don't bother to read the PIL anymore, I think. OK, it's the same drug. It doesn't matter what brand is, so I don't read the,,, the PIL anymore. I will just open the packet and throw it away because it's a nuisance to get the tablets back in the packet. If it's a new drug or drug I haven't tried before, I will read the PIL. But not all of the PIL, just those selected sections that I'm looking for. But I will also ask a pharmacist if it's a new drug that I haven't used before.” (P10; Male, 63)

Generally, they expressed that they read medicine information in terms of side effects, indication, dosage and frequency storage condition, special populations, precaution, manufacturer, intolerance, ingredient, food and drink, drug interaction, contraindication, adverse drug reactions (ADRs), mechanism of action. Side effects were the most frequent issue that all participants mentioned. Some of the participants, who had multiple medicines from various sources, used leaflets as a reference to check whether each medicine had an interaction with another. However, some of them ignored reading PILs because they got used to taking the medicine for a chronic condition. The PILs seemed less useful for these people.

“I read all of the first page and then I thought on and I, I sort of glanced over then after that at the possible side effects of 1 in 100 people and 1 in 1000 people. And I thought God now there's too much information. But I mean it says here that you know if, if I, I could be affected by the high blood pressure and it says it's on here that it could give me low blood pressure or headaches or dizziness, or I might feel sick. I might not be able to drive and I'm thinking It bothers me more than anything else.” (P15; Female,77)

Most participants informed that PILs contained a lot of information that was not relevant to their conditions. They sometimes felt worried and scared about the information provided.

“but what I feel……what I found is that there's too much information on it, but it's not relevant necessarily for what I want.” (P05; Male, 63)

“but they can confuse you and can worry you and can also possibly make you think I'm not going to take this 'cause I've read the leaflet.” (P01; male, 63)

They also mentioned about difficulty of the language used in PILs which were written with medical jargon and technical terms. The font and text size written in the leaflets were difficult to find information and not attractive to read.

“but it can be a bit full of medical jargon, and it's not always patient friendly” (P06; Male, 25)

In terms of trustworthiness, most participants accepted that PILs were made by the drug company. They knew that PILs were developed under the Medicines and Healthcare products Regulatory Agency (MHRA) approval, and therefore the fact that the manufacturer produced the PIL did not interfere with the PILs perceived trustworthiness.

“On balance, I will trust it if it makes the medicine has been approved by the MHRA. I think I would trust it. So as long as the medicine itself and the information leaflet has been approved.” (P14; Female, 58)

“ They just wouldn't be able to live with the consequences, so I trust the PIL if that's if that's your question, really I don't mind that it's written by the manufacturer. I don't see who else could write it. I suppose the regulator could write it, but that's a lot of extra admin, isn't it? On the service, it's probably already very busy, so I'm quite happy for the manufacturer to write it.” (P10; Male, 63)

10.4.2.2 Theme 2: Opinion on sample PILs and Improvements

The Boots Ibuprofen PIL was shown as an example PIL. The first reflection of the example PIL which all participants expressed was the huge amount of information contained in the two pages. They expressed the view that this might affect their willingness to read the information.

“The first word that comes to mind is bloated, which probably doesn't describe it very well, but I mean, it's full, you don't really know where to start. Well, I guess you start from the beginning, but it’s not easy to access each piece of information.” (P06; Male, 25)

“ I still think that there's far too much information and I think you'd lose the will to live once you started reading it, um, and heaven forbid, if…if I couldn't read. What would? what would happen? What would ?...how would I know whether I should be taking this or not? That's my first impression.” (P08; Female, 71)

Contents

In terms of content, participants mentioned the uniform pattern and the information format and that most of the medicine leaflets available in the UK were printed with the same pattern. Some of the participants who had experience taking ibuprofen stated that they understood the content. Because of a long list of side effects information provided, they also thought that people who

never have taken Ibuprofen before might feel worried and fear the side effects information provided.

" If I put myself in somebody else's shoes who'd never taken it, I would probably not even bother. Um, because yes, it sounds horrendous. So I mean, goodness me, I don't know. Do people actually get all these problems?...perhaps I'm the lucky one, I don't know." (P08; Female, 71)

" Well, you could worry a lot about all those side effects. I mean, there's a whole list there you think really… if you were taking this medicine from the first time and you've never heard of ibuprofen, you might worry about it because it covers a lot of different side effects there. So it depends on what your medical situation already is isn't it? If your reasonably fit and healthy to start with, I think most people wouldn't worry too much about those side effects." (P10; Male, 63)

In this sample PILs, there was only showing the side effect information without any possibility of the evidence. Therefore, some participants mentioned about the possibility of side effects that the likelihood percentage or proportion of each side effect must be indicated so that they could aware and take more concern of these side effects.

"So one thing that is missing from this particular form of document is something that I like in the others and that tells me on the side effects is the occurrence it tells me 1 in 10 will get these side effects One in 100 will get the Side, 1 in 10,000 will get this, one in a million will get these if I find that there are Yeah, one in a million of dying of meningitis and taking ibuprofen, I'm prepared to take that risk. There's no feeling to my own personal risk assessment on this particular format, which is disappointing for me.?" (P12; Male, 53)

Layout and design

With regards to layout and design, the heading with bold could draw attention from most participants. It was a good practice in written the main topics with bold letters. The bigger bold titles were more stand out and clear, so most participants could find what they need to read quite quickly. The outstanding table which contained information about frequency and dosages was obviously giving the snapshot key information the vast majority of people need.

"I think that table is clear and quite apart from anything else is because it seems bigger. It's got more space in it. When you're reading a lot of prints, so let's go to the right of the table into the right-hand column, which begins a severe skin reaction and you go down and you've got a quite

a lot of a print there, even though you can kind of glaze over, you may lose your place." (P11; Male, 62)

"Where it says "What is this medicine for" in a bigger type and it's in a heavier type, whereas mine it is also similar size. So this is actually setting out into you could actually pick if you want you to say the possible side effects. It wouldn't take you long to find the paragraph entitled possible side effects. Where is this? I have to look. To find it, it's not it's not so clear on this one is it? It's here because it is set out In, in paragraphs with bigger headings." (P15; Female, 77)

The majority of participants felt disappointed with the ratio between the paper size and font size. There was too much text which was printed in small font and contained in a small size of paper. They felt that it looks very cramped. Some of them thought that they may need their reading glasses if they had to read this PIL in their real life.

" it looks very cramped and one of the things I would say is they are usually very tiny writing. I mean I have to wear glasses to read, but I would need to put my reading glasses on to read a patient information leaflet and I'm sure some people, particularly older people, must really struggle with the tiny writing" (P10; Male, 63)

"It's so squashed together it's quite difficult to read." (P14; Female, 58)

10.4.2.3 Theme 3: Source of medicine information preferences and preferred way to receive medicine information

Verbal medicine information

For the scenario of getting medicine information in the future or getting any adverse medical events when taking medicines, verbal medicine information was the main source of medicine information which most participants would prefer. Half of the participants stated that they needed verbal information from a HCP to guide them as to which aspects of the PIL were most relevant to them. The participants also mentioned that it was important to be able to ask their own questions which were specific to their needs. They also trusted in the experience and knowledge of their health care professionals.

"I would ask. I have asked in the past and when I get my review by my consultant on the prostate, I would say well why am I having this particular pill when it says it's for hypertension and other things because I already take for hypertension pills…… hypertension medicine so. The actual leaflet is saying it's all sorts of things." (P05; Male, 77)

" I always like to hear things from someone, hopefully with experience and knowledgeable because it has a much more natural calming effect. I think to hear it out loud in person when just reading it from a sheet and it always looks much more daunting in black and white ink on a page" (P06; Male, 25)

Emotional support and tailored information for individual conditions were also reasons for preferring verbal discussions. Especially, in the case of suspected long-term side effects, discussing or even online chatting with health care professionals was the most wanted medicine information source. Some participants were impressed with pharmacy services, saying that pharmacists could provide more information than they did in the past.

"If I thought it was a medical problem, I would go back to the doctor if…If I couldn't get to see a doctor, I suppose I'd go and see the pharmacist I do… I do. I'm grateful now that pharmacists are able to give more information over the counter than they have done in the past. It does alleviate the problems with. You know with the fact that there are fewer … doctors that you can get hold of and you do get extremely good advice. So yes, that's what I'd do if there was a problem with my medication, I would.. it would be dependent, but it would either be the doctor or the pharmacist." (P08; Female, 71)

"Having spoken about that with you, I think the only thing they could perhaps do is to have a link where you could go somewhere on a website, and actually, if you wanted to look up more, or even then, if you want to, then chat something like you know we get this "chat with me now" type box. But I mean I appreciate time is in NHS I don't know, but that would be helpful I suppose if you could do that in at least feel you're talking to somebody and then you could think things through and chat about it. Be quite nice." (P09; Female, 45)

When asking about how the health service could be improved in terms of providing medicine information, they stated that pharmacists could play an important role in providing medicine information because pharmacists seem more accessible compared with doctors.

"I think really it's the pharmacist is the key. So I think that's the easiest way. I mean, trying to get advice from a doctor now it's very difficult, not their fault, but because now you have to book telephone appointments and it's just you're not going to ring a doctor and pester them just to ask information about a drug. So pharmacists are the answer" (P10; Male, 63)

Written medicine information

Written medicine information alone seemed less preferred than verbal information alone. Participants perceived that PILs were a medicine information reference that were always supplied with prescribed medicines. Information that seemed important and the participants normally wanted to look at consisted of indication, frequency and dosage, side effects, interaction with other medicines and foods, and drink and drive information, and any traveling medicine restrictions. In the case of any suspected side effects, PILs were still one of the choices of medicine information source in hand; however, for most participants, when side effects occurred, they may need more information than was contained in the leaflet. They wished they could consult HCPs for more information.

"but if it was something instant like a rash or a tight throat or something, as soon as I've taken the medicine that I would look back at the leaflet and think is that a known side effect? You know, should I be reporting that? Um.. But not for long term effects" (P10; Male, 63)

The ability to tailor information for individual conditions, and provide simplified, short, and concise information were the attributes that participants wanted from PILs. Some of the participants appreciated receiving a 'pharmacy letter' which was comprehensive and tailored with their information.

" I think that the actual information sheet that, when is prescribed by a doctor or even,,,, even a pharmacist these days if it's prescribed, then it should be tailored to that particular person or that particular condition that.. that person is... has got rather than a generalization pill information sheet, that covers a whole range of things." (P05; Male, 77)

"I think it would be nice if it told you what you could and could not travel with 'cause I know that's never on there. I will have to look it up separately." (P09; Female, 45)

"The pharmacy letter that I get. Is even better than the verbal information I get from the pharmacist when they're handing it over at the counter…Straightforward means that the pharmacy writes up a letter and it's it's a personal well. It's not a letter, it's a note. It's a list of notes, but they've been tailored to the combination of drugs that I've got, so they must have done it in a personal level" (P12; Male, 53)

The participants also provided some suggestions for improving the ibuprofen PIL. They suggested that the PILs could be colour coded so that this could help to signpost them to the information they needed. The main information and all the technical information could be left as black font

because most people would not read through that. Some pictures or icons should also be added to draw the patient's attention to a particular section. PILs could be written in braille language for the blind.

"Which was the traffic light situation which is red, amber and green, something bright, something where you know exactly where you're going to. The red could be the very important information you need and the risks that are umm are possible of taking that medication that the amber could be the things that you should know…Uh, and the green would be." (P08; Female, 71)

"Um I am a visual person so um. Yeah, this is. Um, this is a bit like reading a newspaper to me, which is just I don't ever do it. I read, I read a lot, but. I think, um maybe some imagery would be good. How you would actually do that, I don't know. Like what could you put into images? I don't know. Um, I do think somehow it needs to be a bit more accessible and it needs to say read me, I'm important. Which is actually, is not what it does. It doesn't say read me." (P07; Female, 61)

Some of them were concerned about an environmental issue that the PILs were printed on paper. The PILs might be the waste eventually. Therefore, the electronic PILs were suggested to replace the paper version. However, there were some concerns in using the technology in elderly people.

" I always get the leaflet in every pack I get. I think about the waste of paper and the resources when I actually don't need it anymore unless there is some change in the. the risks or the benefits. So again, you know we're trying to clean up the planet and there we are. We're throwing loads of stuff to people that just throw it away, because I haven't read one for 40 odd years until… until today and that's terrible, isn't it? But that's the way it is." (P09; Female, 45)

"I suppose online might be one way, but I don't know how I would go about that. I suppose I could look up the brand of the drug and I could probably download the PIL. I've never tried to do that, but I assume that's an option. It wouldn't…wouldn't occur to me to do that to be honest." (P10; Male, 63)

The combination of verbal and PILs seemed to be the perfect source of medicine information with PILs supporting and providing back up for the instruction the participants had received verbally. In the situation that they might forget, or could not catch up on the information from their HCP, the PILs were still available and accessible to them. The leaflets were also thought to provide reassurance; to confirm and support verbal information that they received from their HCPs, and information obtained from other sources such as the Internet.

"I think it's nice for a doctor just to quickly go over the instructions on the medication, but also to have written because I think certainly for us who are in the third age we… we tend to forget things very easily. At least you have a leaflet to refer to. When you're younger, you know, just the verbal will probably be OK." (P08; Female, 71)

"I think initially I prefer it verbally the basics this is what it is. This is what it's for. These the possible side effects and this are when you take it, but I also want the backup information in the leaflet in the, in the box." (P14; Female, 58)

10.5 Discussion

10.5.1 Verbal medicine information

Verbal information from health care professionals was the major source of obtaining medicines information for the general public because, within the healthcare system in the UK, most medicines, particularly if they are taken on a regular basis, are prescribed by the patients' General Practitioner (GP) or an independent prescriber, and then dispensed by a community pharmacist. The patient therefore has access to the community pharmacist, doctors, nurses and other HCPs in healthcare centres within the community. Verbal information was the major source of medicines information, which most patients were familiar with.

Furthermore, verbal medicine information was the main source of medicine information which most participants said that they would prefer if they had to take a medicine. Trust in the experience and knowledge of the HCP was the major reason for this. Participants wanted the opportunity to receive tailored information and ask any questions which were specific to their needs. Participants indicated that they wanted more information about the possible long term side effects of a medicine, and that they wanted the opportunity to discuss this with their HCPs. A previous study found that physicians and pharmacists were the most commonly used sources of medicine information for patients.[10] Earlier studies in Armenia, Australia, Sri Lanka, and the UK have shown similar results which revealed that medicine information from pharmacists was judged to be important for patients and the majority of them trusted the information received.[78,97,104,297]

The major factor which limited the provision of verbal information was time restrictions. Participants wanted that they could spend more time with their HCP. Community pharmacists' workload has increased since the introduction of the contracts introduced on 1 April 2005 in England and Wales, especially around the core activity of dispensing prescriptions and medicines use reviews.[315] Therefore the pharmacy staff in the UK do not have as much time to spend with

individual patients because their time is limited by the number of items that they to dispense and the workload associated with this. A prior study also found the greatest increases in clinical workload in UK primary care. There was a substantial increase in practice consultation rates, average consultation duration, and total patient-facing clinical workload in English general practice.[320] It is unsurprising that verbal information was also judged to be much less accessible than written information. This has been found in previous studies.[293,296,298] A systematic review in 2018 which focused on patient and public perspectives of community pharmacies in the United Kingdom also found that there were some who questioned whether pharmacists had enough time to carry out additional services due to their high workload which may lead to a lack of continuity for service provision.[321]

However, there was an advanced service for community pharmacy called New Medicine Service (NMS) which was designed to provide early support to patients about their medications. The NMS was designed to help patients get the most out of their medicines. This advanced service can help with the patient presenting a prescription for certain new medicines for a long-term condition. This may help patients who need to talk with a pharmacist when they are prescribed certain new medicines.[322]

10.5.2 The Internet

The Internet was another source of medicine information which some participants talked about. In general, websites available on the Internet seem to be accepted as a source of knowledge. It is also easy to search for specific information which may be needed at any time via information technology devices such as a mobile phone, or laptop. A prior study found that the Internet plays an important role as convenience, timeliness, and privacy medicine information source for searching health-related information.[10] A literature review and some studies conducted in the UK, also found the Internet to be easily accessible and cited as the most frequent used source of general health information.[10,296]

However, trustworthiness of information on the Internet was still the concerning issue for the participants in this study. The earlier study also showed that people perceived that it was difficult to find reliable information on the Internet.[10,296]

10.5.3 Patient information leaflets

All participants acknowledged that patient information leaflets were an important source of medicine information. They had all experienced reading their own PILs. This is similar to studies which have found that 67-75% of people in England read the PILs.[113,120,293] Apart from in the UK,

studies from Saudi Arabia, Palestine, and Nigeria have revealed that the percentage of the public reading the patient information leaflet ranged from 45%-90.6%.[84,86,91]

The example PIL was representative of most of the medicine leaflets available in the UK in that it had the same uniform pattern and information format. In EU countries, all licensed medicines are legally provided with a PIL. The content of the PIL is approved as part of the medicine's license approval process, and must include the following headings 1. What the medicine is and what it is used for 2. What you need to know before you take the medicine 3. How to take the medicine 4. Possible side effects 5. How to store the medicine 6. Contents of the pack and other information.[15,200]

The participants revealed they normally read the PILs when they first obtained their medicines. Mostly they reported only scanning and skimming important information, but some, a minority, did read the whole information carefully. These findings support former studies in Egypt, Palestine, Saudi Arabia, Armenia, and the UK that found that most patients read the information the first-time of using a medicine.[76,83,86,91,95,97]

The side effect section was the topic that all participants read, followed by indication, dosage and frequency, storage conditions, special populations, precautions, intolerance, ingredients, food and drink incompatibilities, drug interactions, contraindications, and mechanism of action. The results were similar to the previous studies in Armenia, Singapore, Korea, Saudi Arabia, Nigeria, Egypt, and the UK, which that found that the information viewed as most important and needed by patients/ the general public were adverse effects, dosage, indications, and method of administration, duration of treatment, expiry date, and contraindications [10,83,84,91,97,106,120]

There were both positive and negative points of view on the leaflet. The leaflet with the medicine is the general public's knowledge source which could be retained for reference. This supports previous research conducted in Palestine and the UK that some people thought that the leaflet could generate new knowledge and may have a positive impact on behaviour.[76,86,114,119] The information was easy to access, read and understand.

However, negative views on PILs were mentioned. The PILs contained a lot of information, and it was not all relevant to the medical conditions for which they were taking the medicine. PILs sometimes made participants feel worried and scared about the information that they provided. The language used in PILs included medical jargon and technical terms. The thin font and small text size were difficult to read and not attractive.

These findings support a large number of studies which found that people in many countries were dissatisfied with the poor format and language used in medicine leaflets. The existing leaflets do not meet patients' needs and appear ineffective. They had some difficulty in comprehension or understanding related to the language used, technical terms, and the small font size used. They felt that PILs could raise fears and concerns.[79,84,87,91,95,107,248,249]

In terms of how to improve PILs, the PILs could be the tool which can support the safe and effective use of medicines. The design and content of leaflets impact on patients' willingness to read them. Application of good design principles improves readability, comprehension, and ability to locate information.[249] The titles were more prominent and clear with bold characters so that the information was clearly distinguished and easy to find. This was correlated with the recommendation in the guideline on the readability of the label and package leaflet of medicinal products for human use regulated by the European Commission.[15] Tables can be an option for containing the key information such as frequency and dosages.

Participants in this study thought that it would be better if the PILs could be printed with colour codes to signpost the target information patients seek. This finding correlates with a previous view on new approaches to pharmaceutical benefit–risk communication tools. These authors considered that the food safety sector (traffic-light labelling) system has shown great promise for being usefully adapted to the pharmaceutical context.[323]

Additionally, some participants suggested that some pictures or icons can also draw the patient's attention. Several studies have been conducted to develop and test new pictograms in leaflets for use in low-literate patients with HIV, older people, and general patients. [126,130–132,134,324–327] They found that the pictogram significantly improved the comprehension of medicines, and played an important role in increasing understanding and promoting adherence to prescribing medicines. However, pictograms should be developed in accordance with the cultures, beliefs, attitudes, and expectations of the target population. Pictograms needed to be validated and culturally adapted before use.

The participants in this study suggested that the percentage or proportion of experiencing the possible side effect must be indicated, not showing simply a list of the side effects alone without any indication of how likely someone is to experience these. For the EU Guidance, it was updated in 2006 and 2009, the presentation of adverse effects was recommended to combine each of the five verbal terms with a numerical frequency. Many studies have been conducted to evaluate the optimum way that adverse effects should be described. Previous studies conducted in the UK in 2008 and 2012 found that a wide range of methods was used to describe adverse effects, and 23-

40% of the leaflets did not provide the likelihood of adverse effects occurring, while in those that did different formats were found, such as recommended EU terms, verbal descriptors, numerical indication, or long lists of adverse effects.[198,200]

Some suggestions for presenting side effect information have been suggested within the published literature. The absolute frequency format achieved greater accuracy in estimating the likelihood of experiencing side effects with more participants also being satisfied with this format. The use of numerical descriptors was positively related to the perceived influence of the information on the decision to take the medicine and was negatively related to ratings of satisfaction with the information.[18,22,328] Some studies found that patients overestimated the probability of occurrence of side effects in general and found that textual format or verbal risk descriptors were associated with higher estimation and mislead patients with respect to the actual risk associated with a particular medicine than the numerical format[19,20,328] However, in practice, patients found numerical data difficult to interpret and textual information was preferred.[21]

The majority of participants in this study expressed that they would like PILs to provide tailored information so that it can be relevant to and specific with the disease or context of an individual patient. Tailoring information leaflets to patient characteristics and requirements would enhance their effectiveness. In previous studies, patients have also welcomed the concept of tailored information, preferring information tailored to their condition, age and gender.[75,249] The study from 2017 carried out in New Zealand also has shown that passive information of pre-printed leaflets was perceived as outdated, unvalued and ineffective. Leaflet tailoring by using automated computer systems for with the ability to further adapt patients' information might be the best way to provide specific medicine information for individuals.[249]However, the automated tailored leaflets would be the duty of HPC rather than the manufacturer. This is therefore still only found and feasible in developed countries.

Most participants trusted in the PILs made by the drug company because, in the UK, the PILs were developed under the Medicines and Healthcare Products Regulatory Agency (MHRA) approval. Environmental protection was an issue of concern as the PILs wasted paper with participants often simply throwing these away without reading them, particularly if the medicine was being taken on a long term basis for a chronic condition. In the UK, the paper waste was approximately 7 million tons (3.2%) of waste material in 2016.[329] An improvement therefore would be that all PILS should be either printed on environmentally friendly materials or replaced with technological approaches that circumvent printing.

The participants indicated that their HPCs neither told nor encouraged them to read the PILs. A previous study from Ghana found that more people read leaflets if told to do so by a pharmacist. No similar study has been conducted in the UK. Pharmacists should advocate reading the leaflet and promote the PILs as a useful resource. [80,330] Therefore, pharmacists and other HPCs should provide verbally information while encouraging the patient to read the leaflet. Especially, it is clear that people normally read the PIL when they started a new medicine, but then when they got used to and used the medicines for a long-term, many ignored it and threw the PIL away. Therefore, if there were any change in the benefits or the risks, and the updated information was included in the PILs, they wouldn't know. The MHRA normally informs doctors and pharmacists when a new risk is discovered, therefore HPCs must inform and encourage patients to read the PILs. However, it also suggested that the leaflet should not replace the pharmacist's obligation to provide verbal counseling.[330]

The combination of verbal information and written information was the perfect match. The participants needed PILs for reference. They might forget, or could not remember all the verbal information provided by their HCP, so it was desirable to have the PILs as a source of medicine information in their hand. This finding supported those from a previous study that only relying on verbal information might be inadequate and leaflet on its own also seemed to be suboptimal. Providing more patient-centred leaflets would make them more accessible could improve the leaflet's value. Automation of tailored information would be beneficial.[331]

10.6 Conclusions

Verbal information from HPCs was the primary and important source of medicine information. This source was considered a trustworthy source, the information provided can be tailored to individual needs. However, time consuming was a concerning issue for this source. The Internet seems to be an option for medicine information seeking. Accessible easily was the advantage of the Internet. However, reliability of the information on the Internet was still questionable.

Written information was acknowledged as an important of medicine information. Normally, people read the PILs at the first time of being given their medicine by scan and skim the information provided. The side effect section was likely to be the most frequent reading topic. However, it was found that existing leaflets do not meet patients' needs regarding the information provided, layout, and design. The design and content of leaflets did not convince patients to read them. Tailoring information leaflets to patient's individual conditions were required to enhance effectiveness. Verbal coupled with written medicine information was confirmed as the most preferred source of medicine information.

10.7 Strengths and limitations

The study was carried out by using semi-structured online interviews with a range of participants, in terms of their age, gender, education, diseases and the number of medicines taken. We could also generate more insightful responses by having greater opportunity to ask follow-up questions, seeking additional information, and returning to any questions later on in the interview to further understanding. Because a standard real PIL was provided to aid discussion rather than an imitation PIL, the opinion and suggestions from the participants are relevant to practice.This study was originally intended to be carried out using focus group discussion to observe the effect of idea gathering and group dynamics. As the data collection period fell within the coronavirus pandemic in 2020, the focus group discussion was not allowed. The online face to face interview with participants was conducted instead. Therefore, the emotional responses which was the aim to explore were difficult to probe and were not fully explored by the online platform.

As on-line in-depth interviews, the authentic example PIL was not shown. It was shown on the computer screen. Therefore, the feeling of touching the real material in terms of the texture, size of paper could not be captured. However, all participants had their own experience in reading PILs which they could recall.

10.8 Recommendations for research and practice

Even though the PIL used in this study was well designed and contained all the information required by the MHRA, it did not meet patients' needs. New research must be conducted to update and redesign/ further improve and optimise the PIL. Tailoring information specifically to an individual patient's needs must be explored to identify what core information is needed, which design is optimal, and PILs could be better integrated into routine general practice. Information technology (IT) can contribute to this, and what and how technology can be used to support the provision of medicine information needs to be further explored.

With regards to practice verbal combination with written information is the preferred in the source of medicine information. This not only encourages patients to read the PILs, but also informs them about the information that is most relevant to them. It also gives patients opportunity to ask questions. Tailoring information leaflets to individual patients would enhance patients' satisfaction.

Chapter 11 General Discussion

11.1 General introduction

This study was started by conducting a scoping review. Overall, there was a limited amount of literature published in Africa and Asia with most of these studies having occurred within the last decade. A greater number of studies were conducted in the United Kingdom. Studies tended to be concentrated in specific countries and many were carried out by certain research groups. It was evident that there was a difference between the studies conducted in the UK, in which PILs regulations have been established for four decades, and countries in Asia and Africa in some of which regulation have been developed much more recently. In the UK, the studies were focused not only on the completeness of the medicine information provided, or which data were provided when compared with the EU standard regulations, but were focused on how medicine information could be improved to enhance patients' understanding. This shows that the standard provision of PILs or PIs within the different countries affected the type of research conducted.

Generally, the main focus of studies included in this review were as sources of patient's medicine information, impact of WMI on patient's knowledge and behaviour, the development and use of pictograms, factors affecting reading and usefulness of PILs, content, design and format, and regulatory aspects of PILs.

The scoping review enabled some knowledge gaps to be identified. These were the needs and preferences for medicine Information sources and the wider public's views on PILs, which can impact on practice and policy in the future, helping to improve the regulations. There were an increasing number of studies focusing on WMI, particularly medicine content related to the regulatory issues in Asian countries since 2013, which could be regarded as a significant sign of development and improvement of patient safety. The studies identified from Thailand also included surveys of patients and several studies seeking to improve patient knowledge through providing WMI.

WMI research is gaining interest in the United Kingdom, Asia, and Africa. However, most studies had limitations of small-scale, and local surveys which may be unrepresentative of larger populations. Furthermore no studies at all were identified from many countries illustrating a paucity of evidence and research from these geographical areas.

The quality of the studies also varied. There was a lack of critical information, for example, blinding measures, sample size calculation, characteristics of participants, refusal rates, and follow-up period details. Therefore there is a need not just for more research but for high-quality research studies to be conducted so that the evidence from these is reliable, valid and can be used to improve practice..

Furthermore, more research studies are needed to learn more about what people want, prefer, and need from written medicine information, as well as to evaluate the quality and benefits of making this information available using internationally accepted methods and regulations. For example user-testing of all information leaflets should be adopted following standard methodologies but also acknowledging the cultural and societal context that the PILs are intended to be used within.

More intervention studies are required, but first good quality PILs are needed, so it is critical to focus on identifying the most desirable format and content of PILs. In order to ensure breadth and depth, both quantitative studies, such as surveys, and qualitative studies, such as focus groups, are required to investigate these needs and preferences, and to provide more insight into people's cultural and societal contexts. Future studies could also aim to investigate whether WMI can improve patient empowerment in making health-related decisions.

The development and validation of a standard measure to assess the impact of WMI on knowledge, which can be applicable to all medicines, would be a valuable research tool for future use so that this can allow comparisons and meta-analysis across studies.

One of the main purposes of this thesis was to undertake comparisons firstly of the regulations between countries, then of available leaflets, and finally the use of medicine information sources and opinions on these sources. Regulations and guidelines were compared between several countries, and the key factors which should be included in a PIL identified. Comparison of leaflets from the UK and Thailand was then conducted with reference to the 'gold standard' of guidance/ regulations from across the globe (including USA and Australia). Both this and the studies into use and opinions of WMI among the general public were made between the UK, where medicine information systems are well established, and Thailand, where the system is developing. A critical analysis was conducted with the aim of identifying best practice from both countries which potentially could be taken forward to improve PILs in both countries. The qualitative study in the UK was undertaken, to further understand what people in the UK want from WMI, given that it has been widely available for many years.

11.2 Discussion of key findings from empirical studies

11.2.1 Sources of medicine information

Opinions of the end users of WMI are vitally important and should be frequently sought. Therefore studies obtaining user opinions in term of sources of medicine information they use, preferences for medicine information, and preferred ways of getting medicine information were included in this thesis. It was anticipated that differences would be found between the UK and Thailand, since patient information with medicines has been established and regulated in the United Kingdom for many years, while, in Thailand, PIL regulation is still in the starting phase.

The two surveys were conducted using similar methods in the UK and Thailand. Comparison of the survey findings demonstrated that how established the enforced PIL regulation was within a country impacted on the points of view of participants on their preferences for the source of medicine information. These differences in context were clearly observed between the general public in Thailand and in the UK. In the UK, the major source of medicine information was written information whereas, among Thai participants, the number of participants receiving written medicine was significantly lower.

The survey also found that the general public in the UK were more familiar with written medicine information than people in Thailand. It was not surprising that written information was not the main source of medicine information among Thai respondents in the past as they were less likely to have experienced this format. Even when WMI was received, it was most frequently in the form of PIs, and people have difficulties in understanding PIs even when written in the Thai language. In addition, these have such a wide range of text design and format. Also, limitations in the availability of PILs meant that the majority of participants were not familiar with this format. These were the main challenges to the provision of written information in Thailand.

From the survey, Information on the medicine container was the major source of WMI in Thailand. There is good pharmacy practice guidance regarding to information on the medicine container (a plastic envelope) which should contain, at least, information in terms of the name of pharmacy store, and contact, patient's name, medicine generic and trade name, indication, how to use the medicine, and precautions.[332] This practice is covered by the regulations relating to the permission and the issuance of licenses of sale of medicines in community pharmacy in Thailand. Importantly, there have been no studies on whether this information is actually provided, or how appropriate or sufficient it is to be used as medicine information for patient. However, obviously, the information provided on the medicine container (a plastic envelope) does not include any instructions on what to do if any side effects occur. Therefore, future studies on the impact of

using such medicine containers, in particular a plastic envelope, must be conducted so that empirical results can be used to change practice in order to improve patient safety. Regardless of what the medicine information on the plastic envelope is, the gold standard medicine information for patients must be PILs that have been standardised by an authorised organisation in order to reduce patient confusion.

11.2.2 Perceptions of the general public on different medicine information sources, preferences for medicine information sources

The triangulation of data from the survey in Thailand and in the UK, face to face interviews in the UK, and the scoping review, confirmed that verbal information was perceived as trustworthy, easier to understand, provided an opportunity to ask questions, and could be fit to a patient's health conditions. The survey both in Thailand and in the UK also found that obtaining medicine information verbally from a health worker was the most preferable source of medicine information. Comparing with other sources of medicine information, it also found that obtaining medicine information verbally from a health worker was the most preferred source of medicine information. Furthermore, when participants would have a medicine in the future, the majority of participants in both countries preferred receiving information both verbally and in writing. It could be the ideal form of medicine information source because verbal information can be tailored to individual patient conditions and characteristics, and patients trust their HCP. Patients can also keep the written information as a reference for remembering and managing any side effects that occur.

Receiving verbal medicine information from the HPC was identified as the most fundamental and trustworthy source of health information. However, health professionals' information was sometimes perceived as too technical, and safety information was limited.[78] The results also found in the face to face interview carried out with UK participants confirmed that time restrictions were the major factor which limited the provision of verbal information. The participants would like to be able to spend more time with their physician. However, in practice, it is not feasible for physicians to give patients more time as they have high workloads. The pharmacist must therefore play an important role and be responsible for giving information about both OTC and prescribed medicines, especially, at the first time of providing a medicine; this particularly important for certain medicines with high associated risks in both UK and Thailand. Furthermore, the patient may be given the opportunity to ask questions about their medication. Pharmacists could follow good pharmacy practice guidance (Thailand)[332] and NHS Community Pharmacy Contractual Framework Essential Service – Dispensing[333] on verbal information provision in providing medicine information to patients.

Specifically focusing on written information, the leaflet provided with the medicine was the most preferred source among the UK participants, whereas the Thai respondents preferred to read medicine information on the dispensing label/ medicine envelope because they thought that it was easy to understand. In general, people's thoughts did not extend much beyond their own past experiences. Participants who were more experienced in the use of medicines in the UK were more likely to be familiar with and to value PILs. Those in Thailand where access to PILs were limited were less likely to appreciate what PILs could offer. There is a potential that people in Thailand would change their opinion if PILs became more widespread because, in comparison with the PIs, PILs should be easier to read. However, there was no research supporting the model PILs or available PILs on what people think about them in Thailand, and more research studies on what people do want are needed before there is widespread use.

Generally, the Thai participants wanted to receive more of every type of information in comparison with participants from the UK. This reflects the fact that the medicine information for patients or the general public provided in Thailand was inadequate, because most current information was difficult to read and designed for HCPs. Thai's still require more information from all sources, as it has been lacking for many years. In contrast, the majority of participants in the United Kingdom said they had far too much information. This could be the result of a long period of time over which WMI provision in the United Kingdom has been established. This is an urgent issue to be solved for Thai people as it affects patient safety.

As in Thailand, the Thai culture is one that discourages information seeking and encourages acceptance of a paternalistic form of medicine, where people simply do what the HCP tells them to. This also needs to be changed. People must be encouraged to seek health information by themselves. This could be started by reinforcement to level up health literacy in Thai people. Furthermore, people could be taught and encouraged to protect their rights as consumers who need to be well-informed in order to manage or use any health care products. In addition, consumer protection legislation must be strengthened.

Whilst the UK studies found greater public awareness and acceptance of PILs which were adherent to the regulations on WMI, the findings from both the UK and Thai studies in this thesis concluded that the general public were dissatisfied with the poor format and language of medicine leaflets. It can be concluded therefore that existing leaflets do not meet patients' needs and appear ineffective.

This critical finding suggests that the current PILs guidelines may not be fit for purpose. Despite the fact that the guidelines in the UK are well prepared and established, and are all subjected to user-testing, some of the recommendations are not aligned to patients' needs and preferences.

The majority of the general public in both countries stated that they normally read the information when they were first given the medicine. This key finding supports the findings from the scoping review that patients read PILs at first-time of using a medicine.[76,83,86,91,95,97] Well-designed PILs may be able to capture patients' attention and entice them to read the leaflet the first time they receive it.

11.2.3 PIs and PILs guideline and ideal PILs

The provision and regulation about PILs is vital in terms of guiding and directing the content of PILs, and how people should access them. The scoping review and the results of empirical studies in this thesis found that the regulatory framework within a country also had an impact on research conducted. Therefore, reviewing the different guidelines from different countries and investigating the available PILs was conducted to find out the differences and problems. Ideally all guidelines should ensure that the information contained in leaflets for patients is accessible to and could be understood by those who receive it, so that they could use their medicine safely and appropriately. By comparing the guidelines across four countries: EU, US, Australia and Thailand, it was found that all important medication information which patients should know were covered in all regulations. However, the detail and information contained in guidelines varied between the different countries, dependent on their contexts and backgrounds. The varying detail could be due to the fact that regulations were adopted and altered to match specific situations. The critical point is that the guidance should be updated routinely to provide acceptable standard and appropriate formats which should be based on the findings of research.

Investigating the available PILs from the UK and Thailand was also conducted to find out the differences and problems. The results found that the UK leaflets were uniform in terms of content and design, while the Thai PIs were varied both in content and design. The different formats could be linked to lack of non-standard formats, as well as lack of post-regulation control and monitoring. Some pharmaceutical companies would like to cut costs by reducing the quality of paper and the size of PIs. However, the leaflets from both countries were difficult to read. More importantly, the serious problem was that Thai PI was not appropriate to be the main medicine information source for patients. This suggests that the Thai regulatory authority should require a unified approach to PIs and PILs through setting standards and introducing regulations, then enforcing these, including the need to provide PILs with all medicine.

From the scoping review and empirical studies in this thesis, some aspects can be used to generate ideal PILs. More prominent and clearer titles could be desirable with bold characters to ensure that the information was distinguishable and easy to find. Tables can be used to describe important information such as frequency and dosages. PILs could also be printed with colour codes to direct patients to the specific information they seek. Some images or icons may also be useful to catch the patient's attention and draw them towards reading the PILs. The language used, words, font and font size, and specific information have to be set out in a particular order and written in terms which the patient could understand, and read easily. Medical technical terms must be avoided. PILs could also be printed on good quality of paper. BALD criteria could be a guidance in designing leaflets for patients. In term of content, the percentage or proportion of the possible side effects must be indicated, rather than simply listing the side effects without indicating the degree to which they occur.[18–22,328]

People liked the idea of tailoring medicine information to their specific conditions or diseases.[75,78,86,96] The tailoring of medicine information to age and gender were also needed.[75,249]Leaflet tailoring by using automated computer systems could be the best way to provide specific medicine information for individuals.[249] The feasibility of tailoring of medicine information needs more investigation. Importantly, people who have experience in using medicine could take part in leaflet development and improvement. User testing is also a vital process before launching a leaflet to the market. However, there is user testing in UK but PILs do still not meet all needs. Post-marketing review in terms of adhering to the PILs provision and general customers' satisfaction could be routine research.

There are such model PILs for an increasing number of medicines, produced by the Thai FDA. This could be exemplar for drug companies to reproduce the PILs to their products, and can be also source of patient information. However, there was no evidence on whether patients used that source. None of the study participants mentioned being aware of it. HPCs, in particular pharmacists, should increase their awareness of these leaflets and suggest patients seek information from this source. As web-based information was also the favoured form of WMI in Thailand, Thai FDA should encourage pharmacists at community pharmacies and hospitals to promote the model PILs and the website.

11.3 Summary of key contributions to knowledge

There was a systematic review on WMI published in 2007 for which most studies identified were conducted in developed countries. To update this, a new scoping review of the literature conducted in the areas of interest, Africa and Asia was, therefore, undertaken. This was the first

ever literature review to focus on research from these continents which excluded research from countries with long-standing and highly developed WMI, except the UK, which was included for comparison. The scoping review identified a large number of papers of many different types, which meant that a systematic review of intervention studies and surveys was also possible.

One of the important lessons learned from the literature review was that the provision of PILs or PIs in each country affected the type of research conducted and that the participants' usual context affected the research findings. It was also clear that the PILs and PI regulations and guidelines in any country are a key factor that influences what WMI is available and how the leaflet is created.

No study, to date, has been conducted in Thailand to investigate the PIL Regulations and assess the suitability of written medicine information available. The findings from this study have begun to fill the gaps identified in the literature review and contribute to knowledge. The comprehensive comparison of ibuprofen leaflets which were available in the UK and Thailand markets was the first such evaluation. The evaluation used methods for assessing design and readability for the first time, as well as assessing content.

Furthermore, the surveys were the first to determine information on the general public's needs for medicine information in the UK or Thailand, and to compare these. In both nations, the majority of participants preferred to receive both verbal and written information. While WMI was recognised by the public as an essential source of medicine information, the evaluation of the available leaflets showed that these do not match their expectations in terms of information, layout, and design in either country. The qualitative study carried out in the UK was a novel approach to gathering peoples' views and provided more detailed opinions on PILs in this country.

11.4 Implications for pharmacy practice

To support patient safety, and encourage self-care, the most distinguishing result was that the general public in both countries preferred receiving both verbal and written information. The verbal information provides the opportunity to tailor health information to the individual patient, which they desire. Therefore, the healthcare professionals should pay attention to patients as individuals when providing medicine information and self-care information, to support their individual needs.[316] There is a need for HCPs to evaluate patient comprehension and need for medicine information. They should direct people to the WMI which is provided, but also advise them as to which sections are really important and relevant for them. Especially, pharmacists may begin by recommending the adverse drug sections, which were frequently the main sections of a

patient's interest.[113,123] Pharmacists, in particular, must also be aware of some patients' desire for tailored medicine information and ensure they meet these needs during consultations.[75]

The evaluation of ibuprofen leaflets demonstrated that some Thai PIs lack critical information. HCPs in Thailand therefore need greater awareness of the type of written information which patients receive with their medicines and should provide further information where important points are lacking. They should also be more concerned about providing patients with specific medication information by identifying those who need more information, and spending more time with these patients. Additionally, the establishment of more specialist HPC positions in providing medicine information to patients e.g. patient-focused drug information unit, and counselling via telephone or video-link may also be helpful.

As previously stated, the Thai FDA has created model PILs for some medicines. No research has determined whether pharmacists are aware of these, but it is essential that pharmacists become aware of them and advise patients to obtain medicine information from this source. The Thai FDA could encourage pharmacists to promote the model PILs and websites, and support pharmacists by supplying model PILs to all pharmacies to provide to patients or developing dispensing support systems which include a link/ QR code on the dispensing container so that patients can access on-line information at any time.

11.5 Implications for policy and research

In terms of policy, providing PILs to all medicines given to patients must become compulsory in Thailand; without a change in policy or a legal requirements to provide information to patients practice will not change. The policy or guidelines that were adopted from other countries may lead in the wrong direction because each country has its own context in term of health systems, people's demographic, health literacy and needs. It must be written in the context of a specific country. Research and routine practices in certain contexts could be used to develop and improve the WMI. This means that the country could have its own study to suit the context and people. More importantly, all stakeholders, including regulatory bodies, the manufacturing sector, HCPs, independent researchers and the general public or patients, should be involved in developing and improving patient guidelines and leaflets. An authorised organisation, such as the FDA in Thailand, should provide a prototype of PILs that provided all key details, were well designed, and passed user testing for each medicine during the first stage of development.

Then, the regulation revision must further be based on evidence of effective practice. Research to gather evidence of current practices to determine whether they are effective in improving

patients' knowledge could be conducted alongside any changes in regulation. The content, design and layout of available leaflets must also be routinely assessed by both FDA and independent researchers to ensure that leaflets are following the guidelines.

User testing does not guarantee patient satisfaction. It could be used in further research to improve PILs guidelines both in Thailand and in the UK. In the development of PILs, the patient's point of view must be considered. The representative patients involved in the development process must be recruited from real users so that the results can have strong external validity to be applied to a certain context. Differences in reading behaviour, familiarity with health and medicine information, health literacy, and shifting the paradigm from dependency to self-care should be taken into account and investigated further. More intervention studies are required. It is critical to focus on identifying the most desirable format and content of PILs.

Mass customisation— building a unique product and service for each customer- is the next wave of the business world. Furthermore, the new generation that grew up with the Internet and its tailored delivery of information and recommendations is likely to expect personalised products that are tech-enabled. The customization is likely to be possible in many industries, in particular health care e.g. drug combinations customized for the patient. To tailor products and services, technologies are making it easier to individual customers' preferences.[334] Therefore, customised PILs through tech-enabled personalized services could be the new interesting topic for research.

11.6 Overall strengths and limitations

The multiple methods used in this thesis are a strength, enabling triangulation of findings. The scoping review, document comparison, qualitative, and quantitative research all showed similar findings relating to WMI provision.

The new review of the literature conducted in the UK, Asia and Africa was undertaken with a scoping review approach which allows a wide range of relevant literature and studies using various methodologies to be included in the review. However, for the scoping review and study appraisal, the publications written entirely in a language other than English were excluded, only those with an English abstract were included.

The comparison of ibuprofen leaflets which were available in the UK and Thailand market was the first such evaluation. Many studies which assessed WMI were included in the review, which enabled learning from them and incorporating relevant methods from them into the PILs and PIs comparison study. All leaflets were collected at random in various pharmacies. Therefore, the findings reflect the real situation in Thai and UK pharmaceutical markets. However, this study

focused on only the Ibuprofen leaflet, a small number of leaflets, and collection in one region. The collection of leaflets was carried out in the same areas of both countries. The leaflets for other medications, those produced by other manufacturers and available in other regions were in question.

Furthermore, information on the general public's needs for medicine information in the UK and Thailand, and the comparison was the first such study. These two studies utilized a quota sampling technique aimed at maximising diversity and at ensuring a representative sample of population factors, including the gender, age, and locations of the people involved. Again, many of the survey studies included in the review were used to develop the questionnaire used in these surveys. The questionnaire was designed to include all aspects of receiving information on medicines. However, even though the quota sampling was used, a higher proportion of women and those with higher educational level were included in the actual sample recruited. The time-consuming nature of the questionnaire could also be the obstacle to this survey. This might have reduced the concentration and interest of the participants. The surveys were restricted to small areas of both countries, and the qualitative study was also restricted to the same location, resulting in a lack of generalisability and a need for more widespread research.

Finally, in the face-to-face interview study, this could generate more insightful solutions by being better able to ask further questions, search for more information, especially concerning emotional reactions to PILs, and return to questions in order to gain further understanding later in the interview. The findings could be triangulated with the survey findings. Originally, this study was designed to gather the results through a focus group discussion, but due to the coronavirus pandemic in 2020, was conducted as individual online face-to-face interviews instead. No similar study was conducted in Thailand for comparison.

11.7 Conclusion

WMI is an important tool for improving patient understanding of their medications and facilitating communication between health care professionals and patients. As a consequence, healthcare services in particular; medicines are delivered in the safest possible way. The WMI is created from policy, regulations, and guidelines. Research and routine practices could be used to develop and improve the WMI policies, regulations, standard guidelines.

Vitally, PIs are not appropriate as patient information. The PILs must be mandatory in Thailand. Despite the fact that some PILs follow the guidelines accurately, patient satisfaction, which changes over time, is not being achieved. As a result, patients are unwilling to read the WMI

provided with their medicines; in most cases this is the PIs. The guidelines may be updated and revised by cooperation with all stakeholders; patients, health care providers, policymakers, and drug companies. The electronic and/or customised PILs to suit individual conditions; age and gender by using technology were suggested to replace the paper version. Integration of different sciences e.g. health care, behavioural psychology and information technology could provide new and beneficial challenges.

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Appendix 1 Full search strategy for Scoping review

CINAHL Plus and MEDLINE (EBSCOHOST)

Search ID#	Search Terms	Search options	Results
S1	Patient information leaflet	Limiters - Full Text; Abstract Available; Published Date: 20040101-20210731 Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Boolean/Phrase	1474
S2	Medic* AND Information	Limiters - Full Text; Abstract Available; Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Search modes - Boolean/Phrase	420,786
S3	Medic* AND Information AND patient	Limiters - Full Text; Abstract Available; Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Boolean/Phrase	290,056
S4	TI Medic* AND TI Information AND TI patient	Limiters - Full Text; Abstract Available; Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Boolean/Phrase	418
S5	TI Drug AND TI Information AND TI patient	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Boolean/Phrase	167
S6	AB Drug AND AB Information AND AB patient	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Boolean/Phrase	31,677
S7	Drug AND labelling AND Information	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	2,194

Search ID#	Search Terms	Search options	Results
S8	illustrated AND Medic* AND Information	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	10,469
S9	illustrated AND Medic* AND Information AND patient	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	6,854
S10	Medic* AND package AND Leaflet	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	864
S11	Medic* AND package AND Leaflet AND patient	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	708
S12	Medic* AND Information AND Leaflet	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	6,131
S13	Medic* AND Information AND Leaflet AND patient	Date: 20040101- 20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	5,108
S14	package AND Insert	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	2,812

Search ID#	Search Terms	Search options	Results
S15	package AND Insert AND patient	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	2,091
S16	package AND Insert ND Medic*	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	2,276
S17	package AND Insert AND Medic* AND patient	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	1,803
S18	package AND leaflet	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	1,042
S19	package AND leaflet AND patient	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	800
S20	package AND leaflet AND medic*	Limiters - Published Date: 20040101-20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	864
S21	package AND leaflet AND medic* AND patient	Limiters - Published Date: 20040101- 20210731; Geographic Subset: Africa, Asia, UK & Ireland Expanders - Apply related words; Also search within the full text of the articles; Apply equivalent subjects Search modes - Find all my search terms	708

Scopus

ID	Query	Documents
1	ALL ("patient information leaflet") AND PUBYEAR > 2003 AND PUBYEAR < 2022	2,816
2	TITLE-ABS-KEY (medic* AND information AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	19,318
3	TITLE-ABS-KEY (medic* AND information AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	9,095
4	TITLE-ABS-KEY (drug AND information AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	4,105
5	TITLE-ABS-KEY (drug AND labelling AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	292
6	TITLE-ABS-KEY (illustrated AND medic* AND information AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	70
7	ALL (illustrated AND medic* AND information AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	13,863
8	ALL (drug AND information AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	159,342
9	TITLE-ABS-KEY (illustrated AND medic* AND information AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	23
10	ALL (illustrated AND medic* AND information AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	4,924
11	ALL (medic* AND package AND leaflet AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	1,043
12	TITLE-ABS-KEY (medic* AND package AND leaflet AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	16
13	ALL (medic* AND package AND leaflet AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	779
14	ALL (medic* AND information AND leaflet AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	7,158
15	TITLE-ABS-KEY (medic* AND information AND leaflet AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	182
16	ALL (medic* AND information AND leaflet AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	5,459
17	TITLE-ABS-KEY (medic* AND information AND leaflet AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	140
18	ALL (package AND insert AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	6,058
19	TITLE-ABS-KEY (package AND insert AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	42
20	ALL (package AND insert AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	4,973
21	TITLE-ABS-KEY (package AND insert AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	17
22	ALL (package AND insert AND medic* AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	5,582
23	TITLE-ABS-KEY (package AND insert AND medic* AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	18
24	ALL (package AND insert AND medic* AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	4,900
25	TITLE-ABS-KEY (package AND insert AND medic* AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	9
26	ALL (package AND leaflet AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	1,463
27	ALL (package AND leaflet AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	785

ID	Query	Documents
28	ALL (package AND leaflet AND medic* AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	1,043
29	ALL (package AND leaflet AND medic* AND patient AND (uk OR asia OR africa)) AND PUBYEAR > 2003 AND PUBYEAR < 2022	779

Web of Science

ID	Search Query	Results
1	ALL=(Package AND leaflet AND Medic*)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	190
2	ALL=(Package AND leaflet AND patient AND Medic*)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	114
3	ALL=(Package AND leaflet AND patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	149
4	ALL=(Package AND leaflet) Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	312
5	ALL=(Package AND inserts and Medic* AND Patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	449
6	ALL=(Package AND inserts and Medic*)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	818
7	ALL=(Package AND inserts and Patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	750
8	ALL=(Package AND inserts) Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	2,918
9	ALL=(Medic* AND information AND Leaflet AND patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	865
10	ALL=(Medic* AND information AND Leaflet)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	114
11	ALL=(Medic* AND package AND Leaflet)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	190
12	AB=(Illustrated AND medic* AND information AND Patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	1,237
13	ALL=(Illustrated AND medic* AND information AND Patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	2,487
14	AB=(Illustrated AND medic* AND information)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	3,106
15	ALL=(Illustrated AND medic* AND information)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	7,596
16	TI=(Drug AND information AND Patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	210
17	AB=(Drug AND information AND Patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	27,009

ID	Search Query	Results
18	TI=(Medic* AND information)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	4,436
19	ALL=(Medic* AND information)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	388,286
20	TI=(Medic* AND information AND Patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	652
21	AB=(Medic* AND information AND Patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	83,345
22	ALL= (Drug AND labelling AND Patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	24,980
23	ALL=(Drug AND information AND Patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	39,077
24	ALL=(Medic* AND information AND Patient)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	161,843
25	AB=(Medic* AND information)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	170,452
26	ALL=(Patient information leaflet)Timespan: 2004-01-01 to 2021-07-31 (Publication Date)	1,582

Appendix 2 Full table of provision in each country including of EU, USA, Australia and Thailand

	EU	USA	Australia	Thailand
Content				
Name	-The name, the active substance(s): the (invented) name of the medicinal product and the active substance(s) included in it. - Pharmacotherapeutic group of type pf activity.	Provide established or proper name and brand name also including the phonetic spelling of the brand name, or the established name if a brand name does not exist.	Provide medicine brand name in the title of the full CMI. Provide a tabulated list of all active and inactive ingredients found in the medicine. Provide medicine name and a plain English explanation of what the medicine is used to treat (in indication).] Phonetic pronunciation is optional	Medicine name and trade name :What is in the medicine? (+ salt) Description of product, What is in the medicine? (Qualitative and Quantitative composition)
Pharmaceutical form	the pharmaceutical form	N/A	N/A	dosage form
Strength	strength of the product should be stated.	the CMI should be considered a stand-alone document in meeting this criterion. The label and packaging of the dispensed medication may also contain such information (e.g., name, strength, dosage, brief directions for use), but should not be considered as part of CMI.	N/A	strength :show in Metric system with no abbreviation e.g. 200,400 milligram) or international scale Refer to The European Directorate for the Quality of Medicines & HealthCare (EDQM)
Indication	Therapeutic indications: the therapeutic indications in line with section 4.1 of the SmPC should be stated here.	All FDA-approved indications listed in the PI for the medication. The information in the CMI about the use of or indication for use of the drug should be consistent with or derived from the PI, unless the CMI is customized for a specific patient. FDA-approved indications could also be listed with the customized information.	Summarise the approved indications for your product using Plain English.	What is this medicine used for? : the therapeutic indications should be referred from US FDA, Micomedex, and EMA, eMC.

	EU	USA	Australia	Thailand
Contra-indications	Do not <take> <use> X :All contraindications mentioned in section 4.3 of the SmPC should be included here in the same order as presented in the SmPC.	Information about circumstances in which the medication should not be used for its labelled indication. Include all contraindications listed in the PI.	When should you not take this medicine? Summarise any significant contraindications and/or precautions that apply to the medicine.	What you need to know before you : the contraindications should be referred from US FDA, Micromedex, and EMA, eMC.
Before taking medicine	What you need to know before you <take> <use> X: the information which patients/users should be aware of before they start taking the medicine and while using it.			
Other information for contraindication		Directions about what to do if any of the contraindications apply to the patient, such as contacting the healthcare provider before taking the medicine or discussing with him or her situations that would warrant discontinuing use of the medication. Include a general statement such as, Talk to your healthcare provider before taking this medicine if you have any of these conditions. Information on any contraindication that could result in serious injury or death if it is disregarded. A statement of precaution about any circumstances (such as past or current medical conditions or use of other medications, vitamins, or supplements) in which the use of the medication could lead to serious injury or death.		When should you consult your doctor?

	EU	USA	Australia	Thailand
Dosage	Dosage refer to SmPC section 4.2. When available, information on maximum single, daily and/or total dose should also be included. - Use in children and Adolescents	The Action Plan recommends that information regarding the "usual dosing instructions" be included. To avoid confusion between the usual dosing instructions and the prescribed dose, FDA suggests that the CMI refer the patient to the prescription label for specific dosing instructions. A statement should be included in the CMI stressing that it is important to follow the dosing instructions provided by the patient's healthcare provider, which is usually found on the prescription label for the medicine.	How much to take / use When to take / use [medicine name]	How should you use this medicine?: :Add statement "it is important to follow the dosing instructions provided by the patient's healthcare provider"
How to use	Duration of treatment (SmPC section 4.2) • the usual duration of the therapy; • the maximum duration of the therapy; • the intervals with no treatment; • the cases in which the duration of treatment should be limited.	If specified in the PI, include information on how to use the medication, such as whether to take it with or without food or water, times of day to take the medication, and any other instructions, for example, statements such as (1) Do not chew, (2) Do not split or crush, and (3) Do not lie down for 30 minutes after taking this medicine.	• Follow the instructions provided and use [medicine name] until your doctor tells you to stop. [for antibiotics, replace with 'Follow the instructions provided when [medicine name] was prescribed, including the number of days it should be taken.']	How often should you use this medicine? :Add statement "it is important to follow the dosing instructions provided by the patient's healthcare provider"
How to administer	How to <take> <use> X :When available, information on maximum single, daily and/or total dose should also be included. <Use in children <and adolescents>> :When the medicine is indicated in different age groups with a different dose, method of administration, frequency of administration or duration of treatment, specific instructions for	If detailed instructions describing how to administer the medication (instructions for use) are included in the manufacturer's patient labelling for the product (for example, instructions for inhalers, injections, and patches), include a statement to alert the patient to read the instructions for use contained in the package.	How to [insert appropriate verb] [medicine name] (relevant for devices)	Instructions describing how to administer the medication, pictures may be needed.

	EU	USA	Australia	Thailand
	use for each age group should be clearly identified.			
Route of administration	Route(s) and/or method of administration (SmPC section 4.2) :Route(s) of administration according to "Standard Terms" published by the Council of Europe and an additional patient-friendly explanation may be given if necessary.	State the route of administration. Examples of information about the route of administration are skin use only if a patch and do not swallow if a suppository.		Route(s) and/or method of administration
Missed Doses	<If you forget to <take> <use> X> :Make clear to patients what they should do after irregular use of a medicine, e.g.: if information is available, try to include information on the maximum interval the missed dose can be caught up as per SmPC section 4.2.	Describe what patients can do if they miss a scheduled dose, if this information is in the PI.	[medicine name] should be used regularly at the same time each day [week or month]. If you miss your dose at the usual time, [insert appropriate explanation]. If it is almost time for your next dose, skip the dose you missed and take your next dose when you are meant to. Do not take a double dose to make up for the dose you missed. • [include explanation of what "almost time for your next dose" refers to for the specific medicine where possible, e.g. oral contraceptives] • [include any other medicine-specific action and advice about missed dose, as appropriate]	What should you do if you miss a dose?
Overdoses	<If you <take> <use> more X than you should> :Describe how to recognise symptoms if someone has taken an overdose and what to do as per SmPC section 4.9.	State what to do in case of an overdose. If overdose is a significant issue for a particular medication, include text describing signs of overdose so that patients can recognize the symptoms. In all cases, we recommend that symptoms of overdose be directly followed by	Provide medicine specific information to consumers, e.g. overdose information If you use too much [medicine name] If you think that you have used too much [medicine name], you may need urgent medical attention. You should immediately:	What to do when you have taken more than the recommended dosage? (Over dosage) Sign & symptom of over dosage should be provided.

	EU	USA	Australia	Thailand
		instructions for what to do should these signs or symptoms occur, such as calling a poison control centre, the doctor, or other emergency telephone number.	• phone the Poisons Information Centre (by calling 13 11 26), or • contact your doctor, or • go to the Emergency Department at your nearest hospital. **You should do this even if there are no signs of discomfort or poisoning.**	
Stopping taking	<If you stop <taking> <using> X> :Indicate withdrawal effects and how to minimise them as per SmPC section(s) 4.2 and/or 4.4			
Monitoring effectiveness of treatment	You must talk to a doctor if you do not feel better or if you feel worse <after {number of} days>.> If you get any side effects, talk to your <doctor> <,> <or> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet. See section 4.>	Information regarding how to monitor the effectiveness of the treatment by correctly interpreting physical reactions to the medicine, if this information is in the PI. This would include, for example, informing patients about when to call their healthcare provider if they do not notice signs of improvement. "You must contact a doctor or pharmacist if your symptioms worson or do not improve.""	Call your doctor straight away if you: • [include relevant statements about monitoring of the condition and relevant action(s) to be taken] • [include relevant statement(s) about action to be taken if the condition worsens / does not improve] Remind any doctor, dentist or pharmacist [add other health professionals as appropriate] you visit that you are using [medicine name].	Add statement “you must contact a doctor or pharmacist if your symptom worsens or do not improve”
Warnings and precautions	Warnings and precautions: :All warnings and precautions for use included in section 4.4 of the SmPC should be provided in this section Specific warning -Children - Interactions with other medicines - Interactions with food and drink	the CMI include all information stated in the PI regarding what precautions the patient should take while using the drug to avoid serious situations. For example, the following information should be included, if relevant to the medication - Interactions with other medicines	What should I know while using the medicine? - Relevant condition-specific or medicine-specific subheading - Driving or using machines - Drinking alcohol	Care that should be taken when taking this medicine

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	- use by pregnant or breast-feeding woman, information on fertility - Effects on the ability to drive or to use machines -Excipients warnings	- Interactions with food and other substances - Tolerance to or dependence on the drug product - Patient activities and behaviours to avoid. Examples of such activities include smoking tobacco, drinking alcohol, being exposed to the sun, or driving a vehicle or operating dangerous machinery. - use by pregnant or breast-feeding woman, information on fertility -Specific risks to identifiable patient populations		
Boxed warnings		If the PI contains any boxed warnings that relate to important knowledge the consumer should have or actions the consumer should take, we recommend that a prominently displayed statement which is consistent with or derived from the boxed warnings be included in the CMI. FDA believes that most boxed warnings have information that is relevant to the consumer. N/A No PI	Include Black Triangle statement and/or boxed warnings if applicable an in accordance with guidance provided on the TGA website – Black Triangle Scheme and boxed warning.	
Side-effects	Possible side effects :The section should generally be divided into two sections 1) the most serious side effects need to be listed prominently first with clear instructions to the patients on what action to take (e.g. to stop taking the medicine and/or seek urgent medical	CMI is not expected to contain a full listing of all possible side effects. Because the most serious potential adverse reactions will most likely appear in the Warnings and Precautions sections of the PI, we recommend that this information also be included in CMI. In addition, we	Side effects should be grouped and prioritised in CMI (and summary) by their seriousness, as indicated by the actions that the consumer needs to take. It may be possible and helpful to group a number of potential side effects by type,	Undesirable effects :should be referred from US FDA, Micromedex, and EMA, eMC. : there are two side-effects included: SE which patient must stop taking medicine and see the doctor immediate, SE which patient do not

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	advice. The use of the words “straight away” or “immediately” may be helpful in this context). 2) then a list of all other side effects, listed by frequency and starting with the most frequent (without repeating the most serious included above). <Additional side effects in children <and adolescents > : If appropriate (and in line with information stated in section 4.8 of the SmPC), a subsection should highlight any clinically relevant differences in terms of side effects in any relevant subset of the paediatric population compared to another or to the adult population. Start with the highest frequency. Not setting side effects by organ/system/class Reporting of side effects	recommend that CMI include a list of the symptoms of the most frequently occurring (common) adverse reactions. Include a statement telling patients that the side effects given are not a complete list and instructing them to ask their doctor or pharmacist for more information.	such as ‘stomach complaints’, ‘skin problems’, or ‘breathing issues’. Reporting side effects After you have received medical advice for any side effects you experience, you can report side effects to the Therapeutic Goods Administration online at www.tga.gov.au/reporting-problems. By reporting side effects, you can help provide more information on the safety of this medicine.	stop taking medicine , but patient must contact a doctor or pharmacist if the symptioms worson.
Tolerance/ dependence/ Withdrawal of treatment		A description of the risks, if any, to the patient of developing a tolerance to or dependence on the drug product. Such risks would be described in the PI. Any signs and symptoms of tolerance or dependence should be stated in terms that the patient would be able to understand to recognize them.	If the medicine is potentially habit-forming or addictive, it should be addressed.	

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Drug Interactions	Other medicines and X: :Describe the effects of other medicines on the medicine in question and *vice versa* as per section 4.5 of the SmPC.	Drugs to avoid because of drug-drug interactions. FDA notes that some drugs have few labelled drug-drug interactions, while other drugs list numerous interactions. We do not recommend that CMI list every possible interaction. We do recommend, at minimum, including all drugs listed in the Contraindications section of the PI, and we encourage including interactions listed in the Warnings and Precautions sections of the PI. If there are interactions in the PI that will not be included in CMI, we recommend that a consumer-friendly statement appear in CMI explaining that the list is not complete, telling patients that other medicines they are taking may interact with the product, and encouraging patients to keep a list of all the medicines they take to share it with their doctor or pharmacist. We also recommend that if specific drugs are listed as interactions in CMI, both generic and trade names be included.	Tell your doctor or pharmacist if you are taking any other medicines, including any medicines, vitamins or supplements that you buy without a prescription from your pharmacy, supermarket or health food shop. [Options here include either: - subdividing and listing the medicines depending on the nature of their interaction – an example of this is included below, or; - tabulating these medicines that have been grouped according to the nature of their interaction, or; - if there is only one list of medicines, then ensuring that the information is presented consistently.] • Some medicines may interfere with [medicine name] and affect how it works. • [Include an explanation of the nature of the interaction where possible] e.g. • • Medicines that may increase the effect of [medicine name] include: • [list medicines as appropriate]	Drug Interactions are included in contraindication section.
Food interactions	Interactions with food and drink :Interactions not related to medicines should be mentioned here if reference is made in section 4.5 of the SmPC.	Foods and other substances (e.g., dietary supplements) to avoid because of the potential for interactions. Since the Action Plan was written, there has been increased awareness of dietary supplement interactions with medications. If such interactions are included in the PI, include them in the	Consider if you need additional subheading for interactions with other things such as “food and drink” or “tobacco”.	What other medicines or food which should be avoided whilst taking this medicine are included in conn precaution section.

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		CMI in the same way as drug and food interactions.		
Special populations	Children Adolescents :When the medicine is indicated in children, the warnings and precautions which are specific to this population	Specific risks to identifiable patient populations, such as **children, elderly** patients, people with **compromised immune systems**, or people with **impaired kidney or liver** functioning, if such information is in the PI. Provide enough information for the consumer to understand the importance of the hazard described.	Consider whether you need to include a subheading for different categories of users, e.g. the elderly, children, infants or people with specific pathological conditions. This refers to any medical condition-specific, medicine-specific, and/or age-specific subheading(s) relevant for inclusion for certain categories/groups of users, as applicable to the medicine.	When the medicine is indicated in children Adolescents, and elderly patients, the dosage ,warnings and precautions which are specific to this population must present.
	Pregnancy Breast feeding Fertility: :Where the information is significantly different, pregnancy, breast-feeding and fertility information can be presented under separate sub-headings.	Any risks to the mother and the fetus or the infant from use of the drug during pregnancy, labor, or breast-feeding. If the risks are unknown, include a statement such as, Talk to your doctor if you are pregnant or breast-feeding	Pregnancy and breastfeeding Check with your doctor if you are pregnant or intend to become pregnant. Talk to your doctor if you are breastfeeding or intend to breastfeed. [Include any other relevant pregnancy information specific to the medicine].	When the medicine is indicated in these patients, the dosage ,warnings and precautions which are specific to this population must present.
Driving and using machines	Driving and using machines :Where there is cautionary advice in section 4.7 of the SmPC this should be translated into meaningful colloquial language for the patient.	Warning about patient activities and behaviours to avoid. Examples of such activities include smoking tobacco, drinking alcohol, being exposed to the sun, or driving a vehicle or operating dangerous machinery.	Driving or using machines Be careful before you drive or use any machines or tools until you know how [medicine name] affects you. [medicine name] may cause dizziness in some people [or insert relevant information, as appropriate].	Driving and using machines
Storage	Storage conditions :Storage condition, Expiry date , shelf life after reconstitution, dilution or after first opening the container, warnings	Include storage instructions.	Looking after your medicine • [include device-specific storage information] • [include storage information].	How should you keep this medicine? : The storage condition could be adapted with medicines : Keep away from children

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	against certain visible signs of deterioration Keep this medicine out of sight and reach of chidren		Follow the instructions in the carton on how to take care of your medicine properly. Store it in a cool dry place away from moisture, heat or sunlight; for example, do not store it: • in the bathroom or near a sink, or • in the car or on window sills. Keep it where young children cannot reach it. - When to discard your medicine (as relevant) - Getting rid of any unwanted medicine	
Package labelling		The label and packaging of the dispensed medication may also contain such information (e.g., name, strength, dosage, brief directions for use), but should not be considered as part of CMI.		
Person-centred advice			Provide targeted information that directly relates to a person or their situation so they can take action or make a decision. Provide targeted information and step by step guidance.	
Contents of the pack and other information	Contents of the pack and other information -			
All excipient(s)	What X contains : The active substance(s) (expressed qualitatively and quantitatively) and the other ingredients (expressed		Active ingredient (main ingredient) Other ingredients (inactive ingredients)	All excipient(s) : Description of product ,active ingredient and all excipient in the medicine.

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	qualitatively) should be identified using their names as given in sections 2 and 6.1 of the SmPC and in the language of the text. What X looks like and contents of the pack :The pharmaceutical form should be stated according to the full “Standard Terms” published by the Council of Europe and an additional patient-friendly explanation may be given if necessary. :If appropriate, warnings of those excipients knowledge of which is important for the safe and effective use of the medicine and included in the guideline on “Excipients in the Label and Package Leaflet of Medicinal Products for Human Use” (The rules governing medicinal products in the European Union, Volume 3B), as per section 4.4 of the SmPC, should be mentioned here.		Potential allergens	
Other info	A statement Keep this leaflet. You may need to read it again. <- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.>	A statement that the medicine should only be used by the patient for whom it is prescribed and should not be given to other people.		

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Sign post to HCP	A statement - If you have any further questions, ask your <doctor> <,> <or> <pharmacist> <or nurse>."	A statement encouraging discussion with a healthcare professional about the prescription medicine. A statement that the healthcare professional who prescribed the medicine has additional information about the medicine as well as about the patient's specific health needs, and that the healthcare professional can provide this information to the patient and answer the patient's questions. An example of a statement that covers both recommendations could be: This leaflet summarizes the most important information about <insert medication name>. If you would like more information, talk with your doctor.	Tell your doctor or pharmacist if you notice anything else that may be making you feel unwell. Other side effects not listed here may occur in some people. Always make sure you speak to your doctor or pharmacist before you decide to stop taking any of your medicines.	When should you consult your doctor? (SideEffect)
Sign post to further information			Provide direct information on where links go and use short URL links to external information. Links need to go directly to the relevant content – and not require additional navigation. Ensure links are short, in case consumers need to type in the link manually. Explain where external links go in simple language so the consumer knows what to expect when they follow it.	
Marketing Authorisation Holder	Name and address of the MAH : State the name and address of the MAH as per section 7 of the SmPC and identify as such, e.g. "Marketing		Insert name of distributor, address, and contact details Who distributes [medicine name]	Name/ logo of importer, or Marketing Authorization Holder; MAH

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	Authorisation Holder: ABC Ltd, etc." (Full address: name of the country to be stated in the language of the text. Telephone, fax numbers or e-mail addresses may be included (no websites, no e-mails linking to websites).			
Manufacturer	Name and address of Manufacturer			Name/ logo of manufacturer
CMI publisher		The name of the publisher of the CMI.		
Date CMI	This leaflet was last revised in <{MM/YYYY}><{month YYYY}>. :Date of granting of the marketing authorisation/approval of latest variation or transfer (as per section 9 or 10 of the SmPC	The date that the CMI was published or the date of the most recent revision or review for adequacy and accuracy of content.	Insert month and year of when document was last reviewed.	Date of revision of PIL
Other info	<Other sources of information> :This section should include references to other sources of information which will be useful for the patient.	The CMI should be considered a stand-alone document in meeting this criterion. A disclaimer stating that the CMI is a summary and does not contain all possible information about the medicine. Scientific accuracy is an essential characteristic of CMI. The entire CMI will be assessed for scientific accuracy and bias. The text of the CMI should be unbiased in content and tone and should meet the accepted standards of scientific literature. That is, the text should be explanatory; neutral; without comparative adjectives, untruthful claims about the benefit of a product,	Explain how consumers can access the medicine. Describe what the medicine looks like in simple language and include the registration number for the medicine.	Disclaimer " CMI is a summary and does not contain all information, ask doctor or pharmacist for more information. "

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		or hyperbole; and distinguished from any promotional or other information provided to the patient. CMI should not promote a specific brand, manufacturer, or distributor for the purpose of economic gain.		
Readability		CMI could be provided at the sixth to eighth grade reading level.		
Design+++++++++++++++++				
Font – size	- > 8 point as measured in font Times New Roman - Using different text sizes to enable key informa - tion to stand out and to facilitate navigation in the text - choose lower case text for large blocks of text. - Capitals may be useful for emphasis. - Do not use italics and underlining	Use 10-point or larger type size.		- 14 points bold centre in the box for Medicine name, strength, dosage form and trade name - 14 points bold centre in the box for main topics - > 11 points for general information
Font- type	- Times New Roman - Not narrowed, with a space between lines of at least 3 mm.	Do not use ornate typefaces Choose a bolder type over a thin version of the same style.		Tahoma (General)
Font colour	Contrast between the text and the background is important	Select text colour and paper that give a strong contrast. Black, dark blue, or brown ink on white or pale yellow		Text contrast with the paper colour

	EU	USA	Australia	Thailand
		uncoated paper provides the best contrast.		
Line spacing	A space between lines of at least 3 mm. Space between one line and the next should be at least 1.5 times the space between words on a line	Space between lines) is recommended at least 2.2 millimeters.		line: easy to read/ Space between one line and the next should be at least equal a newspaper line (>2.2 mm US)
Headings	Bold type face for the heading or a different colour Same level headings should appear consistently (numbering, bulleting, colour, indentation, font and size) to aid the reader. No more than 2 levels when multiple levels of heading A different type size or colour is one way of making headings or other important information clearly recognisable.		Use high contrast headings to aid scanning. Use meaningful subheadings, bullet points and tables to aid scanning and navigation through the document. Subheading "Warnings" in bold at the top of this section highlights key information and aids in scanning. Use appropriate tables and/or subheadings to help group information.	Introduction: 14 points bold centre in the box Main topic: 14 points bold centre text in the box for topic Subtopic: bold, Align left
How to emphasise certain points	Consideration Using different sizes to enable key information to stand out Instructions should come first, followed by the reasoning, (n/a)	Use bold-face type or a box to call attention to important information.	Provide the most important information higher up in the relevant CMI section. Then follow up with supporting information if necessary. Consumers expect critical information to be up-front. Provide the most important information first.	Introduction: 14 points bold centre in the box Main topic: 14 points bold centre in the box for topic Subtopic: bold, Align left

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			Ensure action information is highly visible to consumers, by ensuring the call to action is: • In tables or at the beginning of related information • Bolded in black for important information • Short and to the point" Bold key actions and messages for emphasis	
Use of Capital letters	Don't use widespread use of capitals	Use upper- and lower-case lettering, not all capitals.		N/A
Use of Italics	Don't use italics	Do not use italics.		N/A
Use of underlining	Don't use underlining	Do not use underlining		N/A
Use of highlighting		Do not use highlighting		N/A
Justification of text	Don't use justification			N/A
Length of line		Do not use a line length that is too long optimal line length is approximately 40 letters long.		N/A
Layout of columns	Consideration should be given to using a landscape layout which can be helpful to patients			3 column (suggestion)
Multi-lingual leaflets	Where a multi- lingual leaflet is proposed there should be a clear demarcation between the different languages used (n/a)			N/A
Sentence construction	An active style should be used		Use plain English - be direct Use active voice rather than passive voice in the CMI document, to support consumers to take action.	Use plain language e.g. "take, swallow"

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			Use pronouns to direct your message to the consumer. Ensure consistent expression of information within the CMI document. Ensure appropriate information has been included under the relevant section and where the consumer would expect to find this information. Provide step-by-step guidance where consumers need to know how to complete a task. Ensure all steps are within the relevant section, rather than split across sections. Explain the why to help consumers understand why they should act or make a decision. e.g. why not to stop taking a medicine suddenly. Use plain English and provide plain language explanations.	
Sentence length	Long sentences should not be used.		Use short sentences	short sentences
Paragraphs/ Bullet points/ Tables		Use short paragraphs and bullets where possible.	Use short paragraphs Use meaningful bullet points and tables to aid scanning and navigation through the document.	Short paragraphs

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Scientific symbols	Scientific symbols (e.g. > or <) are not well understood and should not be used			N/A
Numbers				All Arabic
Abbreviations/ acronyms	Abbreviations are not well understood and should not be used		Minimise the use of acronyms whenever possible. Many people scan CMI for the information they want rather than reading it from top to bottom, therefore acronyms spelled out earlier in the document may get missed and cause confusion if found only in acronym form later in the document. The asterix (*) should be replaced with trademark symbols as appropriate.	N/A
Symbols/ Pictograms	Symbols and pictograms can be useful provided the meaning of the symbol is clear and the size of the graphic makes it easily legible. (n/a)		Use images or diagrams of the medicine to help consumers to ensure they are taking the correct medicine by being able to view medicine packaging and the dosage form (e.g. tablet, liquid, injectable).	If there are symbols and pictograms, descriptions must be written.
Language				Thai language
Medical terminology	Medical terms should be translated into language which patients can understand.		Use plain English - common words Use examples of everyday items or concepts to explain or replace medical terminology and aid understanding, e.g. the use of the	Common words which patients can understand.

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			term ‘crushing’ chest pain helps consumers understand the condition and highlights the severity of the side effect. Provide a plain language explanation of necessary medical terms. Don’t assume a person using a medicine has knowledge of their condition or the medicine they are taking. Use common terms for medicine types and medical conditions, where appropriate, to aid understanding."	
Links within the document			List links to other sections in the full CMI to improve document navigation.	
Paper Size/ orientation	The paper is sufficiently thick to reduce transparency	Select text colour and paper that give a strong contrast. Black, dark blue, or brown ink on white or pale yellow uncoated paper provides the best contrast. We suggest that other combinations be avoided.		A4 - Landscape
Paper quality and colour	Use the uncoated paper			Text contrast with the paper colour
Layout	Make sure that when the leaflet is folded the creases do not interfere with the readability of the information.			

Appendix 3 Participant information sheet for cognitive interview

medway school of pharmacy

PARTICIPANT INFORMATION SHEET

Title of Project: Sources of medicine information in the UK: A public perspective

Name of Researcher (s): P Nualdaisri, J Krska, S Corlett, M Abdulla, P Berchie, S Ishiekwene

You are being invited to take part in a study, which is seeking views on information about medicines they use. Before you decide if you want to take part, you must understand why the study is being done and what it involves. Please take time to read the following information. Ask if anything is not clear or if you would like more information. Take time to decide if you want to take part or not.

Why is the study being done?

There is a lot of information available in this country about medicines, including an information leaflet provided with every medicine supplied, information on websites and also in the media. We want to find out whether different people prefer and use different ways of getting information about medicines.

Do I have to take part?

No. It is up to you to decide whether or not to take part. Even if you agree to take part, you can change your mind at any time without giving any reason. If you decide not to take part in the study, you will not be affected in any way.

If I do take part, what would I have to do and what would be done to me?

You will be invited to take part in an interview with a researcher, at a time and place of your choosing, during which you will be asked to complete our revised questionnaire while talking out loud about what you are thinking whilst completing it. The researcher may ask you questions about how you interpret words or phrases. This is to make sure that you are interpreting all parts of the questionnaire in the way it was meant to be understood. There are no right or wrong answers. The researcher will make notes of what you say during the interview, but will also audio-record it to make sure that any misunderstanding is acted on. If you agree to take part, you will be asked to sign a consent form, prior to the interview.

Are there any risks if I take part?

There are no risks to taking part in this study. However if you wish to stop the interview at any time, the researcher will be happy to do so.

Are there any benefits if I take part?

There are no personal identifiable benefits to taking part.

Will anyone know that I've taken part?

We will not tell anyone that you have taken part in the study.

What will happen to the results?

The results of your interview will be used to make sure that the final version of the online questionnaire is understandable. This online questionnaire will then be used to get the views of the general public about medicine information in a further study.

Any personal contact details you provide will be stored securely and will only be used for the purpose of arranging the interview and will be destroyed once all interviews have been completed.

Who should I contact if I want to know more about the study?

Professor Janet Krska, Medway School of Pharmacy

Who should I contact if I have any concerns about the study or the way it has been conducted?

If you have concerns about how this research study has been conducted please contact the Chair of the MSoP Research Ethics Committee on S.A.Corlett@kent.ac.uk

Further notice on how the University uses personally-identifiable information can be found here: https://research.kent.ac.uk/researchservices/wp-content/uploads/sites/51/2018/05/GDPR-Privacy-Notice-Research.pdf

Thank you for taking time to consider taking part in this study.

This project has been looked at and approved by the MSoP Research Ethics Committee

Appendix 4 Consent form for cognitive interview

medway school of pharmacy

CONSENT FORM for INTERVIEW

Project title Sources of medicine information in the UK: A public perspective

Name of researchers: P Nualdaisri, J Krska, S Corlett, M Abdulla, S Ishiekwene

I have read and understand the information provided for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily	Initial Here
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason.	Initial Here
I understand that the interview will be digitally audio recorded.	Initial Here
I agree to an interview to discuss the Questionnaire with a researcher, which will last no more than 30 minutes.	Initial Here

_____

___

Name of Participant (Print) Signature Date

_____

Name of person taking consent Signature Date

(if different from the researcher) Where possible, this is normally signed and dated in presence of the participant

_____

Lead researcher Signature Date

Appendix 5 survey questionnaire

Experiences, use and preferences for information about medicines among the general public:

A multi-country survey

Pre-survey screening questions:

Are you aged 18 or over?
YES/NO
Are you able to communicate in English or _____ (INSERT LOCAL LANGUAGE)?
YES/NO
Do you use any regular medicine OR have you used a medicine in the last 3 months?
YES/NO
If yes, are you a health professional or training to become one?
YES/NO

If no, proceed to obtain verbal consent, and record using the survey form:
Do you understand fully what this study involved?
YES/NO
Have all your questions been answered to your satisfaction?
YES/NO
Do you agree to complete the questionnaire with me today?
YES/NO
Are you happy for your responses to be shared with other researchers in the study team?
YES/NO

If yes to all, proceed with the questionnaire.

Section 1: Demographic information

1. What is your age (years)? _____
2. What is your gender? (male/female/gender diverse/prefer not to say)
3. How would you describe your ethnicity?_____
4. What is your first language? _____
5. Can you read English? (Yes/No)
6. What is your highest level of education? (no education/primary/secondary/technical college/university)
7. Have you used any medicines regularly (on most days) in the past 3 months? (Yes/No)
    a. If yes, how many different medicines do you use (prescribed and any you buy)? _____

Section 2: Thinking about any medicines you have used in the past 3 months

1. Where have you obtained medicines from? (select all that apply)
    □ Hospital □ Community pharmacy (Drug shop, Chemist, Drugstore, Dispensary)
    □ Online pharmacy □ Online purchasing e.g. Amazon
    □ Primary care unit □ Private clinic □ Dispensing doctor

    □ Friends and family □ Doctor/ Health centre
    □ Retail outlet (Grocery, store, Shop, Supermarket)

2. Have you received any information about these medicines? (Yes/No)
    If no is selected, go to Section 3

3. What types of information have you received (please select all that apply) ***(Respondents are directed to different sets of questions depending on response to this question.)***
    a. Patient information leaflet/package insert, website, information on the medicine container
    b. Verbal information from doctor, nurse, pharmacist
    c. TV, radio, newspaper, magazine, mobile app, social media, family member or friend, digital platform [e.g. Alexa, Siri]

   If a is selected, with or without b and/or c, answer questions 4-10.
   If b is selected, with or without c, go to questions 11 and 12.
   If only c is selected, go to question 13.

4. What type of written information did you receive? (tick all that apply) ***(Respondents are required to answer each relevant sub-question, depending on response to this question.)***
    a. a leaflet about your medicine (go to question 5)
    b. information on the medicine container (go to question 6)
    c. a website (go to question 7)

5. When/how did you get the leaflet?
   □ in medicine pack □given by doctor or other health worker [e.g. pharmacist , nurse]
6. What was the information on the container like? (tick all that apply)
   □ printed on a label by the person who dispensed the medicine,

   □ written on the medicine envelope by the person who dispensed the medicine,

   □ printed on the container by the manufacturer

7. Which website(s) have you looked at for information about your medicine?
   □Government organisation website[NHS, NICE] □ drug company website [GSK, Pfizer]

   □ Pharmacy website [Lloyds] □ Patient organisation website [Diabetes UK, British Heart Foundation]

   □ Hospital website [East Kent Hospital],

   □ Other website ……. □ I can't remember)

8. Thinking about the overall written information you have received, when did you look at the information?
    a. when you were first given the medicine
    b. when something unexpected happened
    c. when you wanted to find out whether you were able to drink or drive or use machinery
    d. when you wanted to check if it was safe to take another medicine
    e. other time……..
    f. I never looked at the information (go to question 16)

9. How often have you looked at the information? (once only, two or three times, more than three times)
10. How have you used the information? (select all that apply)
    a. to check when to use the medicine
    b. to check if the medicine was suitable for you
    c. to make sure you avoided certain other medicines
    d. to make sure you avoided certain foods or drinks

e. to identify possible side effects
f. to decide if it was safe to drink or drive or work with machinery
g. to find out what to do when I missed a dose
h. other way……

11. Who talked to you about your medicine(s)? (select all that apply)
(□ doctor, □ pharmacist, □ nurse, □ health worker, □ other person…)
12. When did they talk to you?
(□ when you were prescribed the medicine, □ when you had a prescription dispensed for the first time or for refills, □ when you bought the medicine, □when you asked them questions, when you had a review, other time…)
13. Where did you get the information from?
(□TV, □ radio, □mobile application, □social media, □ newspaper, □magazine, □advertisements, □ family member or friend, □ digital platform, □ other)

Thinking about all the information you have had about your medicines(s)

14. How easy was the information to understand? (choose one box)

Very easy				Very difficult

15. Was the information enough for what you needed? (choose one box)

Needed a lot more				More than I needed

Section 3: Your views on different information sources

16. For each of the following possible places you may get information about medicines in general, **please indicate whether you would use this** and <u>if yes</u> whether you think each is: easy to access, easy to understand, relevant to you and trustworthy.

Source	Tick if would use	Easy to access	Easy to understand	Relevant to me	Trustworthy
Verbal from health professional					
Drug company information on medicine container					
Dispensing label/ medicine envelope					
Leaflet with medicine					
Leaflet from health worker					
Government website (e.g. NHS,NICE)					
Manufacturer website (e.eg. GSK, Pfizer)					
Patient support group website (e.g. Diabetes UK)					
Pharmacy website (e.g. Lloyds, Boots)					
Hospital website (e.g. East Kent Hospital)					
Advertising on TV/radio/magazine					
News reports					
Mobile application					
Social media/family and friends					
Digital platform (e.g. Alexa, Siri)					

Section 4: Your needs for medicine information in future

17. If you were to be given a new medicine you had not used before, what information would you want to be given about it and when?

Information	Tick if would want	When first given	Later after using for some time
Name of medicine			
What it's for			
How to use it			
Possible side effects			
What you should avoid (other medicines, foods, drinks)			
Anything which means the medicine may not be right for you (such as another medical condition)			
How to store it			
What to do if you miss a dose			
How to get more information			
Anything else…….			

18. What would be your preferred way of getting this information (tick one option)? ***(Respondents are directed to different questions depending on response to this question.)***
    a. As a leaflet, label or written on the medicine container, or from a website (go to question 20)
    b. Verbal from a doctor, nurse, pharmacist or other health worker (go to question 23 and 24)
    c. Both a and b (go to question 19)
    d. Other way (e.g. TV, social media, family or friends, advertisements) (go to question 24)

19. Why would you want both written and verbal information? (go to question 20)

    ……
    ……..

20. How would you prefer to get written information (tick one option)? ***(Respondents are directed to different questions depending on response to this question.)***
    a. leaflet with your medicine (go to question 21)
    b. information on the medicine container (go to question 25)
    c. information on a website (go to question 22)

21. What are the reasons you would prefer a leaflet with medicines over a website?…….

    ……

22. What are the reasons you would prefer a website over a leaflet with medicines?.....

    ……

23. Why do you want verbal information?

    ……

24. Why do you not want written information?

    ……

25. How important is it to you that a leaflet for patients is given with all medicines (choose one box)?

Very important				Not at all important

26. How important is it to you that information about all medicines is available on a government website (choose one box)?

Very important				Not at all important

Thank you for completing this survey

Appendix 6 Participant information sheet for survey

medway school of pharmacy

PARTICIPANT INFORMATION SHEET

Title of Project: Sources of medicine information in the UK: A public perspective

Name of Researcher (s): P Nualdaisri, J Krska, S Corlett, M Abdulla, P Berchie, S Ishiekwene

You are being invited to take part in a study, which is seeking views on information about medicines they use. We are asking members of the public in Kent to take part in this survey.

Before you decide if you want to take part, you must understand why the study is being done and what it involves. Please take time to read the following information. Ask if anything is not clear or if you would like more information. Take time to decide if you want to take part or not.

Why is the study being done?

There is a lot of information available in this country about medicines, including an information leaflet provided with every medicine supplied, information on websites and also in the media. We want to find out whether different people prefer and use different ways of getting information about medicines.

If I take part, what would I have to do?

You do not have to take part. If you say yes, I will go through a questionnaire with you, here, asking you each question in turn and recording your answers. This will take no more than 15 minutes. If you don't want to take part, you can say no now or if you start, you can also stop the survey at any time.

What are risks and benefits if I take part?

There are no risks or individual benefits to taking part. There are no right or wrong answers, we just want to know about your experience and your opinion. I will not ask for your name or any other personal information, so the answers you give will all be anonymous, and no-one will know you have taken part.

What will happen to the results?

We will combine the results of all the surveys together and use them to write reports and academic papers. We hope what we learn will help health workers to get a better understanding of what information people want about medicines. We will make the survey responses available to other researchers, but nothing can be traced back to you.

When we have analysed the survey, we will put a short summary of the results on a website: https://www.msp.ac.uk/research/pips-events.html

This study is funded by Medway School of Pharmacy and is being carried out by students at Medway School of Pharmacy.

Who should I contact if I want to know more about the study?

Dr Sarah Corlett, Medway School of Pharmacy: S.A.Corlett@kent.ac.uk Telephone 01634 888909

Who should I contact if I have any concerns about the study or the way it has been conducted?

If you have concerns about how this research study has been conducted, please contact Dr Gurprit Lall, Deputy Head, Medway School of Pharmacy: G.Lall@kent.ac.uk Telephone 01634 202964

Further notice on how the University uses personally-identifiable information can be found here: https://research.kent.ac.uk/researchservices/wp content/uploads/sites/51/2018/05/GDPR-Privacy-Notice-Research.pdf

If you have any questions about your medicines, please contact your local community pharmacist. The researchers are students; therefore, they will not be able to advise.

Thank you for taking time to consider taking part in this study.

This project has been looked at and approved by the MSoP Research Ethics Committee

Appendix 7 Ethical approval letter for study entitled Source of medicine information in the UK: A public perspective

medway school of pharmacy

12th July 2019

Your application for ethical approval for project entitled *Sources of medicine information in the UK: A public perspective* has now been considered on behalf of the Medway School of Pharmacy School Research Ethics Committee (SREC).

Your project is approved, subject to minor amendments, as listed below;

- The patient information sheet "May 2019" mentions the Thai government funds the project. Please clarify in the documentation (PIL) how the government is involved.
- If the data collection takes place in a private area, for example a shopping centre or pedestrianized street then you must ensure that the appropriate permissions are obtained. A gatekeeper information/ permissions letter should be included in the ethics documentation.
- Researcher safety measures please refer to MSoP school policy.
- On patient information sheet, include referral/ signposting information for people who have questions about their medicines and would like more information. Researchers will not be able to advise.
- Clarify the timeline for interviews.

Please submit the amended documents for Chair's review to Joanna Mowbray j.mowbray@kent.ac.uk

I must remind you of the following:

1. that if you are intending to work unaccompanied with children or with vulnerable adults, you will need to apply for a DBS check; the project must be conducted under the supervision of someone who has an up-to-date DBS check; you must not be in the presence of children alone except if you have completed a DBS check;
2. that you must comply with the Data Protection Act (1998);
3. that you must comply throughout the conduct of the study with good research practice standards;
4. If you are completing this project off site, you must obtain prior approval from relevant authorities and adhere to the MSOP off site protocol.
5. to refer any amendment to the protocol to the School Research Ethics Committee (SREC) for approval.
6. You are required to complete an annual monitoring report or end of project report and submit to j.mowbray@kent.ac.uk

Yours sincerely

Dr Sarah Corlett

Appendix 8 Appendix 8 Ethical approval letter for study entitled Source of medicine information in Thailand: A public perspective

คณะกรรมการจริยธรรมการวิจัยในมนุษย์
สาขาวิทยาศาสตร์สุขภาพ มหาวิทยาลัยสงขลานครินทร์

หนังสือรับรองฉบับนี้ให้ไว้เพื่อแสดงว่า

รหัสโครงการ: HSc-HREC-62-24-1-1

ชื่อโครงการ: การสำรวจแหล่งข้อมูลยาและความคิดเห็นต่อแหล่งข้อมูลยาในมุมมองของประชาชนทั่วไป

นักวิจัยหลัก: อ.พิชญา นวลได้ศรี **สังกัด:** คณะเภสัชศาสตร์
นักวิจัยร่วม: น.ส.เพชรนภา เพชรรัตน์ **สังกัด:** คณะเภสัชศาสตร์
นักวิจัยร่วม: นายภิพพัฒน์ จุติสงขลา **สังกัด:** คณะเภสัชศาสตร์

เอกสารที่รับรอง:

1. แบบเสนอเพื่อขอรับการพิจารณาจริยธรรมการวิจัยในมนุษย์ ฉบับที่ 3 ลงวันที่ 16 มีนาคม 2563
2. โครงการวิจัยฉบับสมบูรณ์ ฉบับที่ 3 ลงวันที่ 16 มีนาคม 2563
3. เอกสารชี้แจงอาสาสมัคร ฉบับที่ 2 ลงวันที่ 6 มกราคม 2563
4. แบบบันทึก/แบบรวบรวมข้อมูล ฉบับที่ 2 ลงวันที่ 6 มกราคม 2563
5. ประวัตินักวิจัยทุกคน

ได้ผ่านการพิจารณาและรับรองจากคณะกรรมการจริยธรรมการวิจัยในมนุษย์ สาขาวิทยาศาสตร์สุขภาพ มหาวิทยาลัยสงขลานครินทร์ โดยยึดหลักจริยธรรมของประกาศเฮลซิงกิ (Declaration of Helsinki) และแนวทางการปฏิบัติการวิจัยทางคลินิกที่ดี (The International Conference on Harmonization in Good Clinical Practice)
ข้อมูลการพิจารณา ในบันทึกการประชุมคณะกรรมการจริยธรรมฯ ครั้งที่ 9/2562 วาระที่ 3.4.02 วันที่ 12 พฤศจิกายน 2562

ขอให้นักวิจัยรายงานความก้าวหน้าโครงการวิจัย ทุก 6 เดือน และยื่นต่ออายุก่อนถึงวันหมดอายุอย่างน้อย 30 วันปฏิทิน (กรณีเป็นรายงานผู้ป่วย ไม่ต้องรายงานความก้าวหน้าต่อคณะกรรมการจริยธรรมฯ แต่ขอให้รายงานสรุปผลการวิจัยเมื่อสิ้นสุดโครงการ)

(ศาสตราจารย์ ดร.ฉวีวรรณ จั่นสกุล)
ประธานคณะกรรมการจริยธรรมการวิจัยในมนุษย์
สาขาวิทยาศาสตร์สุขภาพ มหาวิทยาลัยสงขลานครินทร์

วันที่รับรอง: 14 เมษายน 2563
วันหมดอายุ: 13 เมษายน 2564

สำนักงานคณะกรรมการจริยธรรมการวิจัยในมนุษย์
สาขาวิทยาศาสตร์สุขภาพ มหาวิทยาลัยสงขลานครินทร์
15 ถ.กาญจนวณิชย์ สำนักวิจัยและพัฒนา อ.หาดใหญ่ จ.สงขลา 90110
โทรศัพท์ 0-7428-6955
โทรสาร 0-7428-6961

Appendix 9 Participant information sheet for face-to-face interview

Introduction

Thank you for your interest in this study. We would like you to take part if you are living in England, are older than 18 years of age, and are taking medicines on a regular basis. These can be prescribed by your GP or bought from a pharmacy or retail store.

This leaflet tells you about us, why we are carrying out this study, and what we are asking you to do. Please take time to read this information sheet and feel free to discuss this project with others. You can also **contact Sarah – see details below -** if you have any questions or would like more information.

This research project is funded by the Medway School of Pharmacy, University of Kent and is being run by a research team led by Dr Sarah Corlett, a registered pharmacist and Lecturer. Sarah is supervising student pharmacists (Kendra Banjoko, Shameera Chandrarajah, and Yousra Elalami) and a PhD researcher (Pitchaya Nualdaisri) who are undertaking this project as part of their degrees. The project team are supported by Prof. Janet Krska who retired from the School in February 2020.

1. What is the purpose of the study?

Regulations directing that written medicine information must be provided with all medicines supplied to patients and the general public in the UK have been in force for a number of years. However despite this and guidelines created to help Manufacturers to improve the quality of patient information leaflets (PILs) we know that often they do not meet individuals' needs.

We would like to better understand what information you want from PILs and how you currently use them. We would like to explore with you your thoughts and feelings when you read a PIL; We will share with you one PIL for a commonly used pain killer called ibuprofen. We would like to know how you think PILs and medicine information generally could be improved.

2. Do I have to take part?

No. It is your choice. If you decide to take part you are still free to change your mind or withdraw at any time. You will not need to give a reason.

3. What are you asking me to do?

We would like you to share your thoughts about your medicines with us by taking part in a virtual/ on-line chat using Skype, Zoom or Microsoft teams. We will arrange the discussion for a time that is convenient to you. We would like to digitally record sound from our discussion because this helps us to ensure that we have an accurate record of your views. We will NOT record your image. The recording will be stored on a password protected drive at the University to which only

the research team have access until it is deleted. We will transcribe the interview and delete the recording no longer than one week after the transcription has been checked. When we transcribe the interview we will give you a pseudonym so that you will not be identifiable. We may use quotes from the interview in our write up but they will not be traceable or attributed to you. Nobody will know that you have participated in this study.

4. What are the possible benefits?

In recognition of the time you have given to prepare for and take part in this study we will give each participant a £10 shopping voucher. We also hope that the information you provide will shape improvements to written medicine information leaflets/ PILs.

5. What are the possible disadvantages?

There are no risks if you take part in the study. We estimate that it will take 30 minutes to complete.

6. Will anyone know that I've taken part?

No one will be told about your participation in this study. Your name and contact details will be deleted immediately after the interview has taken place. Prior to this they will stored securely on password protected University computers and only accessible to the research team. No unauthorised person will have access to your contact details or the transcripts from the interviews.

7. What will happen to the results?

The data will be analysed and published as part of this research project in academic journals and conferences. A summary will be made available on the Medway School of Pharmacy (MSoP) website after the completion of the project. We hope the results will lead to further projects on this topic. The anonymous data (transcripts) collected will be stored for 5 years on password protected files at the University and deleted 5 years after the last publication.

8. Who has reviewed this study?

The Medway School of Pharmacy reviewed this research project and gave permission for this study to take place. This does not mean that you have to take part, it is completely your choice.

9. Contact Details:

Project lead: Dr Sarah Corlett

Email: S.A.Corlett@kent.ac.uk

10. Further Information

Please contact your local pharmacy or your GP if you are experiencing any difficulties with your regular medicines or if have any questions about your medicines.

11. Who should I contact if I have any concerns about the study or the way it has been conducted?

If you have a complaint or any concerns about this research project please contact the, Deputy Head of School, Medway School of Pharmacy Dr Trudy Thomas (T.Thomas@gre.ac.uk).

12. General Data Protection Regulation (GDPR) Privacy notice for research – University-level

The University of Kent uses personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation we have to ensure that we use and safeguard your data according to the law. You can find more information or contact The University of Kent's Data Protection Officer at:

https://research.kent.ac.uk/researchservices/privacy-notice/#

Thank you for your time.

Appendix 10 Consent form for interview

medway school of pharmacy

Exploring medicine information needs for people taking regular medicines

Pitchaya Nualdaisri, Yousra Elalami, Shameera Chandrarajah, Kendra Banjoko, Prof Janet Krska and Dr Sarah Corlett

I have read and understand the information provided for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily	Initial Here
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason. Contact: Sarah Corlett (S.A.Corlett@kent.ac.uk)	Initial Here
I understand that if any personal information is collected during the study the information will be pseudonymised and remain confidential	Initial Here
I understand that the interview will be digitally audio recorded and that this recording will be transcribed verbatim	Initial Here
I understand that verbatim quotes taken from the recording of our conversation may be used in publications and reports, but that I will not be identifiable from these.	Initial Here

Name of Participant: (Print)

Signature: Date:

Please sign and return to S.A.Corlett@kent.ac.uk.

Please print and sign and then e-mail a scanned copy, photograph, or the document completed with your initials in each box and confirmation of your consent to take part in the accompanying e-mail.

Name of researcher confirming consent prior to interview:

Signature : Date:

Appendix 11 Topic guide for interview

medway school of pharmacy

Briefly explain purpose of interview and check consent.

1. The UK requires that a PIL is supplied to the public with all medicines. How important is it for people to be given written information about their medicines?
   Why do you think this?
   What are the key things that you need to know when you are taking a medicine?
   What information do you think a PIL should include?

2. Tell me about the last time that you took a new medicine.

Prompts:

- What was the medicine for?
- Who recommended it or prescribed it for you? (lots of on-line/ telephone prescribing during Covid which may affect face to face/ verbal advice given)
- Were you given any advice by the healthcare professional? What was this? Did you have opportunity to ask questions?
- Did you look at the PIL that was supplied with the medicine?
- Was there anything particularly that you wanted to know about (for example ….how to take the medicine, side-effects)
- Have you looked at the PIL since? For what purpose?
- Are you still taking the medicine/ have you had any issues with it?

3. If you had an issue with the medicine now – for example you noticed that you were putting on weight although you seemed to be eating the same amount as usual and you thought that it might be something to do with your new medicine - what you would do? {prompts - discuss with HCP, check information on PIL to see if reported previously, talk to friends, look on the internet, nothing – wait and see}..and why?
   If you wanted to look at a PIL for one of your medicines right now could you put your hand on one easily? What do you do with them?

4. Please look at the example PIL that I have loaded up onto the screen? (Ibuprofen PIL)

   Without looking at the detail what are your first impressions? (prompt - font, layout/ design).

   You said at the beginning of this discussion that the information you wanted to know was X, Y, Z. Can you find that information on the PIL on the screen? How easy was the information to find? What would improve the layout/ design of the PIL?

5. Imagine that you have had a telephone consultation with a nurse prescriber from your local practice because you have been suffering with pain in your right hip for the last week. They have given you a month supply of the pain killer ibuprofen and advised you to start taking it straightaway and to have one tablet three times a day after you have had something to eat. Please spend a few minutes looking through the PIL on screen. Tell me what your thoughts are as you read through the PIL? (language) How do you feel about starting this medicine now? (emotion - concern re risk/ benefit and impact on your own judgement or behaviour) You said earlier that you like to know about X (answer from Q1) reading the section within this PIL how does it make your feel? Are you reassured/ or concerned? Does it give you all the information that you would want to know? Is there anything here which is not relevant or of interest to you?

6. Many people have told us that they would like to receive both verbal and written information about their medicines.
   What are your views on this? Why? (Tailoring information to needs of patient/ sign-posting most relevant information)
   How could this (a patient-centred information service) be delivered within the current NHS ? (by whom, how public access service, access to information, networks/ communication between HCPs). What would the benefits of this approach be? Would there be any barriers or problems?

7. PILs are created by the medicine manufacturer. How do you feel about this? Do you trust this information? Does knowing that it is written by the manufacturer change your view of it?

8. Is there anything else that you would like to tell me about PILs that I haven't asked about?

Appendix 12 Demographic information form

Exploring medicine information needs for people taking regular medicines - Demographic information

Please complete the form and return it with your consent form to S.A.Corlett@kent.ac.uk

1. What is your age (years)?

2. What is your gender? (male/female/gender diverse/prefer not to say)

3. How would you describe your ethnicity?

4. What is your first language? _____

5. Can you read English? (Yes/No)

6. What is your highest level of education? (no education/primary/secondary/technical college/university)

7. Have you used any medicines regularly (on most days) in the past 3 months? (Yes/No)

a. If yes, how many different medicines do you use (prescribed and any you buy)? _____

Appendix 13 Appendix 13 Ethical approval letter for study entitled Exploring medicine information needs for people taking regular medicines

medway school of pharmacy

30 October 2020

Dear Sarah

Your application for ethical approval for project entitled *Exploring medicine information needs for people taking regular medicines* has now been considered on behalf of the Medway School of Pharmacy School Research Ethics Committee (SREC).

I am pleased to inform you that your study has been approved, with immediate effect.

I must remind you of the following:

- that if you are intending to work unaccompanied with children or with vulnerable adults, you will need to apply for a DBS check; the project must be conducted under the supervision of someone who has an up-to-date DBS check; you must not be in the presence of children alone except if you have completed a DBS check;
- that you must comply with the Data Protection Act (1998);
- that you must comply throughout the conduct of the study with good research practice standards;
- If you are completing this project off site, you must obtain prior approval from relevant authorities and adhere to the MSOP off site protocol.
- to refer any amendment to the protocol to the School Research Ethics Committee (SREC) for approval.
- You are required to complete an annual monitoring report or end of project report and submit to j.mowbray@kent.ac.uk

On behalf of the MSoP ethics committee