The inclusion of a headline section and information about the benefits of medicines in written medicines information.

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The candidate confirms that the work submitted is her own and that appropriate credit has been given where reference has been made to the work of others.

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> *"Scientists have calculated that the chances of something so patently absurd actually existing are millions to one. But magicians have calculated that million-to-one chances crop up nine times out of ten." (Pratchett, 1987)*

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Abstract

Introduction: Criticisms of the mandated patient information leaflets (PILs) supplied with all medicines include being difficult to read and overly negative. Two adaptations suggested to address this are:

1) Inclusion of **headline** section
2) Inclusion of additional information about potential **benefits** of the medicine.

Aims: To explore the impact of a headline section and benefit information in PILs on patients' satisfaction, understanding and medicine-taking behaviour.

Methods: Two scoping literature reviews informed the nature of exemplar PILs with a headline section and benefit information to be presented to medicine users. These PILs were used first in focus groups to explore opinions of the adaptions, and then the headline section was user-tested. A survey assessed the nature and availability of benefit information in current PILs. Finally an interview study explored the thoughts of actual medicine users about the inclusion of benefit information.

Findings: The reviews found a small body of literature about a headline section. In contrast, there was a large body of heterogeneous research on benefit information - used to develop exemplar PILs. Focus group participants viewed headline sections positively and, when user-tested, was used about a third of the time to locate key information. Benefit information was more controversial; many struggled to understand it, with an emotional response in some, who appear to over-estimate medicine benefits. The emotional response was less pronounced in the actual-user group, although some surprise and disappointment remained at the perceived low level of benefits.

Conclusions: A headline section was viewed positively, and in user testing it was used to find key information. However, perceived low level of benefit proved a significant barrier to benefit information, with some unwilling to engage with it. More research is needed to allow informing patients about both the potential benefits and harms of medicines – allowing them to make informed decisions.

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Symbols and abbreviations

AR	Absolute risk
ARR	Absolute risk reduction
ASB	Absolute survival benefit
CABG	Coronary artery bypass graft
CVD	Coronary vascular disease
DTC	Direct-to-consumer (drug advert)
EMA	European Medicines Agency
ER	Events rates
EU	European Union
FDA	Food and Drug Administration
JANA	Janatriptan
GP	General Practitioner
HPS	Heart Protection Study
MHRA	Medicines and Healthcare products Regulatory Agency
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NNS	Numbers need to screen
NNT	Numbers need to treat
OR	Odds ratio
PIL	Patient information leaflet
PL	Package leaflet
QRD	Quality Review of Documents
REBA	Rebastatin
RCT	Randomised controlled trial
RR	Relative risk
RRR	Relative risk reduction
SmPC	Summary of Product Characteristics
TNT	Tablets needed to take
WN	Whole numbers

Chapter 1: Introduction

Chapter 1 Introduction

The inclusion of a headline section and information about the benefits of medicines in patient information leaflets.

1.1 Introduction

Medicines are the most common intervention in the NHS. Most people will take a medicine at some point in their life. In the UK and across Europe all licensed medicines are legally required to be provided with written medicines information; this takes the form of a patient information leaflet or PIL. This thesis focuses upon potential ways to improve the content and format of patient information leaflets in order to better support patients to access and understand information about their medicines. The principal aim is to explore the inclusion of two distinct adaptations that have been considered for use in a PIL. These adaptations relate to the following:

[1] The **format** of the information: an exploration of the inclusion of a **headline** or summary section in patient information leaflets

[2] The **content** of the information: an exploration of the inclusion of information about the **benefits** of medicines in patient information leaflets.

Including both a headline section and 'benefit' information in a PIL have been identified as developments that may have potential in assisting patients to better access information about their medicines. They might also help patients to understand more about their medicines and encourage them to make informed decisions about their use. This thesis aims to explore patient perspectives on the inclusion of a headline section and 'benefit' information in a PIL.

Initially this doctoral research focused solely upon the impact of providing a headline section in a patient information leaflet. The focus of the work was broadened in order to incorporate additional research into the inclusion of benefit information, which was a focus of interest of the researcher prior to commencement of the PhD studies. An international research project, examining the inclusion of one type of benefit information had previously been undertaken and provided some of the foundation for part of this PhD research (Hamrosi et al., 2012).

This introductory chapter begins with an overview of the history and role of patient information leaflets for medicines. There is also a discussion about the nature and context of a headline section and benefit information. The chapter ends with a summary of the rationale for the PhD research and its aims and objectives.

1.2 The history and legislation of patient information leaflets

The term patient information leaflet (PIL) specifically refers to the mandated leaflet that is legally required to be provided with all packs of licensed medicine, whether the medicine has been prescribed or bought without prescription. The UK has regulated the patient information provided with medicines since 1977, although until 1999, few medicines came with leaflets similar to those available today.

In 1992 a directive from the European Commission on the labelling of medicinal products for human use and on package leaflets paved the way for the introduction of leaflets for the patient with all medicines (Council of the European Communities, 1992). It should be noted that the legislative term is a Package Leaflet or PL. However researchers and practitioners in the UK generally use the term Patient Information Leaflet or PIL, and that will be the term used in this thesis.

The aim of the directive was to provide a standardised format of leaflet intended for the patient, which would provide a high degree of consumer protection and ensure access to full and comprehensible information about medicines (Council of the European Communities, 1992). The directive came into force in 1999, from which time member states had 18 months to implement the directive into national legislation to ensure medicines were accompanied by a PIL within a 5 year transition period.

The leaflets were required to reflect the content of the Summary of Product Characteristics (SmPC), which is a document required by the European Commission before a medicinal product can be marketed. The Summary provides a description of the product in terms of its chemical, pharmacological and pharmaceutical properties. Detailed guidance on the order and content of the PIL is provided by the Quality Review of Documents product information templates (QRD template) provided by the European Medicines Agency (Co-ordination Group for Mutual Recognition and Decentralized Procedures - Human, 2011). The order of the information should be:

- Identification of the medicine
- Therapeutic indications
- Information necessary before taking the medicine
- Dosage
- Description of side effects
- Additional information

The information provided must be in a format that is accessible and comprehensible to patients. Design of the leaflet is not something covered in either the Directive or national legislation, but it has been stipulated that it must be written in clear and

understandable terms for the patient and be clearly legible (Council of the European Communities, 1992). The nature of what type of information must be provided has since been more clearly defined following the leaflets becoming mandatory.

The introduction of PILs improved access to written information about medicines, and these leaflets are frequently the only written information that a patient will receive about their medicines (Medicines and Healthcare Products Regulatory Agency, 2012a). Provision of these leaflets also responded to patients' desire for information about their medicines which include information about the following:

- Side effects
- What it does and what it's for
- Dos and don'ts
- How to take it. (Dickinson and Raynor, 2003)

The inclusion of these leaflets in medicine packs has been shown to have some positive impact on knowledge and satisfaction, however, a criticism patients frequently made about leaflets is that they are too difficult to read and contain too much jargon (Raynor et al., 2007, Ley, 1988)

In 2005 the EU published a further directive which required that pharmaceutical companies undertake '*consultations with target patient groups'* in order to ensure that the leaflets provided with medicines meet a specific standard which facilitates ease of use for the general population (European Commission, 2004) . As a result, all leaflets now undergo a performance-based testing process, usually the technique known as 'user-testing'. This is a type of diagnostic testing, concerned with finding out what is wrong with a document. In a user-test people who are representative of likely users of the medicine are recruited to read the leaflet and answer questions which measure its performance (Ley, 1988, Raynor et al., 2011). This Directive was designed to lead to the development of PILs which better meet patients' needs for clearly written and presented patient information.

Also in 2005, the MHRA commissioned a report from the Committee on Safety of Medicines Working Group on Patient Information called "Always Read the Leaflet" (Medicines and Healthcare Products Regulatory Agency, 2005a). The aims of this report were:

- To advise on a strategy to improve the quality of information provided with medicines within the regulatory environment, in order to meet patient needs
- To propose criteria against which the quality of patient information can be assessed to assure the safe and appropriate use of the medicine and the process by which these will all be monitored

- To advise on key cases which could impact significantly on public health and to set standards for other products.

The report suggested a number of ways of improving the information provided with medicines highlighting changes to the leaflet to incorporate:

- The use of a headline or key information section on a PIL.
- The inclusion of more information about the benefits of the medicine.

Consideration regarding the use of these interventions has been given a higher profile recently in EU pharmacovigilance proposals (European Commission, 2009). Other international organisations, such as the US Food and Drug Administration (FDA), have also recognised the importance of providing critical drug information in a highlighted section of a written document and have made recommendations on moving towards better risk communication by striking a balance and conveying information on benefits as well as harms (Fischhoff et al., 2011, Food and Drug Administration, 2009).

Currently, little is known about patient preference for, and the effectiveness, of these two interventions. There is need for research; to explore the potential impact of both a headline section and benefit information on patient satisfaction, knowledge and potential medicine-taking behaviour. This research aims to explore how such changes might be implemented in current patient information leaflets by evaluating the impact of including a headline section and benefit information in PILs for patients in the UK.

1.3 Medicines information and the empowered patient

For people to optimise the safe and effective use of their medicines it is important that they receive good quality and easy to use information that informs them about their treatments (Raynor et al., 2007). The use of medicines is often sub-optimal (National Institute for Health and Care Excellence, 2009) and the role of good quality information is important in ensuring that patients:

- Get the right medicine
- Take medicines correctly (which can improve health outcomes)
- Take medicines safely
- Reduce wastage (Picton and Wright, 2013).

Providing patient information can fulfil several distinct roles. In an analysis of published discourses on patient information leaflets Dixon-Woods (2001) described patient information leaflets as being developed with systematic differences depending upon the discourse from which they originated. The two different discourses described are:

- Patient education
- Patient empowerment.

The dominant discourse on the role of patient information leaflets has been described by Dixon-Woods (2001) as grounded in patient education. The patient education approach is biomedical in origin and it tends to use patient information as a means of educating the patient from a health professional perspective, rather than from a patient perspective (Dixon-Woods, 2001).

The patient education approach presumes that the purpose of the leaflet is to reinforce the values and views of the healthcare professional. PILs are frequently being viewed as something that can compensate for patients' inadequacies in knowledge, understanding and medicine-taking behaviour. The goal of information provided for the purpose of patient education is to improve adherence to medicines. According to this discourse patients are frequently viewed as incompetent, non-compliant entities that need educating about medicines in order to achieve the desired effect of adherence to medicines (Dixon-Woods, 2001).

However, in recent years there has been a shift away from what might be termed paternalistic concepts of compliance and adherence to medicines. Healthcare providers are now encouraged to facilitate shared-decision making with patients and use information to support patients making informed-choices, as opposed to educate about compliance with treatments (Charles et al., 1997). Consequently, the concept of adherence, and the ways in which healthcare providers address it, has changed and this in turn has impacted upon the role of medicines information.

Non-adherence to medicines is no longer viewed as something which arises from patient incompetence or non-compliance, but instead is viewed as a normal state of being which is influenced by multiple factors such as patient knowledge, beliefs and concerns about medicines and perceptions of treatment and health (National Institute for Health and Care Excellence, 2009, Horne et al., 1999).

Using this approach the role of medicines information should be to focus less on education and more on patient empowerment with an aim to provide information that facilitates informed choices. This helps patients develop their knowledge and understanding about medicines whilst addressing any concerns associated with the medicine in an accurate and balanced way.

Dixon-Woods describes 'patient empowerment' as an approach that views patients as "experts in their own needs or preferences" (Dixon-Woods, 2001). This approach acknowledges that patients may have difficulties in understanding complex medical information, but views them as competent with engaging with information according to their own beliefs and experiences. The aim of patient empowerment is to *"build up the capacity of patients to help them become active partners in their own care, to enable*

them to share in clinical decision-making, and to contribute to a wider perspective in the health care system" (van den Berg and Donyai, 2010).

As perspectives on engaging patients in medicine-taking have changed over the years, so has the role of the patient information leaflet. Initially the PIL was instructional information about medicines designed to educate patients. However, initial PILs were often full of jargon and as something to protect the manufacturers, rather than to support the patient with their medicine-taking. As a result leaflets were subject to a great deal of criticism regarding the quality of the information they included (Raynor et al., 2007).

An increased interest in creating PILs which meet the needs of patients over the last decade has meant that the potential users of medicines are now actively recruited in order to test the design and readability of the leaflets to ensure that they meet patients' needs. There has also been a body of research developing the best methods of communicating written information about medicines (Nicolson et al., 2009, Grime et al., 2007, Raynor et al., 2007). From this research it is apparent that patients want medicines information that provides sufficient detail to enhance their understanding about medicines; also that written information should not be a substitute for spoken information from healthcare professionals (Grime et al., 2007). It is apparent that patients' desire information that can help them make decisions about their treatments, both when initially prescribed a medicine and also throughout the course of their treatment.

Research undertaken recently has highlighted the desire for information about the benefits of medicines which needs to be provided to balance the information about the potential harms of the medicines (Hamrosi et al., 2012). Also there is evidence of a growing desire for medicines information to be tailored to an individual's personal needs in order to facilitate decision-making using targeted information (Dickinson et al., 2013).

The information landscape continues to change and patients are increasingly becoming interested in having information that meets their specific needs and which helps provide them with knowledge about a medicine, rather than information which is purely prescriptive. The EU has responded to patient need for high quality information by mandating the user-testing of leaflets to ensure they are written in a manner comprehensible to the layperson. User-testing is a type of diagnostic testing that focuses on the layout and wording of PILs, however does not necessarily address issues with content and the scope of the information provided. Improvements have been made to the leaflets as a result, although common criticisms of leaflets remain and user-testing can only respond to patient need and preference to a limited amount. PILs

are still viewed as too lengthy and full of jargon. Patients desire information that is clear and reliable, which they can use to help make decisions about treatments. In order to make decisions about treatments patients need good quality information which they can easily read and understand and they also need information about the likelihood of benefit and risk of harm presented concomitantly in the leaflet.

The idea of a headline section is something which is designed to respond to the challenges that patients have to face when reading a PIL which they may view as complex and lengthy. The inclusion of information about the benefits of treatment will ideally provide balance and enhance positive judgements about medicines (Bersellini and Berry, 2007b).

1.4 Headline section background

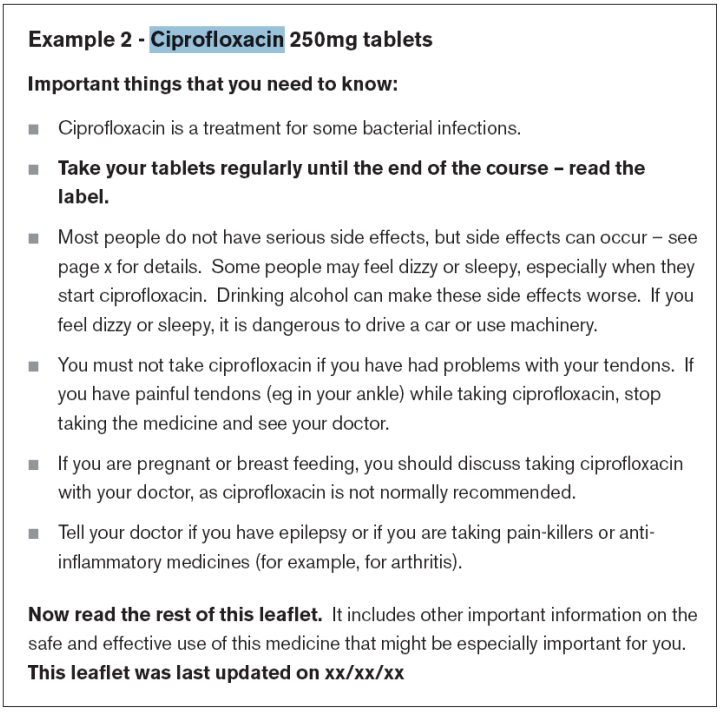
A **headline** section is an adaptation, suggested by the MHRA report as something that might be used to address some of the concerns that patients express about the length and complexity of PILs. These concerns can be a disincentive for patients to read the PIL (Medicines and Healthcare Products Regulatory Agency, 2005a). It is known that not all patients read the PIL and that some only read part of the leaflet and therefore might miss out on reading important information about their medicine. Research measuring the proportion of patients who read a PIL has shown varied findings. Lower proportions of readership, at 40%, were reported by Raynor and Knapp (2000) compared to higher proportions of 89% reported by Vander Stichele et al (1991).

The inclusion in a PIL of a headline section has been considered as something which might address this. A headline consists of a summary of the key messages on the safe and appropriate use of the medicine. It should be presented at the beginning of the PIL in order to maximise visibility and the likelihood of it being read (Medicines and Healthcare Products Regulatory Agency, 2005a)

A headline section could be presented in a number of different ways with the key information being highlighted using techniques such as bold, italics, large or small type or the use of boxes and outlines. The following type of information has been suggested as having potential for inclusion in a headline section.

- Why the patient should take the product
- The maximum dose of duration of treatment
- Potential side effects/ withdrawal reactions (symptoms to look out for, especially for common or serious side effects)
- Contraindications
- Important drug interactions

- Circumstances in which the drug should be stopped
- What to do if the medicine doesn't work
- Where to find further information.



Example 2 - Ciprofloxacin 250mg tablets

Important things that you need to know:

- Ciprofloxacin is a treatment for some bacterial infections.
- **Take your tablets regularly until the end of the course – read the label.**
- Most people do not have serious side effects, but side effects can occur – see page x for details. Some people may feel dizzy or sleepy, especially when they start ciprofloxacin. Drinking alcohol can make these side effects worse. If you feel dizzy or sleepy, it is dangerous to drive a car or use machinery.
- You must not take ciprofloxacin if you have had problems with your tendons. If you have painful tendons (eg in your ankle) while taking ciprofloxacin, stop taking the medicine and see your doctor.
- If you are pregnant or breast feeding, you should discuss taking ciprofloxacin with your doctor, as ciprofloxacin is not normally recommended.
- Tell your doctor if you have epilepsy or if you are taking pain-killers or anti-inflammatory medicines (for example, for arthritis).

Now read the rest of this leaflet. It includes other important information on the safe and effective use of this medicine that might be especially important for you.
This leaflet was last updated on xx/xx/xx

Figure 1: MHRA example of a headline section using an outlined box.

The use of a **headline** or summary section in written instructions is not a widely researched area. There is a small amount of literature which suggests that a summary in text can be useful to aid patient recall of information (Hartley and Truman, 1982, Hartley, 2004) However there are some concerns that the use of certain techniques, such as boxes and outlines can separate the information from the main body of text and this can impact negatively upon a reader's comprehension. Hartley suggests that there is little evidence for these concerns, but the use of boxes and outlines remains controversial (Hartley, 2004).

The MHRA gives no specific guidance on techniques to summarise key information, suggesting only that it should be at the beginning of the leaflet and that it should contain bullet-pointed information about key safety messages (Medicines and Healthcare Products Regulatory Agency, 2005a). Little is known about patient preferences for format of a headline section and whether the addition of this adaptation will encourage those who usually do not read PILs to access more information about their medicines.

This research aims to address this gap in the evidence-base and evaluate whether patients can find and understand key safety messages presented in this way.

1.5 Harm information background

While there is little research into the most effective method of presenting a headline section, in comparison the field of ***risk communication*** is well studied. There is a large and diverse research-base exploring the presentation of information about **harms and benefits** to patients, although the research-base examining the impact of presenting the **benefits** of treatments is smaller.

Patient information leaflets currently contain both textual and numerical descriptions of the possible harms associated with taking the medicine. The provision of this information is important for a number of reasons. Firstly it informs patients about the potential adverse effects of their treatments for which they can identify and seek help if needed. It is also important to assist them in making informed decisions about whether to take the treatment (Knapp et al., 2001, Knapp et al., 2009a).

The risk of harm described in a patient information leaflet relates to the likelihood of experiencing a side effect from taking the treatment. In order to communicate the potential for harm the European Union initially recommended use of qualitative descriptions (also called 'verbal terms') for five bands of risk, ranging from very rare (affecting < 0·01% of the population), to very common (>10%) (European Commission, 1998).

Patients value information about the side-effects of their treatments, and side-effect information is frequently cited as the most important information that patients wish to be told. However, research has shown that these frequency descriptors can lead to over-estimations of risk estimates (Berry et al., 2003b). This may in turn lead to patients making decision about their medicines which are not based on accurate assessments of the information.

In their document 'Always Read the Leaflet', the MHRA acknowledge that patients express concerns after reading about the potential side effects of the medicine. They suggest the possibility of the inclusion of additional 'positive' information in a PIL as means of providing more balance in a leaflet which in turn could minimise these concerns. This has been subsequently referred to as 'benefit' information.

Patients are limited in their ability to make informed decisions due to the lack of information available on both the risk of harm and the likelihood of benefit (Peters et al., 2014). Both are needed to support patient decision-making and initially this thesis aimed to assess inclusion of improved information about both risk and benefit

information. However a decision was made to narrow the focus to information about benefits alone for the following reasons:

1) There is a large field of research on the presentation of harm information, including good quality systematic reviews (Akl et al., 2011a, Waldron et al., 2011). There has been no similar 'systematic' collation of the research on benefit information.
2) PILs already contain information about risks but little about benefits. As patients want balance, it can be argued that there is a greater need to research best methods of presentation of benefit information in a PIL.

1.6 Benefit section background

Patients want both information about the risk of harm and the likelihood of benefit presented in medicines information, although as the previous section highlights, previously patient information leaflets were only mandated to include information about the potential harms of a treatment (Raynor et al., 2007). There are fewer studies that focus upon the provision of benefit information to patients, when compared to those with a focus on the presentation of risk of harm, and these suggest a mix of consequences associated with presenting benefit information to patients.

Some studies have shown that presenting benefit information has a positive effect upon patient judgement and intention to take a medicine (Bersellini and Berry, 2007b, Amery, 1999). Others have found that patients are more influenced by information on the adverse effects of medicines, rather than the benefits (Fried et al., 2011). It has been shown that there can be significant concerns associated with the provision of benefit information to patients. Previous work to which the author contributed found that the provision of benefit information provoked strong feelings of shock and anxiety when the benefits of an anti-platelet medicine were presented to a representative sample of medicine-users from both the UK and Australia (Hamrosi et al., 2012).

There is no agreed definition of what benefit information encompasses. Benefit information tends to refer to information about how the medicine works and how effective it is. In 'Always Read the Leaflet' the MHRA describe benefit information as additional information that describes the positive effects of taking a medicines and refers to several key points it might include:

- Why it is important to treat the disease and what the likely clinical outcome would be if the disease remained untreated;
- Whether the treatment is for short term or chronic use;

- Whether the medicine is being used to treat the underlying disease (i.e. curative) or for control of symptoms. If the latter, which symptoms will be controlled and how long the effects will last;
- Whether the effects will last after the medication is stopped;
- Where the medicine is used to treat two or more discrete indications, all should be succinctly described as above;
- Where to obtain more information on the condition.

Figure 2 shows an example provided by the MHRA which presents such additional textual information about the benefits of a medicine. The MHRA state that any additional information must be compatible with the Summary of Product Characteristics, be useful to the patient and not be promotional (Medicines and Healthcare Products Regulatory Agency, 2005a).

Without benefit information

PRODUCT contains beclometasone propionate which is one of a group of medicines called corticosteroids. These have an anti-inflammatory action and are used to treat asthma.

With benefit information

PRODUCT contains beclometasone propionate which is one of a group of medicines called corticosteroids, or "steroids". Corticosteroids prevent attacks of asthma by reducing swelling of the air passages and are sometimes called "preventers". You should take this medicine regularly every day even if your asthma is not troubling you. Using PRODUCT can help prevent severe asthma attacks which sometimes need hospital treatment and if left untreated could even be life-threatening.
This medicine should not be used to treat a sudden asthma attack; it will not help. You will need to use a different inhaler ("reliever") to deal with these attacks

Figure 1: An example of benefit information as provided in 'Always read the Leaflet'.

There is no agreed best format for the presentation of this type of positive information. In addition it does not encompass numerical benefit information – how likely a person taking the medicine is to benefit personally. This contrasts with the fact that currently PILs are required to contain numerical information about the potential harm a medicine might cause, which is displayed as information on side effects. Alongside this are criticisms of current PILs that they do not achieve a balance in providing patients with

facts about their medicine and are too negative with insufficient information on the benefits of the medicine (Raynor et al., 2007).The MHRA has recommended consideration be given to the inclusion of 'positive', benefit information in PILs in order to address this (Medicines and Healthcare Products Regulatory Agency, 2005a).

A major challenge of risk communication is that it is complex. Patients are vulnerable to 'innumeracy' and can misinterpret both textual and numerical information depending upon its format; different methods have been associated with over-estimations of risk and have been found to be 'biasing' (Gigerenzer, 2002, Knapp et al., 2009c, Berry et al., 2004, Carling et al., 2008, Goodyear-Smith et al., 2011, Berry, 2006). It is unclear which method of numerical presentation is most effective at communicating benefits to patients when presented in a written format.

Further research is essential to identify the most useful formats for communicating benefit information and to assess the impact of making changes in this manner to regulated PILs on patient knowledge and understanding and health-related behaviours.

1.7 The rationale of the research and expected outcomes

The primary purpose of this study is to improve the quality of written information about medicines, by developing evidence-based changes to written medicines information that incorporate the suggestions made above. The key objective is to explore how the users of medicines view the addition of a headline section and benefit information in their PILs and produce recommendations about how to present key safety messages in a headline section and information about benefits in a balanced format that patients find usable.

The motivation behind the research is to support patients to make informed, autonomous decisions, and help them get the most out of their medicines. It fits within the remit of the NHS White Paper which aimed to put patients first and states *'no decision about me without me'* (Department of Health, 2010). As a result the patient will be placed at the focus of the research as participants, but also as assessors of the readability and usability of the PILs which will be developed. This will be done through the process of user-testing, which assesses the performance of a written document (Raynor et al., 2011, Raynor, 2008).

The project aims to build up an existing base of knowledge in the two fields of:

1) ***information design***, specifically with regards to the **headline** section and;
2) ***harm/ benefit communication***.

The research aims to investigate how the inclusion of benefit information might impact upon a patient's knowledge, understanding and future health behaviours.

The expected outcomes of the research are the development of evidence-based PILs containing changes to format and content, a deeper insight into patient preferences about the use of a headline section and benefit information and the ways that these impact upon health-seeking and information-seeking behaviour. The research will also test the potential of providing this information to patients for the first time and assess understanding and behavioural intentions and whether this can impact upon the safe and effective use of medicines.

1.8 Research aims and objectives

1.8.1 Research question

What is the impact of the inclusion of a headline section and information about the benefits of medicines in patient information leaflets on patients' satisfaction and potential understanding and medicine-taking behaviour?

1.8.2 Research aims

- To investigate methods for the presentation of a **headline** section in a regulated PIL.
- To investigate methods for the inclusion of information about **benefits** in a regulated PIL.
- To explore patient preference for a headline section and information about the benefits of medicines.
- To explore how the inclusion of both headline and benefit information in a regulated PIL can impact upon patient knowledge and understanding of medicines.
- To explore the impact of the inclusion of both a headline section and benefit information on potential medicine-taking.

An initial aim of the research was to investigate the effect of combining the headline section with the benefit information into one adaptation. As the research progressed it was apparent that participants responded to the two adaptations differently and that these differences made it difficult to research the effect of combining benefit information in a headline section within the timescale of the work. As a result an investigation of this has not been included as part of the over-arching aims of the work.

The thesis presents 5 empirical studies. They are as follows:

Chapter two describes 2 literature reviews which were conducted concurrently and which review the breadth and depth of the literature on the optimum methods of

presenting information in a **headline** section and the presentation of information about **benefits** in written medicines information.

Chapter three presents the findings from a focus group study which explores the opinions and attitudes of users of medicines on the inclusion of both a headline section and information about the benefits of medicines. This chapter focuses upon preference for format and explores the potential impact on self-reported knowledge and medicine-taking behavior with the aim to identify the range of response that the interventions provoke.

Chapter four reports the use of 'user-testing' to explore how readers use a headline section in a PIL in a scenario-based test of the finding and understanding of key information.

Chapter five reports a survey of 100 PILs currently in circulation in the UK. The aim of this chapter is to determine the extent to which information about the benefits of medicines is currently included in a regulated PIL.

Chapter six describes the final study, an exploration of the impact of the provision of benefit information on the attitudes and beliefs that real-life users of medicines hold about their treatments. This study recruited patients receiving a prescription for simvastatin and used semi-structured interviews to explore preferences for format, understanding and the potential impact on behaviour. This study aimed to highlight whether there were any differences between the opinions and attitudes of those receiving hypothetical information and those receiving benefit information about the medicines which they were already using.

1.8.3 Funding and support for the PhD studentship

The research was supported by the Academic Unit of Pharmacy, Radiography and Healthcare Science, University of Leeds and by the UK medicines regulatory body, the Medicines and Healthcare Products Regulatory Agency (MHRA). The MHRA has a role in regulating the quality of the information provided with patient information leaflets. The Academic Unit of Pharmacy, Radiography and Healthcare Science, University of Leeds, has a track record in undertaking research into medicines information.

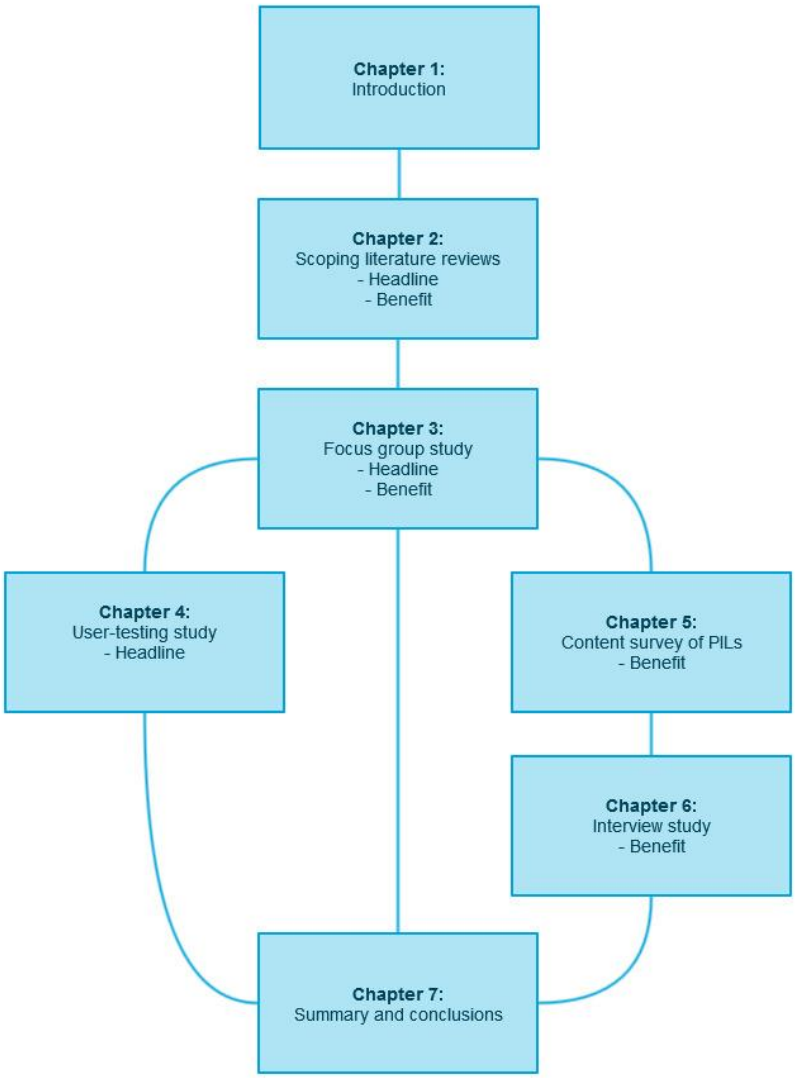


Figure 2: The structure of the thesis.

Chapter 2:

Scoping Literature Review

Chapter 2 Scoping literature reviews. (Study 1)

What does published research tell us about the inclusion of a headline section and the inclusion of information about benefits in written medicines information?

2.1 Introduction

Chapter two reports two scoping literature reviews undertaken to explore the published research on both the inclusion of a headline section and the inclusion of information about the benefits of medicines in written information.

This chapter describes the methods used to undertake the literature reviews and presents a narrative description of the findings of the literature collated. The ultimate aim of the review is to identify potential formats that can be used in the later stages of the PhD to develop leaflets which contain a headline section and information about the benefits of medicines. The chapter is presented in 4 sections:

[1] The methods of the review.

[2] Findings: The use of a headline section in written information.

[3] Findings: Information about the presentation of the information about benefits in written information.

[4] Application of findings to later studies in the thesis.

The aim of this review is not specifically to critically appraise the body of research but instead to collect and collate a range of options that have the potential for use in the later stages of the research. However, a critical evaluation will be part of the review and each study will be evaluated using a generic critical appraisal tool. The aim of such critical appraisal is to provoke discussion on the quality of the research in the field, rather than be used to define the inclusion of research into the review (Long et al., 2002).

The final part of this chapter will present the conclusions of the review and make recommendations about the options that have the most potential for presenting both a headline section and information about the benefits of medicines in PILs that can be used in the next stages of the research.

2.2 Aims and objectives

[1] Headline section

Aims

- To undertake a scoping review to identify published research on the presentation of a 'headline' section.

Objectives

- To identify the extent, range and nature of the research on the use of a headline section to summarise key points of information within a piece of information.
- To summarise the different methods for presenting a 'headline section' and the potential impact on the reader's ability to find and understand key information.

[2] Benefit

Aims:

- To undertake a scoping literature review to identify the best techniques for presentation of information on potential benefits in written health communications that can be replicated in a patient information leaflet.

Objectives:

- To identify the extent, range and nature of the research on the presentation of information about benefits in health communications that can be replicated in a patient information leaflet.
- To explore the different methods and formats of benefit presentation
- To collate and summarise key findings on the best ways to present benefit information in health communications that be replicated in a PIL.
- To explore the impact different methods of benefit presentation might have on satisfaction, knowledge and potential medicine-taking behaviour.

Overview of Method

A scoping literature review was undertaken using the framework developed by (Levac et al., 2010) and building upon the methods described by Arksey and O'Malley (2005).The method is suited to the appraisal of a body of studies which focus on a similar topic but use different methods.

The method differs from a traditional (systematic) review, as it is based on an iterative and interpretative approach to the collection and collation of the literature as opposed to a more rigid process which apply pre-determined criteria of methodological quality to the literature. The aim of this review is not to evaluate efficacy or effectiveness, but instead to *"map the range and scope of the literature and explore its utility and*

importance based upon the relevance, credibility and contribution of evidence" (Davis et al., 2009, P.1389).

Although a scoping literature review differs from a systematic review in several ways, it also shares several similarities, for example the requirement for the review to be conducted in a rigorous and transparent way. A well-executed scoping review requires a framework that is well-defined and robust. In order to ensure that the methods of the review were rigorous and transparent a framework defined by the Centre for Reviews and Dissemination was applied (Centre for Reviews and Dissemination, 2009). This framework uses core principles which can be applied to the review to facilitate rigour and transparency in its various stages. The framework describes the structure of a review which includes the following stages: developing a search strategy; defining inclusion criteria; identifying the research evidence; selecting the studies; extracting the data; assessing the quality of the studies and synthesising data to present a coherent narrative of the scope and range of literature. These stages are applied here to the fields of the headline section and benefit information presentation.

2.3 Search strategy

A search strategy was developed with the assistance of health librarians and an information design expert (BP). Search terms were developed and combined MeSH headings and Boolean operators to expand and refine the review topics (see appendix 1 for the combination of search terms used). Two searches were developed, one for headline and one for benefit and which were run concurrently.

A range of different resources were searched including medical databases and peer-reviewed journals in the fields of pharmacy and information design (see table 2). Only English language papers were retained. The literature searches were run over a period between 24.04.11 and 13.06.11.

Electronic databases:

- CINAHL
- MEDLINE
- The Cochrane Library
- EMBASE
- Web of Science
- PsychINFO

Theses databases:

- ProQuest (Dissertation and Theses database)

- Index to theses

Reference Lists:

- Key papers were searched to help refine the search strategy. The reference lists of all included papers were assessed for their relevance.

Relevant Journals

The contents table of the following journals were searched for potentially relevant literature.

- International Journal of Pharmacy Practice
- Information Design Journal.

2.3.1 Study selection

For both the headline section and the benefit section there were several phases of data selection. Criteria for each phase were developed iteratively and refined in light of the results of the search, based on familiarity with the research.

The different phases for each part of the literature review are described below. The initial screening was undertaken by one reviewer (RD). However, two reviewers (RD & DKR) screened all the full text papers for relevance and eligibility to the study according to the refined inclusion criteria. Differences of opinion were discussed until consensus was reached.

2.3.2 Phases of study selection for headline section

Phase one

Initially references were screened for relevance by viewing the title and, where the scope of the paper was unclear, abstract. Papers were required to meet at least one of the criteria for inclusion to be included in phase two. Criteria for inclusion:

The use of a Headline section to present key information:

- Does the paper refer to a method of presentation of key/ summary/ important information in written information?
- Does the paper refer to instructional design of written information?
- Does the paper refer to the use of boxes and outlines, (occasionally referred to as boxed-asides (Hartley, 2004)) or similar technique to convey information?
- Does the paper refer to the use of a warning sign or the presentation of hazard information within a body of text?

Phase two

A mechanism to eliminate studies that did not relate to the original search question was designed. The inclusion and exclusion criteria were devised and refined iteratively, depending upon the studies that were retrieved during the first stage of the literature search, based on an increasing familiarity with the data. There followed a process of sifting of the data where the inclusion and exclusion criteria were applied to each abstract title in order to evaluate relevance.

Table 1: Inclusion/ exclusion criteria for phase two of the scoping review.

Headline	Include	Exclude
Type of study	All primary empirical Research	Opinion, discussion articles
Population of Interest	Information for patients or consumers	Information for Experts
Intervention	Use of summary section / boxed aside/ headline to communicate key information in written information	

Phase three

The next phase of study selection involved a more detailed process for examining the relevance of the papers. Full copies of each text were obtained. (When copies were unavailable the first author was contacted for further information).

The full text article was read and a decision made about inclusion into the scoping review. The criteria used can be viewed in table 2.

Table 2: Inclusion/ exclusion criteria for phase three of the scoping review.

Types of studies • Empirical qualitative or quantitative primary research, or systematic reviews. • (Exclude non-empirical research) **Population of interest** • Patients, general public • (Exclude information intended for practitioners such as doctors etc.) **Types of interventions: Include** • Presentation of a summary of the most important points of information in a document • Use of a method of highlighting such as a box or shading to present key information. • Attention to the order of key information within an instructional document. **Types of interventions: Exclude** • Use of 'data boxes' for example in computer programming • Interventions that cannot be replicated in a patient information leaflet • Labels, signs and warnings **Types of outcome measure (papers to meet one or all of the criteria)** • Understanding of information • Readability • Knowledge of treatment effects – recall of information • Satisfaction with medicine (treatment) • Decision-making (promotion of informed decision-making) • Adherence to medicines (treatment) – changes to medicine-taking behaviour

2.3.3 Phases of study selection for benefit section.

The initial search was run in Medline The original search terms (see appendix 2) were very broad and there was a lack of precision in the definition of terms which led to the retrieval of large numbers of irrelevant references (England, 2000, Anonymous, 2003). For practical reasons the search strategy was revised and additional limits imposed. The search was limited to references after 1984, a date set after the publication of a key paper in this field (George, 1983).

Large numbers of references were initially identified and, even after limiting the search, approximately 60,000 references were searched. Advice was sought on managing the

volume of references. Tools such as the de-duplication facility don't work on large numbers of references, therefore it was not possible to export reference lists in their entirety into reference managing tools in order to perform de-duplication processes. In consultation with a health librarian (Mark Clowes) a number of smaller searches with less breadth were developed. Methods of searching such as (bracketing terms) and using the **adj3/ SAME** function to provide precision were utilised. These searches were run adjacent to keyword searches already identified. The refined search strategy was used to search the remaining databases (see appendix 3).

The adoption of such limits in a search has the potential to exclude relevant papers. However, for practical reasons, it is sometimes essential to take this risk. The limits reduced the number of references retrieved, however significant numbers of articles were still identified and the number of papers assessed as relevant. Within a scoping review it is acceptable that decisions are made about the length of time span and language and imposed iteratively. A scoping review is not a linear process, but instead requires the researcher to reflect on each stage and adapt the search as required (Arksey and O'Malley, 2005).

Initially the study aimed to assess inclusion of improved information about both risk and benefit information. However the volume of the research on risk information was too large to search within the time constraints of the study a decision was made to narrow the focus to information about benefits alone.

As a result there were four phases of data selection. Criteria for each phase were developed iteratively and refined in light of the results of the search based on familiarity with the research.

Phase one

Initially references were screened for relevance by viewing the title and, where the scope of the paper was unclear, the abstract. Criteria for inclusion were:

- Does the paper refer to presenting, communicating, informing or educating patient about harms, risks, or examine patient perceptions of harms and risk?
- Does the paper refer to presenting, communicating, informing or educating patient about risks, or examine patient perceptions of benefit?
- Does the title make reference to a specific method of communication about risks, for example use of graphical display, icon array, presentation of probability?
- Does the title make reference to a specific method of communication about benefits, for example the Number Needed to Treat (NNT) statistic?
- Does the title make reference to framing of risk?

Phase two

A mechanism to eliminate studies that did not relate to the original search question was designed. Inclusion and exclusion criteria were devised (although to some extent these were refined *post hoc* based on increasing familiarity with the data). The next phase of data sifting employed the application of the inclusion and exclusion criteria to the abstracts of these papers that had been identified as potentially relevant by title alone.

Table 3: Phase two criteria for benefit information

Risk-benefit	**Include**	**Exclude**
Type of study	All primary empirical research	Opinion, discussion articles
Population of interest	Patients, general public	Healthcare professionals
Intervention	Presentation of risk information (side effects/ harms/ adverse events) Presentation of harm information in any format Presentation of benefit information (effectiveness information such as NNTs, efficacy data) Framing of risk information in written information	Verbal communication of risk alone

Table 4: Inclusion/ exclusion criteria for phase three of the scoping literature review - Benefit.

Types of studies

All empirical qualitative and quantitative primary research. Systematic reviews.

(Exclude non-empirical research)

Population of interest

Patients, general public

(Exclude information for specialists such as Doctors etc.)

Types of interventions: Include

- Presentation of patient outcome measures such as mortality
- Presentation of numerical risk/ benefit data such as absolute risks, relative risks, numbers needed to treat, natural frequencies
- Diagrams, graphics and charts
- Use of patient narratives and vignettes
- Framing (loss or gain)

Types of interventions: Exclude

- Spoken presentation of risk (for example during consultation)
- Educational programmes of risk education
- Techniques to calculate and present individualised risk
- Interventions that cannot be replicated in a patient information leaflet
- Computer formatted risk presentations such as interactive web based graphics.
- Decision aids and risk calculation tools
- Interventions where the explicit intention in the paper is to persuade, promote or increase adherence to or participation in health-related behaviours.
- Diagrams, graphics and charts
- Alternative graphic displays for example visual analogue scales and icon arrays (20 papers with a focus on graphical presentations of benefit were initially retrieved however, these were excluded later on in the review)

Types of outcome measure

- Understanding of information
- Readability
- Knowledge of treatment effects – recall of information
- Satisfaction with medicine (treatment) decision-making (promotion of informed decision-making)
- Adherence to medicines (treatment) – changes to medicine-taking behaviour

Phase Four

The following criteria were used to eliminate papers with a focus on risk or harm:

Table 5: Refining the review from risks and benefits to risks

Include: **Benefit** Information

Papers that assess the impact of:

- presenting **survival figures**, such as survival curves and graphs
- **Treatment effects** for example the outcome of choosing a surgical procedure or medicine. This also includes treatment risk reduction
- **Screening effects**
- Information about interventions that lead to a **postponement of, or a reduced likelihood of an adverse event**.

Include papers about the presentation of generic risk/ benefit information. These are papers that assess a specific technique as opposed to a specific type of numerical data. For example the comparison of an icon array to a bar chart. The comparison of an (in full) ARR to an RRR or a probability with no context as to what the figures entail – these papers test numeracy to some extent.

Exclude: **Risk** Information

Papers that assess the impact of only:

- The presentation of information about **side effects**
- The presentation of **mortality figures**
- The presentation of information about the **risk of disease**

In order to ensure the transparent reporting of the process involved in the review, the PRISMA flow chart was adopted to record the flow of information, and the number of references searched for each phase of the review (Moher et al., 2009). See Figure 4 for the PRISMA flow chart.

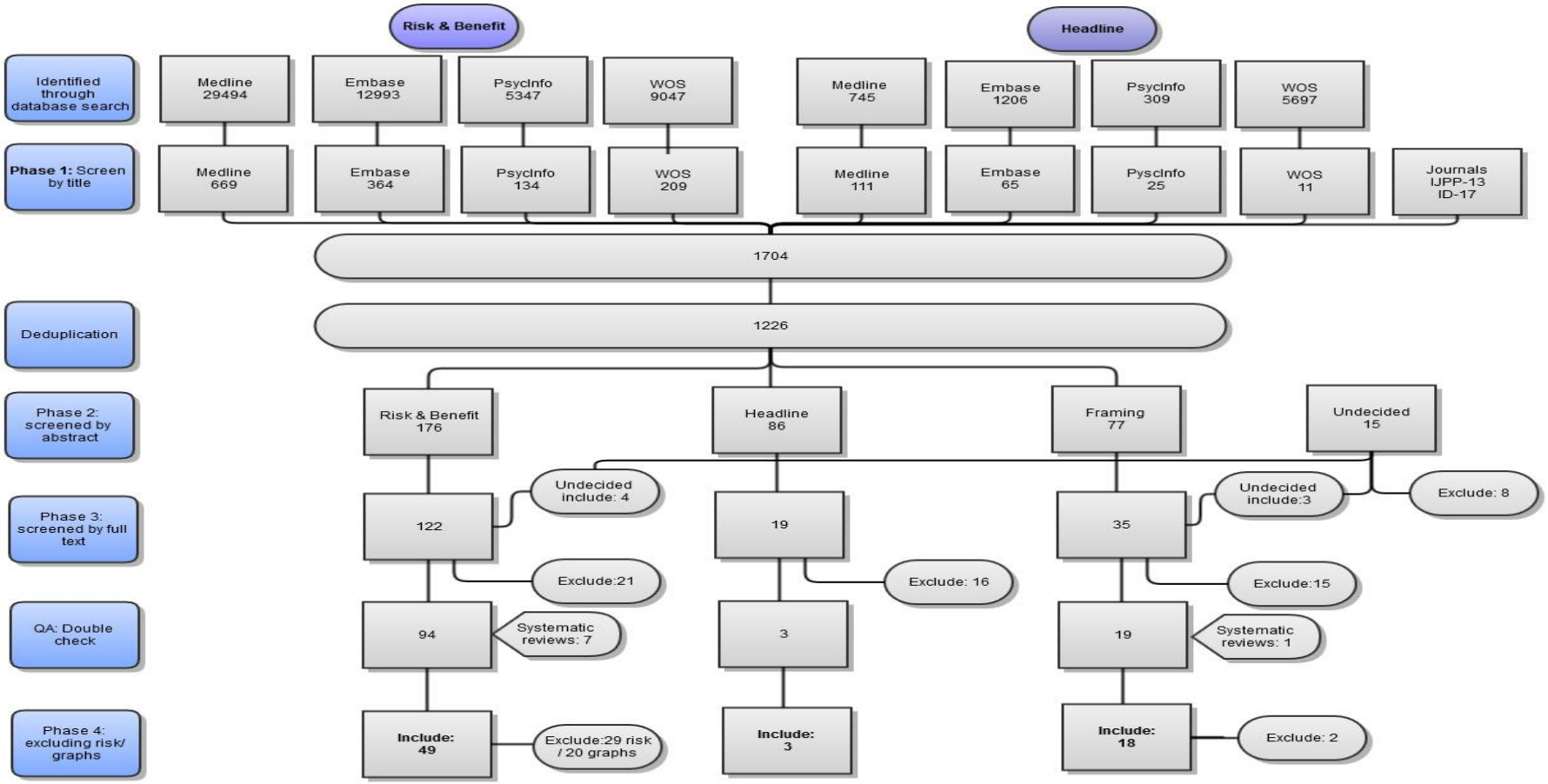


Figure 3: PRISMA diagram to show the flow of the scoping literature review.

2.3.4 Collating and summarising results

Headline: From a search of 8,702 initial references, 3 papers were included in the narrative synthesis.

Benefit: From a search of 64,838 initial references, 87 were included in the narrative synthesis.

Meta-analysis was not possible due to the heterogeneity of the retrieved research in these fields. Instead a descriptive synthesis using the narrative synthesis methodology was undertaken.

"A narrative synthesis refers to an approach to the systematic review and synthesis of findings from multiple studies that relies primarily on the use of words and text to summarise and explain the findings of the synthesis" (Popay et al., 2006, P.5).

The strengths of a narrative synthesis in this context include:

- It is appropriate when the data are heterogeneous and when meta-analysis is not possible, or not the focus of the review.
- It provides a systematic and structured framework to the process which is transparent and replicable.

In order to collate the retrieved data, a data collection form was developed. The form was designed to replicate that used in Cochrane systematic reviews (Higgins and Green, 2001). This is a widely used format, which is commonly understood and presents the essential key findings of a research study (see appendix 4).

The retrieved literature was organised according to different categories and sub-categories and these were evaluated for common linkages, themes and findings. Attempts were made to form groupings and clusters, for example on groups of participants such as age, or on research designs or interventions. The results are presented as a narrative description.

2.4 Study quality assessment

Although the scoping literature review method does not specifically set out the requirement for an in-depth assessment of study quality, the studies retrieved were evaluated for quality using a generic research appraisal tool (Long et al., 2002). This critical assessment was used to illuminate the findings as opposed to being used to determine inclusion or exclusion of the research article into the review.

The findings are presented in two sections; headline and benefit. The benefit information section contains several sub-categories which present the range of formats

of benefit information and how the research identified impacted upon issues such as knowledge, behaviour.

2.5 Study findings: Headline section

2.5.1 General findings

The initial screening (phase 1) identified 86 potentially relevant papers. These were screened by abstract (phase 2) with 19 papers included for screening by full-text (phase 3). Three papers met the inclusion criteria and were included.

Two of these papers used a similar headline method, called a Drugs Facts Box, which used a tabular format to summarise numerical information. (Schwartz et al., 2007, Schwartz et al., 2009)

Dolk et al. (2011) used a headline section as described by the MHRA (Medicines and Healthcare Products Regulatory Agency, 2005a). This was a highlighted section containing key safety information in a textual format and was presented within a body of text (Dolk et al., 2011).

The studies used different methods to evaluate the impact of the headline section. Schwartz et al (2007) recruited a convenience sample (n=274) into a cross-sectional survey which aimed to evaluate whether participants could use and understand a Drugs Facts Box. Schwartz et al. (2009) undertook 2 randomised controlled trials to test whether the Drugs Facts Box improved knowledge and judgements about medicines in comparison to a direct-to-consumer (DTC) drug advert. One trial recruited 231 people into a 'symptom' drug box arm and the second, 219 people into a 'prevention' drug box arm. Dolk et al. (2011) recruited 80 participants to evaluate the value of a headline section on the perception and effectiveness of a PIL using user-testing.

2.5.2 Impact on ability to find information

There is no evidence to show that a headline section impacts positively or negatively upon people's ability to find information. Research into the Drugs Facts Box did not assess this. Dolk et al. (2011) looked at whether patients could find the information and reported that the headline section did not have an impact on the participants' ability to locate information.

2.5.3 Impact on understanding of Information

Dolk et al (2011) compared a regulated PIL with or without a headline section and found that the information presented was comprehended as well with or without the headline section present. However, the sample size was small and real differences may have been undetected.

Schwartz et al. (2007) found that the Drugs Facts Box aided the retrieval and understanding of risk and benefit information. Most participants were able to use the box and retrieve information to answer the questions set. The authors reported a positive correlation between participants' understanding of the information and their educational attainment.

Schwartz et al. (2009) reported that most participants found the Drug Facts Box 'very easy' or 'somewhat easy' to read. The use of the Drugs Facts Box was associated with a decreased perception of the magnitude of side-effects. With regards to the benefits of the medicines, the Drugs Facts Box promoted an accurate perception of the effectiveness of each medicine relatively. It was reported that the Drugs Facts Box resulted in more accurate knowledge about the magnitude of side-effects because of the inclusion of data about the baseline risk.

It was also reported that the use of the Drugs Facts Box improved the accuracy of patients' judgements about their medicines, with participants more likely to choose appropriate drugs and less likely to over-estimate the benefits of the treatments.

Overall, the use of headline section did not negatively impact upon the understanding the participants had about their medicines. Schwartz et al. (2009) were able to show a positive impact upon patient understanding about their medicines.

2.5.4 Preferences for a headline section

There appeared to be no negative concerns about the inclusion of a headline section in general. Participants stated that they felt it 'important' to have an included data summary similar to what was provided in the Drugs Facts Box (Schwartz et al., 2009).

Participants expressed strong positive opinions about the headline section within a PIL; however there was little evidence that participants used the headline to locate information during the user-test (Dolk et al., 2011).

2.5.5 Behavioural impact of a headline section

The research findings on the Drugs Facts Box suggested it might impact upon medicine-taking behaviour. The research showed it could influence a patient's choice so they were less likely to take a medicine after they had read and understood the information about the drug's effectiveness. It could be argued that this is attributable to the content of the risk-benefit information as opposed to the format. There was no evidence of behaviour change resulting from the headline section in the regulated PIL, although this was not a primary outcome measure of that study.

2.6 Headline section discussion

In summary, there is little evidence to suggest that a headline section has either a positive or a negative effect on a participant's ability to find and use key information, although only one of the papers (Dolk et al. 2011) tested this explicitly.

Dolk et al. (2011) was well-designed and used a method appropriate to deliver the objectives outlined. However, there were limitations with the study design which potentially impact upon the strength of the findings. There was limited reporting of participant characteristics, specifically educational attainment. As a result it is difficult to ascertain whether participants were more or less-educated than the average medicine-user. This raises concerns about the applicability of the findings to the general population. While the study found that participants did not necessarily use a headline section, the sample size was small (although this is common in user-testing). As a result there is the possibility that the study failed to measure the positive impact of a headline section and that the finding that patients did not use the headline section may be false. More research is required in this area to ensure a false-negative result has not been reported.

Neither of the Schwartz studies assessed a participant's ability to find information in the headline section in the first instance. The Drugs Facts Box had a different context to the headline section suggested by the MHRA, replacing text within a direct-to-consumer (DTC) drugs advert, which are common in the USA (Dolk et al., 2011, Bell et al., 1999, Wolfe, 2002). DTC adverts tend to be promotional rather than informational and have been criticised for containing incomplete data (Woloshin et al., 2001, Wolfe, 2002). In both studies the Drugs Facts Box was presented in isolation and not embedded within a body of text. This can impact on the applicability of these findings in a European setting, where a headline section in a mandated PIL, would be presented alongside other text.

There are also limitations concerning the lack of representativeness of the sample for both these research studies. Schwartz et al. (2007) recruited participants with above average quantitative skills. Consequently, this makes it difficult to extrapolate from the findings and apply them to a general population of medicine-users. Even with additional quantitative abilities many participants still could not understand the information provided. This was more significant where participants were required to use the Drug Facts Box to work out the absolute difference in the proportion of women with breast cancer in the tamoxifen versus the placebo groups. 71% achieved this, which means 29% could not. Participants of a lower education attainment did less well using the Drugs Facts Box, getting more answers incorrect, although the authors concluded that most participants, even those with lower formal educational attainment, were able to understand and use the tabular data. This has important implications when considering the relevance of these findings to how the intervention might be applied to the general population of medicine-users.

Participants recruited to the 2 randomised trials (Schwartz et al., 2009) also had slightly higher educational attainment than the general population. This might affect the applicability of the findings by leading to an over-estimation of a patient's ability to use and understand the Drugs Facts Box.

It must be noted that the number of people answering questions correctly was variable, ranging from 55%-93% correct answers. While the Drugs Facts Box did increase understanding and knowledge, this was not for all participants. When evaluating the impact of the Drugs Facts Box in the prevention group on the understanding of side-effects, 51% of participants correctly answered questions about side-effects in comparison to 16% of the control group. While this suggests improvements in knowledge in comparison to the control, it is important to note that at least half the participants did not understand the side-effect information, even with the improved intervention.

The survey assessing the outcome measures was completed in the participants' homes and researchers did not observe how the participants used the information, and whether this was intuitive or time-consuming. Between 52% and 71% participants reported that the box's data table was "very easy" or "easy" to understand; this still suggests that many participants did not associate ease of use with the data-table presented.

On the whole the studies included in this review were well-designed and generally methodologically robust. Flaws in their sampling strategies bring into question the applicability of the findings to the wider population of medicine-users. Schwartz et al (2009) fail to address they key issue of whether patients could find and use a summary section in the first instance, and while Dolk et al. (2011) suggests that there is no evidence that a headline section was utilised by participants undertaking user-testing, the small sample does not provide strong evidence for the utility, or lack of utility, of a headline section.

There is a wide range of research, including a systematic review, which supports the view that the provision of good quality information can impact positively on a patient's knowledge and health outcomes (Bishop, 1996, Barlow and Wright, 1998, Macfarlane et al., 1997, Raynor et al., 2007). Evidence suggests that patients value PILs, but there is a gap between the information that is currently provided and the information that patients desire (Raynor et al., 2007). Several key principles, shown to promote patient understanding, can be utilised to facilitate the role that good quality information design can have in improving the content and layout of leaflets so they better meet patient needs. Although these key principles do not specifically suggest the use of a headline section, techniques integral to such a section, including the use of bullet points to organise lists and short headings that stand out, are recommended in order to optimise engagement of the reader with the information.

There is an argument that a section in a piece of written text such as a box or outline may be detrimental to the reader's comprehension (Hartley, 2004). Thomas (1984) suggests that the use of a boxed-aside may 'disrupt the flow of the running text', which may lead the reader to skip over the important information. However, there is lack of empirical research in this area which evaluates the utility of this technique and whether a headline section might impact negatively on a person's ability to find the information contained within the headline text.

Although it did not meet the criteria for inclusion in this review, there is a large body of research on warning design which recommends a number of basic principles to consider when creating warning signs. Wogalter and Vigilante (2003) notes the importance of getting noticed as the first requirement of an effective warning. He also highlights the need to pay attention to layout and placement (Wogalter and Vigilante, 2003). The body of work evaluating the impact of warning sign design raises several issues. A significant proportion of the research was not directly comparable to a 'headline' section, with the interventions differing in purpose and design (for example

much of the research focused on pictorial design, which did not meet the criteria for inclusion in this review).

Dickinson et al (2010) stated that many readers need help with reading documents such as PILs and that highlighting key information with bold text and type size is often appreciated by the less skilled readers of documents. However the paper acknowledges the need for more research in this area (Dickinson et al., 2010). The current review has not included any evidence to suggest that a headline section would be detrimental to the users of medicines information. However, it has also not shown any optimal methods for the presentation of such a section nor whether this intervention is useful for the readers of medicines information.

2.7 Study findings: Benefit

2.7.1 General findings

There was a large body of literature identified that explores the impact of different formats of benefit information. The findings have been organised into several different categories in order to provide a narrative account of the breadth and scope of the literature.

For pragmatic purposes, a decision was made to report, in detail, findings which are most relevant to the use of benefit information in a PIL. As a result, papers which focus upon the presentation of formats such as graphs have not been included for a detailed narrative synthesis in these findings. Graphical formats of benefit presentation are not viewed as a technique that would be feasible for use in a PIL where space is limited – and as good-quality communication using graphs requires significant space. This review therefore focuses on the textual and numerical formats of the presentation of information about the potential benefits of medicines, although the research into some graphical formats will be discussed when the studies are compared with other formats relevant to the review. This is congruent with the methods of the scoping literature which permits selective reporting of the most relevant literature over the least relevant (Arksey and O'Malley, 2005).

In total 87 studies were included for analysis: 7 of the included papers were systematic literature reviews, 5 had a focus on providing probability or generic harm-benefit information, and 2 had a focus on the ‘framing’ of healthcare interventions.

The primary research papers which focused upon presenting benefit information reported on several different methods of presentation (table 5).

Table 6: Type and topic of research papers included in the scoping literature review.

Risk-benefit	Include	Exclude
Type of Study	All primary empirical research	Opinion, discussion articles
Population of interest	Patients, general public	Healthcare professionals
Intervention	Presentation of risk information (side effects/ harms/ adverse events) Presentation of harm information in any format Presentation of benefit information (effectiveness information such as NNTs, efficacy data) Framing of risk information in written information	Verbal communication of risk alone

The majority of the research was published since 2000. Although the earliest publication date was 1989, relatively few studies were published before 2000. The numbers of publications retrieved grew throughout the 2000s, with the largest number of papers being published in 2010 (n=18). This indicates a growing interest in the field of harm and benefit communication.

2.7.2 Studies of different methods of benefit

- **Studies of textual information**

Five papers described research evaluating the provision of benefit information in a textual format. Three were highly relevant and focused upon the provision of a **short written statement** about medicine benefits in a patient information leaflet (Bersellini and Berry, 2007a, Bersellini and Berry, 2007b, Vander Stichele et al., 2002).

These statements highlighted detailed information about the drug action, as well as further information about the relationship between the nature of disease and drug action. The studies were well-described and used different methods: a factorial randomised trial (Bersellini and Berry, 2007a, Bersellini and Berry, 2007b) and a

parallel-groups randomised controlled trial (Vander Stichele et al., 2002). Bersellini (2007a & 2007b) used interventions based on recommended EU guidelines on medicines information. The limitations of these studies were that they were undertaken with healthy volunteers and not necessarily a medicine-taking sample.

- **Studies of numerical information**

20 papers evaluated the presentation of numerical information about benefits. These were all quantitative studies, although one combined this with a qualitative element (Studts et al., 2005). The majority used a controlled-design and many were randomised. Predominantly surveys and questionnaires were used to collect data.

Six studies did not have a control group. These tended to measure patient preference for format and presented a mix of different benefit formats, presented as summary statistics. (Malenka et al., 1993, Sarfati et al., 1998, Hux and Naylor, 1995, Bhandari and Tornetta, 2004, Studts et al., 2005, Misselbrook and Armstrong, 2001).

The research aims were broadly similar; to evaluate the impact of format on understanding and intention to take a treatment. The exceptions to this were studies by Fagerlin et al. (2007) and Fried at al. (2011) which aimed to test whether the provision of comparative risk information changed risk perceptions.

The studies that focussed upon determining the best format can be broadly grouped into 3 categories (a) studies examining summary statistics, (b) studies examining probability formats (c) studies comparing textual formats with numerical formats.

a) Studies examining summary statistics

Several studies examined the impact of presenting *multiple summary statistics* that represented the likelihood of an event occurring. Commonly these included the following:

- absolute risk reduction (ARR)
- relative risk reduction (RRR)
- numbers need to treat (NNT)
- numbers need to screen (NNS)
- odds ratio (OR)
- relative risk (RR)
- events rates (ER)
- tablets needed to take (TNT)
- whole numbers (WN)

- absolute survival benefit (ASB)
- postponement of adverse event.

The papers were varied and used a range of methods. Three studies tested multiple formats against each other in randomised trials.(Carling et al., 2008, Sheridan et al., 2003, Natter and Berry, 2005). Natter et al (2005) also compared forms of absolute risk and relative risk with and without baseline information, using a questionnaire-based study with a two-factor between-subject design to examine patient estimates of risk.

Six papers presented multiple formats of summary statistics to participants and evaluated format based on preference for format and/or willingness to take the treatment (Bhandari and Tornetta, 2004, Halvorsen et al., 2007, Hux and Naylor, 1995, Malenka et al., 1993, Sarfati et al., 1998, Studts et al., 2005)

Finally two papers presented different formats of one type of *single summary statistic.* Kristiansen et al (2002) provided different values of NNT to patients, ranging from an NNT of 10 to an NNT of 400 and measured intention to choose a treatment (Kristiansen et al., 2002). Gyrd-Hansen et al (2003) evaluated the impact of different values of ARR and RRR provided with baseline risks (Gyrd-Hansen et al., 2003).

b) Studies examining probability formats

4 studies evaluated probability statistics such as frequencies, natural frequencies or percentages. Commonly these included the following:

- probabilities
- natural frequencies
- percentages
- variable frequencies
- combined formats e.g. percent and natural frequency.

These studies used different study designs and measured different outcomes such as preference for format, impact of format on decision-making and ability of patient to make ‘trade-offs’ using the data. One experimental study compared how conditional probabilities and natural frequencies could improve understanding in older adults and people with low literacy (Galesic et al., 2009b).

Three studies randomised participants into groups which received different types of probability format. Cuite et al (2008) randomly assigned participants to a variety of studies where participants received either ‘1 in n’, frequency or percentage formats.

They measured a number of different outcomes, including participants' ability to undertake a variety of mathematical operations using the different formats and understanding of different risk level (Cuite et al., 2008). Woloshin & Schwartz (2011) undertook a parallel-group trial, randomising participants to receive information on the risks and benefits of a drug presented in 1 of 5 formats; [1] a natural frequency, [2] a variable frequency [3] percent [4] percent plus natural frequency [5] percent plus variable frequency (Woloshin and Schwartz, 2011). Finally Tait et al (2010a) measured the different risk and benefit trade-offs that patients might make when evaluating benefit information. The study design used an internet survey and randomised participants to four scenarios comparing two hypothetical drugs. Each scenario presented a balance of risk and benefits of the drugs presented in different formats. The balance between perceived risks and benefits and ability to comprehend risk-benefit information was measured according to 2 types of knowledge: **gist knowledge**, which is a measure of ability to understand the essential meaning of the information presented and **verbatim knowledge** which is the ability to correctly identify the numerical risk and benefit statistics.

c) Studies examining a combination of summary statistic and probability format.

Two studies compared a combination of summary statistics and probability formats. Bergus et al (2002) randomly presented different treatments for symptomatic carotid artery disease and also randomised patients to receive information about risk, either before or after benefits with an aim of evaluating whether or not the order of risk-benefit information impacted upon decision-making (Bergus et al., 2002).

Misselbrook and Armstrong (2001) used a postal questionnaire to assess patients' willingness to take a medicine after reading the benefits presented as one of ARR, RRR, NNT and personal probability of benefits. The participants viewed all formats of risk presentation.

- **Descriptive summary of studies testing combined formats**

14 papers presented research evaluating a combination of different formats. These papers tended to compare either textual formats, numerical formats or graphical formats. The papers were varied, recruited a variety of samples and presented multiple formats of benefit information. They were categorised according to two groups:

(a) Studies comparing textual formats with numerical formats

Two studies compared verbal descriptors, where levels of risk were described using words such as 'common', 'uncommon' or 'rare' (France et al., 2008) and 'somewhat likely' or 'moderately greater' (Vahabi, 2010) with percentage and probability formats. The results of these studies were conflicting, France et al (2008) used a short questionnaire survey design to measure whether numerical information, in the form of percentages were better understood, and found that patients found it difficult to accurately predict the frequency of the terms 'uncommon', 'common' and 'rare'. Vahabi et al (2010) randomised participants to receive a breast health information brochure and measured comprehension and preference. The study showed that while nearly two thirds of participants preferred the numeric format, comprehension was highest among participants who received probabilistic information in a verbal format.

(b) Studies comparing numerical and graphical formats

12 studies compared a variety of different formats of numerical and graphical formats. Comparisons included:

- Visual (bar graph) and verbal (textual statement) (Parrott et al., 2005)
- Percentages, frequencies, population figures (Timmermans et al., 2008)
- Text, tables and pictographs (Tait et al., 2010b, Tait et al., 2010a)
- Percentage probability and pictograph (Fuller et al., 2001)
- Bar chart, pictograph, survival curve and textual description (Davis et al., 2010)
- Population frequencies (with varying denominators) and icon arrays (Garcia-Retamero et al., 2009)
- Absolute risk, relative risk and NNT, anchoring to familiar risk, bar charts, thermometer scales, crowd figure formats and a combination (Edwards et al., 2006)
- AR expressed as frequency 'v' RR expressed as percentage and text only 'v' graphical image (Sprague et al., 2011)
- Line plot, bar chart, pie chart, icon array and numerical information in either AR or RR (Garcia-Retamero et al., 2010)
- RR, AR, NNT, OR, natural frequency and graph (bar chart and 10x10 people charts) (Goodyear-Smith et al., 2011)

The methods and settings of the studies were varied. Several studies presented participants with multiple formats and measured preference for format and other

reported outcomes such as understanding or intention to take (Goodyear-Smith et al., 2008, Goodyear-Smith et al., 2011, Fuller et al., 2001, Davis et al., 2010).

Two studies by Garcia-Retamero et al (2009 and 2013) used large samples of German and American participants who were representative of the population. One study measured differences in these samples' abilities to undertake mathematical operations using various graphs compared to numerical information presented as an AR or RR. The second study explored the concept of denominator neglect, which is the focus on the number of times a target event has happened (numerators), without consideration of the overall number of opportunities for it to happen (denominators) (Garcia-Retamero et al., 2013). The findings of this study suggested effective ways to address these phenomena which are of relevance to those presenting risk-benefit information in health communications.

One study by Fried et al (2011) presented various magnitudes of benefits (presented as pictograms). The study has been included for discussion here as the study outcomes are relevant due to their evaluation of patient preference for treatment depending upon the magnitude of benefit compared to the magnitude of adverse effects. The study presented varying degrees of benefit and evaluated a participant's willingness to take a medicine (Fried et al., 2011).

A group of studies randomised participants to different arms receiving various formats in order to measure differences in preference and performance of numerous graphical, numerical and textual formats. The studies had varying aims and used a variety of different settings and populations. Timmermans et al (2008) did not describe whether their study participants were randomised to receive health scenarios. They recruited students who were presented with 4 scenarios which described the benefits of treatments using one specific format; a percentage, frequency or icon array. They measured understanding, risk perception and emotional response.

Two studies undertaken by Tait et al examined different presentations of risk; both compared text, tables and pictograms (icon arrays) (Tait et al., 2010b, Tait et al., 2010a). Both studies recruited large numbers of parents into experiments examining the impact of benefit information about hypothetical analgesics used in a children's clinical trial. They used a randomised controlled trial design, where the control scenario described the benefits and risks using words. The experimental arms presented a table and a pictogram. The study evaluated the impact on both gist and verbatim knowledge as well as perception of risk.

Edwards et al (2006) recruited participants from the Diabetes UK website to a randomised controlled trial which examined different formats of web-based patient information. Intervention groups received either the basic control group information plus additional numerical information (AR, RR and NNT formats), anchoring information, graphical information (bar charts, thermometer charts and icon arrays) or a combination of these. Anchoring information refers to a method which relates the harm and benefit information to more everyday events which the user would be expected to be familiar with, such as the risk of a road accident or of winning the lottery. This study measured both the satisfaction with each format and also the decisional-conflict experienced by the parents.

Sprague et al (2010) assessed how the presentation of risk information influenced the ability of participants to interpret healthcare information using a survey with a 2X2 factorial design. They recruited a sample of Native Americans and presented an icon array and a combination of benefits presented in the form of risk reductions and absolute risks, using a scenario about a hypothetical cancer in which to frame the information.

Finally Parrot et al (2005) randomised participants to receive either a textual or graphical intervention describing LDL cholesterol and LDL receptor genes. Both interventions were lengthy and complex and due to their inappropriateness for inclusion in a PIL the findings from this study shall not be described in significant detail in this review.

Summary

There is a wide range and scope of research which explores the inclusion of information about the benefits of treatments in written information. The breadth of the literature includes several systematic reviews and significant numbers of individual primary data studies which use multiple methods and present a variety of formats of benefit information. These have been broadly categorised as:

- Studies presenting words
- Studies presenting numerical formats
- Studies using graphical formats (not discussed here)
- Studies presenting a combination of formats.

A number of different scenarios have been used to present benefit information and they range from cancer treatments, medicines for cardiovascular disease to pain relief medication presented within the context of clinical trial for children.

Multiple outcome measures have been used to measure the impact of providing benefit information, including:

- Preference for format
- Understanding of format
- Impact upon intent to take treatment.

The findings according to these outcomes will be presented in the following sections.

2.7.3 Preference for and satisfaction with benefit information

- **Studies presenting 'words'**

There is limited evidence that the provision of a short textual statement can enhance patient satisfaction with information when compared to no information or information that does not contain textual information about the benefits of treatments.

Bersellini et al (2006) showed that the inclusion of an effectiveness (benefit) statement and information regarding the rationale for treatment in a PIL positively influenced people's satisfaction with the leaflet. This study is highly relevant due to its specific focus on benefit information in medicines information. The study employed a robust method to measure participant satisfaction and provides empirical justification for the use of a textual benefit statement in a PIL in order to increase satisfaction with information.

- **Studies presenting numbers**

A consistent finding from studies measuring satisfaction with numerical formats was the preference for RRRs over other formats. This format tended to be viewed as easy to understand and as providing a bigger impact on participants (Bhandari and Tornetta, 2004, Natter and Berry, 2005, Malenka et al., 1993, Gyrd-Hansen et al., 2003, Sarfati et al., 1998, Carling et al., 2008).

However, these studies were frequently limited because they lacked a detailed evaluation of the performance of RRRs in enhancing risk perception or understanding. It was apparent from the research that while many participants preferred this format, the RRR statistic had the potential to mislead and encourage participants to be more likely to choose a treatment even if the treatment was associated with significantly increased risk of harm (Natter and Berry, 2005, Bhandari and Tornetta, 2004)

A limited amount of research suggests that the **absolute survival benefit (ASB)** (a method which described the absolute reduction of risk of death attributable to taking

chemotherapy) is a useful format. This technique was noted to be preferable to RRR, ARR and NNT when presenting the benefits of cancer treatments (Studts et al., 2005). Few other studies have assessed the impact of ASB, so the research on this technique is limited. This technique is also one limited to treatments for diseases which have the potential to be terminal, such as cancer, and might not be effective to communicate the benefits of medicines for chronic non-life threatening conditions. The study did not assess the performance of the technique compared to the other formats, focussing upon self-reported preference and influence on decision-making. The use of the ASB statistic appears a feasible option for presenting the survival benefits of cancer treatments but may not be applicable to presenting the benefits of other treatments.

Two studies undertaken by Carling et al (2008 and 2009) identified different preferences for the presentation of benefit information: **RRR** (2008) and **natural frequencies** (2008). These were large sample studies with well-defined methods. The first study showed that participants preferred RRRs (52%) compared to ARR, NNT, ER, TNT and whole numbers (presented as natural frequencies) (25%). However, participants in the second study which used a similar research design reported a similar preference for natural frequencies (31%) compared to RRRs (30%).

To conclude, there is evidence that RRRs are preferred by participants but preference is not indicative of performance, or relevance, and other outcome measures should be considered when considering which format of numerical presentation is suitable for use in a PIL.

- **Studies presenting a combination of formats**

The retrieved studies evaluating the impact of combined formats of benefit presentation on preference and satisfaction were complex and heterogeneous, examining different formats presented in multiple combinations and styles. It is difficult to draw firm conclusions about the most preferred format, but RRRs, natural frequencies, icon arrays and bar charts were consistently preferred when presented.

(a) Words and numbers

Two studies measured the preference for words (with verbal descriptors) versus numbers (Vahabi, 2010, France et al., 2008). Using a survey, they presented participants with either a numeric or textual format, which used terms such as ‘somewhat likely’ or ‘moderately greater’. They found a greater preference for numerical formats compared to textual formats.

(b) Numbers and graphs

12 papers researched a combination of graphical and numerical presentations of benefit. Four of these studies specifically measured preference for format. Parrot et al (2005) suggest that a **textual/numerical** format is better comprehended than a **graphical** format. The research design used and the formats of benefit information presented were very complex. The authors concluded that participants preferred a **textual/numerical format** of benefit presentation (which incorporated percentages) as opposed to a graphical format. However both formats presented were complicated and contained a mix of different types of data. It was also challenging to interpret the message the graph was trying to convey and this may impact upon the usefulness of the findings.

The study did propose that where participants associated quality with the format, they were also more influenced by the persuasiveness of the message. The authors concluded that the textual format was preferred and interpreted correctly more frequently as it was more familiar, although one critique of the study is that the textual/numerical format may have been preferred because the graphical format was too complicated, and that the use of a simple graph might yield different findings.

Goodyear-Smith et al (2008 and 2011) undertook two studies measuring preference for format with patients from medical practices in New Zealand. Of the numerical formats, relative risk or natural frequencies were preferred. NNTs were the least liked format. Graphical format was preferred to numerical format in both studies by about half the sample.

Edwards et al (2006) undertook a qualitative analysis of several different risk presentation formats, including detailed numerical information (AR, RRR, NNTs), anchoring, graphical (bar charts, thermometer scales, crowd figure formats) and a combination of formats. Preference was self-reported. Participants reported that graphical representations, in particular bar charts, were helpful. Numerical information was also perceived as helpful. The participants recruited were well informed about their health and this might affect the applicability of the findings to a wider population.

- **Summary**

Preference for format varied depending upon the type of formats presented. It was apparent that participants appear to prefer some benefit information compared to none,

with additional information about the rationale of treatment impacting positively upon satisfaction with information.

Graphical formats are mostly popular, with icon arrays and bar charts being preferred by many participants. With regards to numerical formats there is a tendency for people to prefer RRRs, however it has also been shown that RRRs can be misleading. Natural frequencies also appeared to show measures of increased satisfaction among some people.

Preference for a particular format is not indicative of performance, although it has been shown to influence how a patient might respond to a particular format of benefit information. This may be because, if participants are satisfied with the format of information, this may facilitate engagement with it.

2.7.4 Effects on participant knowledge and understanding (including risk perception)

The impact on knowledge and understanding was evaluated in a number of studies. There are different types of understanding that can be addressed facilitated; some studies assessed the impact benefit information had upon **verbatim knowledge** such as the ability to correctly identify numerical harm and benefit statistics. Studies assessing verbatim understanding often presented participants with a format of benefit information and requested them to undertake a mathematical operation, which was then evaluated as correct or incorrect.

Other studies examined the impact on understanding in more detail, examining the abilities of participants to use and apply the benefit information to a participant's own situation. There were a small number of studies evaluating **gist knowledge** alongside verbatim information. These studies often used assessments of patient values and/or beliefs about their treatment, to assess whether the decisions made were consistent with patient values and whether the format of benefit information influenced this. Others explored **risk perception** measuring how the information provided placed the benefits in context.

Several key findings were apparent:

- **Studies presenting 'words'**

Three studies evaluated how the inclusion of a textual statement about the benefits of medicines could influence a participant's understanding of their treatment (Bersellini and Berry, 2007a, Bersellini and Berry, 2007b, Vander Stichele et al., 2002).

These studies all compared the inclusion of additional textual information about the benefits of a medicine; including more detailed information on the rationale and effectiveness of treatments. A variety of outcomes were measured, using various rating scales, which included judgements about side effects, (risk perception) (Bersellini and Berry, 2007b, Bersellini and Berry, 2007a) and knowledge about medicines (Vander Stichele et al., 2002). All studies reported that the inclusion of a textual statement about the benefits of medicines increased knowledge about the medicine and the perception that the benefits of the drug were greater than the harms, in comparison to those who received no benefit information. Those who did not receive benefit information reported higher perceptions of risk as opposed to benefit. (Vander Stichele et al., 2002). The provision of benefit information using words was found to improve judgement but not necessarily knowledge (Bersellini and Berry, 2007a, Bersellini and Berry, 2007b), although Vander Stichele et al (2002) reported an increase in knowledge about the medicine. The provision of written benefit information was not shown to improve behaviour or understanding, but led to a more balanced benefit-harm perception.

- **Studies presenting numbers**

The previous section reported that there was evidence that RRRs are a commonly preferred format. However, when measuring how RRRs influence a person's risk perception and understanding of medicines, there is evidence that this format can lead to over-estimations of benefit. Much of the literature comparing RRRs to other summary statistics and probability formats suggests that RRRs are very persuasive and can encourage people to make decisions that are not necessarily in line with their values. (Hux and Naylor, 1995, Sarfati et al., 1998, Carling et al., 2008, Malenka et al., 1993).

This finding is reinforced with the findings of a systematic review and meta-analysis which evaluated the use of alternative statistical formats for presenting risks and risk reductions (Akl et al., 2011a).This study used a clearly reported and robust method for undertaking a systematic review and a well-described and comprehensive search strategy was performed. The review included studies that were undertaken both in patient and healthcare professional populations. The interventions of interest included

presentations of risk (e.g. frequencies and probabilities) or of a risk reduction (e.g. RRR, ARR, NNT) of the same evidence about health. There was a rigorous assessment of study quality, which included RCTs, non-controlled trials and cross-over studies. The meta-analysis was well-executed and included an appropriate I^2 test for heterogeneity, plus several pre-planned subgroup and sensitivity analyses.

35 studies were included for meta-analysis, this included: 8 comparisons of natural frequencies versus probabilities; 31 comparisons of RRR versus ARR; 23 comparisons of RRR versus NNT; and 21 comparisons of ARR versus NNT. Some of the studies were included in this analysis, however many were excluded from the scoping literature review reported here, due to their focus on health professionals. As a result the findings from the systematic review by Akl et al (2011) have only some bearing on the findings of the scoping review as a whole (although it can be argued that the effective understanding of benefit information by healthcare professionals is applicable to a patient population as statistical summaries that perform poorly with healthcare professionals are also likely to be difficult for patients to understand).

The review showed that numerical presentations of harm and benefits are better understood when presented as natural frequencies compared to probabilities (a moderate effect size was noted). RRRs were noted as being more persuasive and were perceived as more effective when compared to ARRs or NNTs. RRRs conveyed a more accurate understanding than NNTs (a large effect size was noted) but not as accurate as that conveyed by ARRs.

This review is the most systematic and up-to-date review of the evidence on summary statistics. However one significant omission in the published studies is that there has been no assessment of the impact of statistics on behaviour. Overall the quality of the evidence was moderate, mostly because of the lack of use of objective measures to assess outcomes; the findings must therefore be interpreted in light of this. This reflects a need for some larger studies, preferably using controlled designs, to evaluate the effectiveness of these types of summary statistics, in particular any upon behaviour.

Research by Carling et al (2008) also highlights the persuasiveness of using RRRs to communicate benefit information. This study explored participants' values and the importance they placed on treatment consequences (Carling et al., 2008). When participants were presented with benefits in the form of RRRs they were more likely to take a statin, than if the benefits were presented in another format. This influence on decision-making existed regardless of the participants' values on taking medicines.

Other studies also examined the interpretation of RRRs and the context in which they were presented. Sheridan et al (2003) used a randomized experiment in which participants were presented with 4 different formats of benefit information: RRR, ARR, NNT or a combination of the three. The findings showed that participants were better able to interpret the benefits of a treatment when an RRR was presented as well as the **baseline risk** of disease (Sheridan et al., 2003).

Two other studies also explored the importance of providing a baseline or comparative risk on risk perception. The provision of baseline risk information can facilitate more accurate understanding of risk estimates (Fagerlin et al., 2007, Natter and Berry, 2005).

Several studies examined the impact of providing **NNT**s and **NNS**'s to participants. The NNT was frequently shown to underperform compared to other formats as it was more frequently misinterpreted (Sheridan et al., 2003, Sarfati et al., 1998). Kristiansen et al (2002) showed that participants were often insensitive to the size of NNTs. A limitation of this study was that it did not present risks alongside benefits and it is possible that participants might be more accepting of NNTs with small value in the absence of having to make trade-offs between risks and benefits. All in all, NNTs were shown to be problematic, but the research was limited as it did not present the NNTs in realistic contexts; it is difficult to draw firm conclusions about the issues associated with their use. More research evaluating the use of NNTs to present information about benefits will be valuable.

Natural frequencies were frequently associated with increased preference and understanding (Carling et al., 2008, Carling et al., 2009). Natural frequencies and **percentages** were shown to perform better than other formats when participants had to undertake three mathematical operations on risk probabilities presented either as a percentage, '1 in n', or a natural frequency. The study showed that natural frequency and percentage formats resulted in a similar degree of accuracy. (Cuite et al., 2008). Natural frequencies were feasible for use in a sample of older participants, although this study only recruited a small sample and contained methodological flaws. Recruitment of older people is a strong feature of this research making the findings representative to the general medicine-taking population. This study concluded that natural frequencies helped both elderly and younger patients understand the predictive values of medical screening tests (Galesic et al., 2009b).

Dahl et al (2007) tested participants' understanding of **postponement of adverse disease events** and concluded that lay people can discriminate between levels of

treatment effectiveness when they are presented in terms of a postponement of an adverse event. Despite the feasibility of these methods in some health contexts, there is little unequivocal evidence to suggest that absolute survival benefit or postponement of an adverse event are preferable to other methods and the use of this technique is limited in a patient information leaflet as it might not be applicable for medicines used for some symptomatic conditions.

- **Studies comparing a combination of formats**

15 studies examined the impact of various **combinations of formats** of numerical, textual and graphical information on participant understanding. The findings were varied.

a) Words compared to numbers

Two studies compared how presenting benefits as either verbal descriptors or a numerical format, such as a natural frequency (Vahabi, 2010) or a percentage (France et al., 2008), could impact on comprehension of benefits. France et al (2008) reported a small study designed to examine whether the use of percentages was a feasible technique to describe risks to patients with chest pain in an emergency room. This study was not designed to examine which method was most effective, but was instead a feasibility of use study. They identified that patients could better understand side-effect frequencies when expressed as a percentage.

Conversely Vahabi et al (2011) identified that verbal descriptors improved the comprehension of probabilistic information regarding breast cancer screening. This study also identified other factors which impact upon comprehension of benefit information such as the participant's format preference, education and perceived benefit of early detection of breast cancer.

The review of the literature in this field does not provide any unequivocal answer regarding the utility of textual benefit information compared to numerical.

b) Numbers compared with graphs

Seven studies showed that graphical formats were better understood than numerical formats and improvements of accuracy of interpretation of risk were associated with graphical formats. So frequently, graphical formats were found to perform better than numerical statements alone (Garcia-Retamero et al., 2010).

Different graphs were identified to perform better in various studies. The following formats were all identified as having the highest impact on measures of comprehension

and understanding: Kaplan-Meier survival curve (Davis et al., 2010), population chart (Fuller et al., 2001) table (Tait et al., 2010b) and bar chart (Garcia-Retamero et al., 2010). The format most likely to be identified as optimal in improving risk perception and understanding was the icon array (Sprague et al., 2011, Garcia-Retamero et al., 2010, Tait et al., 2010a). On the other hand, Timmermans et al (2008) associated the icon array with increased emotional response and described how this had a negative impact upon participants' risk perception. This study had many methodological flaws; the sample was highly educated compared to the general population, no methods of randomisation were reported and the subjective outcome measures might impact upon the veracity of the findings by introducing the potential for biased reporting of outcomes which cannot be objectively measured. (Timmermans et al., 2008).

Many of the studies above assessed understanding of the information, as well as the ability to correctly interpret the information presented. This is known as 'verbatim' knowledge and they did not evaluate how different formats might impact upon 'gist' knowledge. Four studies examined the impact of the provision of a variety of formats of benefit information on both verbatim and gist understanding.

Galesic et al (2009) evaluated both accuracy and perception of risks associated with receiving a number of icon arrays in comparison to numerical information presented as ARR or RRR. These studies found that icon arrays were helpful for both low and high numeracy participants and, contrary to Timmermans' findings, suggested that icon arrays reduced perceptions of risk experienced by participants. (Galesic et al., 2009a)

Two highly relevant and well-designed studies by Tait et al (2010b, 2010c) concluded that the pictograph was optimal in communicating both verbatim and gist knowledge about the benefits of treatment when compared to a numerical statement or a table. Both studies used similar methods of recruitment and similar interventions: numerical statement, tables and pictographs. Participants randomised into a pictograph arm were observed to have higher levels of both gist and verbatim understanding than those receiving either text or a table format. Tables were better comprehended than text.

These findings were corroborated by 3 systematic literature reviews in this field. The most recent of these reviews (Bunge et al, 2009) aimed to survey the quality criteria for evidence-based patient information. The criteria this study used were only partially of relevance to the scoping review, and several categories of 'evidence-based patient information' were not considered relevant . However, it included for review several interventions of interest such as information on the benefit and harm of the intervention,

patient-orientated outcome measures (e.g. mortality and quality of life), the presentation of numerical data, verbal presentation of risks, diagrams, graphics and charts and loss and gain framing; all of which can be techniques used to convey benefit information to patients.

The review was clearly described and, in terms of quality, it used an *a priori* study design and met several of the criteria on the AMSTAR checklist. The methodological quality of the included studies was appraised using both the SIGN and the EPOC checklist. The studies retrieved by the review were heterogeneous and a descriptive approach was undertaken.

There was good evidence for the presentation of numerical data or graphical presentations in comparison to others types of intervention. Natural frequencies were identified as better understood than probabilities. Caution was recommended when using RRR, which resulted in over-estimations of probabilities. It was suggested that ARR leads to better understanding than RRR. When evaluating the impact of textual presentation of risks, a more accurate understanding was reported if numbers were used instead of words. There was a tendency to over-estimate the effect when verbal descriptors were used. Finally it suggested that with regards to diagrams and graphics, there was little consensus as to what were the best methods.

These findings were similar to those made by Visschers et al (2008) who used a literature search method to identify a number of research studies which presented probability information in risk communication. The review used a well-described method to identify and collate the findings of general studies on probability presentation in risk communication. The studies included were heterogeneous and no meta-analysis had been undertaken. However, the researchers used a method of evidence weighting to rank the quality of the findings.

The findings of the descriptive analysis included the following basic recommendations: [1] use the same denominator in probability information throughout the risk communication to avoid denominator neglect; [2] a step by step description of a probability calculation is recommended to present risky situations that include false positives; [3] be careful about presenting risks as RRRs as they can lead to over estimations of risk; [4] information using NNTs should be provided with caution; [5] take the context of the risk communication into account when selecting appropriate verbal probability expressions for a risk message; [6] present both verbal and numerical information in a risk message; [7] graphs are a useful means to present probability of

harm (Visschers et al., 2009). The findings are unsurprising, have been corroborated by other research and ultimately offer no definitive answer to the best method of benefit presentation.

Trevena et al (2006) undertook a systematic review to identify the research literature in a number of areas. One area in particular was relevant to this scoping review and focussed on effective formats for representing probabilistic information. The methods used to undertake the review were of moderate quality. The review included RCTs only and data were extracted by 2 independent data extractors. The search strategy was reasonably comprehensive, although grey literature was excluded. An appraisal of quality assessment undertaken using a quality checklist for the systematic reviews and the Cochrane Handbook grading system for the RCTs.

A descriptive analysis suggested a number of recommendations including that numbers lead to a more accurate perception of the benefits than words when probabilistic information is presented. One RCT suggested that natural frequencies were better understood than probabilities. The utility of presenting baseline risk when presenting risk reductions was highlighted. Graphics were suggested to be useful and there was some evidence that bar charts and survival curves can help participants understand the benefits of interventions. Framing risks as either a loss or a gain can influence patient preferences. Again, these findings echo those from the systematic reviews described already and the findings of the primary research reported elsewhere in this scoping review.

- **Summary**

There is not a definitive answer as to which format is better at promoting understanding and accurate measures of risk perception when different formats are compared. It is apparent that the provision of benefit information in a textual form is useful, but that numerical and graphical formats have been frequently shown to help patients make more accurate estimations about the benefits of their treatment.

RRR formats have been shown to lead to over-estimations of risk and should be avoided. If they are used, then comparative information, such as baseline risk information, should also be provided.

Natural frequencies have been shown to be understandable, particularly if an individual has to undertake a mathematical operation. The interpretation of NNTs has been shown to be problematic, but the research assessing their utility was flawed and did not evaluate their use in context.

Several different graphical formats were found to be useful in improving knowledge and promoting understanding, including survival curves and tabular formats. Some good quality studies found that icon arrays were more understandable in comparison to different formats, although this was not unanimous. Bar charts were also shown to help improve accuracy.

More research in this area would be valuable particularly to evaluate the role of NNTs in benefit communication.

2.7.5 **Effects on participant behaviour**

This review collated a body of evidence that looked at the potential for stimulating behaviour change through the use of different formats of benefit behaviour. However, the literature identified did not assess the long-term impact of providing such information and there is very little research that examined the impact of benefit information in a natural setting or in real-life situations.

Several key themes were identified from the published research literature.

- The persuasive nature of RRRs was tested, with several studies suggesting that RRRs might encourage behaviour change that is not based on an accurate understanding of the treatment effects and which might not be in line with patients' values. Goodyear-Smith et al (2011) used a real-life scenario to assess the impact of benefit information and found that the RRR tended to be persuasive in encouraging a participant to take a particular medicine. The study concluded that RRRs, while simple to understand, can be difficult to comprehend in the absence of any baseline risk information and can lead participants to make decisions that are not in line with their values. So some formats are more persuasive than others, but not necessarily informative. In particular the use of the RRR has been shown to influence choice without helping patients understand or make decisions in line with their values.
- There is also evidence that benefit information can adjust patients' **expectations of treatment** and impacts upon their self-reported **medicine-taking behaviour**. It has been shown that the provision of information about potential benefits, as opposed to no benefit information, helps patients get a deeper understanding of their treatments and also consider their options in more detail. The benefit information presented in Bersellini et al (2006 & 2007) impacted upon a participant's intent to take the treatment. This is important as it

suggests that patients might alter their behaviour in light of receiving more information about a treatment.

- In a RCT which provided improved benefit information in the form of a Drugs Facts Box compared to a direct-to-consumer advert, Schwartz et al (2009) found that the provision of benefit information meant that participants were better informed, but less enthusiastic about the medicines and this reduced their intentions to take the treatments. Fagerlin et al (2007) also reported similar behaviours, noting that providing people with comparative risk information changes their perceptions of risk. In their research they found that people who perceived that they had a higher than average risk may feel compelled to take a treatment and might not consider the trade-offs in risks and benefits.

- **Other influences on patient behaviour.**

Patients do not make decisions about their treatments in isolation and there are a number of other influences on decision-making that were identified in the published research.

a) Context

The **context** of the information is important. Providing patients with comparative risk information changes their perceptions (Fagerlin et al., 2007). Also ensuring benefit information is realistic and relevant means participants are more likely to make decisions that reflect their behaviour in real-life situations. Some of the interventions were also presented in a context that was not transferable to the UK, for example the findings from the studies evaluating the impact of the Drugs Facts Box as a means of improving a DTC advert, might not be relevant in a UK setting due to restrictions on direct-to-consumer advertising. (Schwartz et al., 2007, Schwartz et al., 2009)

b) Numeracy

Participants with higher numeracy appeared to find it easier to undertake any mathematical operations that were required in several of the studies. Numeracy was assessed in most studies using the Subjective Numeracy Score, which is an appropriate validated tool (Zikmund-Fisher et al., 2007). A few studies, for example Garcia-Retemaro et al (2010), found that providing visual aids as well as numerical data to people with lower-numeracy, helps them make more accurate assessments of risk reduction (Garcia-Retamero et al., 2010).

Hess et al (2010) explored the role of subjective numeracy and observed how cognitive differences in the ability of people with low-numeracy in perceiving graphs, compared to people with higher numeracy can lead to problems with the accurate extraction and processing of information (Hess et al., 2011). Other studies concluded that the less numerate population might benefit from graphs but might also also have less ability to interpret the graphs accurately.(Brown et al., 2011, Hawley et al., 2008).

c) Age

It was observed that some older people struggled to interpret benefit information more often than younger adults (Fuller et al., 2001), although formats such as natural frequencies were observed to be helpful to rectify this (Galesic et al., 2009b). It is important to note that many of the research studies recruited samples from the general population, and this means the average age of participants may be younger than the average age of medicine-users, therefore the findings might not be applicable. Older users of medicines are under-represented in the research.

d) Hope and uncertainty

The concept of **hope** was also observed to be an influencing factor on perceptions of treatment benefit. In a qualitative study it was also viewed that inherent uncertainty in life can undermine confidence with probabilistic information and that patients value honesty but that this should not preclude hope (Thorne et al., 2006).

- **Summary**

It is apparent that there is the potential for behaviour change, depending upon the format of benefit information. It has been shown that some formats can mislead patients into making decisions that are not in line with their values. There is evidence that RRRs in particular are persuasive.

Icon arrays and bar charts have also been shown to have the potential to help patients make better informed decisions. The can improve a participant's verbatim and gist understanding of their treatment.

Familiar and simple formats appear to yield more understanding and help patients make better decisions as they reduce the cognitive effort required to make sense of often complex information.

Understanding the right format for the right patients is an ideal, and healthcare practitioners need to be aware that different formats can evoke different responses and behaviours in different people. There are techniques that patients need in order to get

the most out of visual aids. Ideally visual aids should be well-designed to support the participants to do this and to modify any incorrect expectations about treatment risk reduction.

Poorly designed or unclear information is of no use, or worse still misleading and confusing. Therefore the choice of format might be dependent on the goal of the communication.

There is a need to undertake research into the different formats of benefit presentation in a more naturalistic setting to understand the impact on actual, rather than intended behaviours and on long-term behaviours. A need has been highlighted for more research, especially high quality RCTs, assessing the impact of providing different formats of numerical information on patient behaviour.

2.7.6 Studies examining the impact of the framing of information about treatment benefits.

Framing refers to the way in which a scenario or decision might be differently presented, perhaps as having either a negative or positive outcome. It has been noted that the framing effect is a cognitive bias which influences choice between two identical choices when framed as a gain or a loss. Two systematic reviews also met the criteria for inclusion (Tversky and Kahneman, 1981, Edwards et al., 2001, Akl et al., 2011b) .

18 studies were identified which evaluated the impact of 'framing' information about the benefits of treatments on the attitudes, satisfaction, knowledge and behaviours of participants. The studies have been broadly grouped to into 3 categories: Studies which evaluate the impact of framing on treatment choices; Studies which evaluate the impact of framing and other characteristics; Systematic reviews on framing.

a) Studies which evaluate the impact of framing on treatment choices

Attribute (or statistical) framing

Overall, there was a small amount of evidence suggesting that attribute framing, the use of a negative or positive frame in which to present information has the potential to influence attitudes and decision-making regarding different treatments. Four studies were identified which explored a range of different treatments and used different research designs, although only 3 studies are discussed in detail as Zimmerman et al (2000) tested a modified decision board technique that would not be suitable for use in PILs (Zimmermann et al., 2000).

The remainder of the studies tested whether a negative or positive attribute frame impacted upon attitudes or decisions towards treatments. The studies tested different treatments, in different populations and different types of attribute framing. Bigman et al (2008) examined the impact on participant attitude of statements about HPV vaccination framed in a variety of ways. Two key findings were that positive framing was influential and correlated with an increased perception of the effectiveness of the vaccine and that when presented as a mixed frame, the order of the framed information was also influential (Bigman et al., 2010).

O'Connor et al (1989) compared the effects of framing and level of probability on patients' preferences for cancer chemotherapy. Participants were either healthy volunteers or cancer patients and were randomised into one of three groups receiving three different types of framed information: (1) a positive frame in which the probability of survival was given; (2) a negative frame in which the probability of dying was given; and (3) a mixed frame in which the probability of surviving and dying were given. The study was well-designed, and the recruitment of a real-life sample added strength to the findings. An evaluation of preferences for treatment was undertaken and it was found that a positive framing was influential, encouraging a participant to be more likely to choose a treatment than if the same treatment was presented in a negative frame, although this was only statistically significant if there was a 50% probability of survival. The study also noted that participants would make trade-offs about their treatments and that cancer patients were more likely to choose toxic treatments than healthy volunteers. This early study suggests a link between experiences of illness and willingness to accept different values of risks and benefits.

A large-scale randomised trial compared 3 valence framing presentations of the benefits of antihypertensive medication in preventing CVD (Carling et al., 2010). Valence-framing refers to when individual choices are influenced by outcomes that are either positive or negative, whereas 'true' framing refers to the manipulation of objectively equivalent information into either a positive or negative frame (Carling et al., 2010). The study's limitations included that it did not recruit real-life patients making actual decisions about their treatment, although it did recruit a nationally representative sample (from the USA and Germany). Participants were randomised to receive one of three scenarios which contained numerical information about the benefits of an anti-hypertensive, based on realistic clinical trial data. These scenarios were framed either positively or negatively, or negative by year, and one group received no framed numerical information. The participants' values and 'intent to take' were assessed.

Participants were then shown all the different types of information (with the aim that they have the information to make a 'fully-informed' decision) before a final measure of the outcomes was taken.

This study was relevant to the review as it found that providing both the negative and positive framed information resulted in participants being less likely to take a medicine. However, the provision of information about the benefits of a medicine in a positive frame led to participants making decisions that were most consistent with those made by everyone when they were given more complete information and asked to make a more fully-informed decision.

b) Goal (or behavioural) framing

5 studies examined the impact of using 'goal' framing, where the consequences of performing, or not performing an activity are depicted as either a loss or a gain. Often this is emphasised as a specific type of behaviour, for example negative-framed messages emphasise losses, and positive framed messages emphasise gains to health.

Some of the studies were of limited relevance to the outcomes of the review. Two papers undertook multiple experiments using hypothetical scenarios with limited reference to how people make real-life decisions about healthcare treatments (Peters and Levin, 2008, Fischer et al., 2008). Some experiments used scenarios based on theories of risky decision making, such as risky stock trading, and the discussion of these papers has been limited to the studies undertaken which focus specifically on conveying the benefits of treatments.

The remaining studies (Hoffner et al., 2009, Hevey et al., 2010, Brug et al., 2003, Lalor and Hailey, 1989, Leader et al., 2009) examined the impact of providing various health messages which were goal- or loss-framed. These studies used a number of different hypothetical scenarios to convey the health message ranging from breast cancer self-examination (Lalor and Hailey, 1989) to sun screen use (Hoffner et al., 2009, Hevey et al., 2010) to a selection of nutrition education messages (Brug et al., 2003). Questionnaires were used in all these studies to measure the impact of the framed messages. The studies commonly assessed the impact of goal 'v' loss framed messages on the participant's intent to carry out specified health behaviours.

The findings suggested that goal-framed messages were associated with increased uptake of beneficial health behaviours, although many reported subtle nuances that impacted on this general trend. Hoffner et al (2009) reported subtle differences between

the perceptions of men and women and also how having 'involvement' in a particular issue might impact on decision-making. They noted that where participants reported little involvement in the scenario, a loss-frame was effective in changing behaviour (Hoffner et al., 2009).

Hevey et al (2010) noted that the participant's report of body consciousness moderated the effectiveness of the frame, with gain-framed health or appearance messages having the strongest effect on sunscreen use for those high in body consciousness compared to those low in body consciousness (Hevey et al., 2010). Another paper did not report any significant evidence of framing effects, but noted that their use of a non-involved population of students meant that the information they provided was of a very low personal importance to the sample and that this potentially impacted upon the findings (Brug et al., 2003).

Framing different aspects of a goal with regards to influencing a health choice was assessed by Leader et al (2009). They noted that when the benefits of HPV vaccination were framed as a cervical cancer prevention tool, rather than a sexually transmitted infection prevention tool, this increased the reported intention to vaccinate (Leader et al., 2009).

Only one paper assessed the long-term impact of framed messages on health outcomes. The study was a small questionnaire study. It was non-randomised and used a student population (n=55). Although not of high quality, it evaluated the impact of the intervention provided (a pamphlet that described the need to do breast self-examination presented in either a positive or negative frame), after 4 months. The study found that neither the negative- nor the positive-framed interventions were effective in promoting breast self-examination practice unless the individual already felt susceptible to breast cancer (Lalor and Hailey, 1989).

c) Studies that combine both attribute and goal frames

Two hundred undergraduates were recruited to receive 4 variations of pamphlets about a flu vaccination in an experimental survey design which manipulated frame valences (positive or negative) and methods (attribute or goal) in order to explore the effects on perceived risk (Ferguson and Gallagher, 2007).

The results suggested that 'personal outcome effectiveness', that is the perception of how effective the vaccine is, indirectly linked framing to intentions. The study suggested that goal framing increased personal outcome effectiveness (and encouraged more people to think the vaccine was effective) than attribute framing. The study was

theoretical in its approach, using the results to build upon and integrate models of health and non-health behaviour and it made no suggestions on how their findings might be used to improve the communication of benefits of treatments.

- **Studies which evaluate the impact of framing and other characteristics**

A series of studies examined a range of different factors that might also influence how people perceive and interpret framed benefit information. These additional factors included age, cognitive impairment, numeracy, 'involvement' and 'vagueness' (Shamaskin et al., 2010, Zamarian et al., 2010, Kuhn, 1997, Garcia-Retamero and Galesic, 2010). A range of different methods, populations and interventions were described.

Shamaskin et al examined impressions of positively and negatively framed health messages that were presented in in pamphlets to 25 older (age range 64 to 86) and 24 younger adults (age range 18-23). This uncontrolled study found that older adults, relative to younger adults preferred and remembered positive messages, rather than negative ones. Older adults also appeared more likely to misremember negative messages to be positive. To confirm these findings, more research is required.

Zamarian et al (2010) recruited 3 comparative groups of adults (a healthy control, a group with mild cognitive impairment and a group with Alzheimer's disease) who were shown statements about the outcomes of 20 unknown medicines which were described either positively or negatively. All three groups judged the positively-framed medicines more favourably. This was more pronounced in the comparison groups. This small-scale study suggests that framing might be more influential in groups with cognitive impairment, but further research is required to support these findings.

In a series of 3 experiments, Kuhn et al (1997) examined the impact of 'vagueness', presented as vague probabilities, and framing. An example of vague probabilities included the following;

1) a vague point estimate: a verbal qualifier of the base point estimate ("estimated to be around")
2) a low-high range: a range of two probability values centred on the base probability value ("estimated to be between") with the low value presented first; or
3) A high-low range: the same range of two probability values with the high value presented first.(Kuhn, 1997)

These studies were small and used hypothetical scenarios. They reported that participants were averse to vagueness and that framing impacted upon decisions, however they made no suggestions as to the best methods for framing treatment options when the probabilities are vague.

The 'involvement' of adult women in making a decision about child immunisation was evaluated in a 2x2 factorial study undertaken by Donovan and Jalleh (2000). The study found that positively framed messages were more influential, encouraging women to be more likely to seek information or adapt the recommended behaviour, as opposed to the negatively framed behaviour. This was especially so for low-involvement participants. There was no framing effect reported for high-involvement participants. This study was poorly reported and the sample size was not accurately reported (Donovan and Jalleh, 2000).

Two final studies examined **interventions to reduce framing-effects.** The first study explored the impact of a de-biasing technique used to reduce the framing effect (Almashat et al., 2008). The de-biasing technique consisted of a questionnaire which listed advantages and disadvantages of each treatment and is an intervention unlikely to be used in a patient information leaflet.

The second, large-scale study used a randomised questionnaire to measure the impact of providing negatively and positively framed information to high- and low-numeracy participants. In addition, some participants received the framed information presented as a visual aid (an icon array, horizontal bar chart, vertical bar chart, or pie chart). The study reported that low-numeracy participants were more susceptible to framing than those with high- numeracy and that the provision of visual aids was an effective means to reduce the impact of framing (Garcia-Retamero and Galesic, 2010).

- **Systematic reviews on framing**

Two reviews were identified that collated research undertaken into framing effects. Edwards et al (2001) undertook a systematic literature search to identify papers which examined the presentation of risk information. This included a review of the effects of framing and other information manipulations on patient outcomes. The review was partially relevant, but obtained papers excluded by this review (the inclusion/exclusion criteria differed slightly). The literature review searched a variety of sources and there was a review of the quality of the methods of the papers included; however it was not

clear how this was undertaken. The review presented a narrative synthesis of the studies included, although where possible statistical meta-analysis had been undertaken. Analysis of the literature (4 studies) on attribute framing suggested there was no clear pattern of findings regarding the effects of negative and positive framing. With regards to goal framing, it was noted that there was a clear pattern which supports the greater effects of loss framing in promoting behaviour actions to protect against risk.

The final review was a Cochrane systematic review (Akl et al., 2011b) which evaluated the effects of attribute and goal framing of the same information on understanding, perception of effectiveness, persuasiveness and behaviour of health professionals, policy makers and consumers. In terms of quality this study had clear methods, quality assessment and analysis. A meta-synthesis was undertaken of the relevant papers. The review included trials that were not included here, due to their focus on the presentation of risks, as opposed to the benefits of treatment. The review included 35 papers involving 16,342 participants (all health consumers) and reported 51 comparisons. Much of the evidence was reported as low to moderate in quality and a great deal of heterogeneity was reported. The review concluded that both attribute and goal framing had little, if any, consistent effect on health consumers' behaviour. This is contrary to common beliefs about framing and is an interesting finding. The review considers that framing effects are more likely under specific but, as of yet, undetermined conditions and that more research is required to investigate these conditions.

- **Summary**

18 studies and 2 reviews were identified and incorporated in this part of the review. There is a range of research that has been undertaken into how the framing of information about the benefits of treatment impacts upon patient attitudes, knowledge and behaviours in relation to treatments. It was apparent that the research is varied and difficult to compare directly, although similarities exist. Much of the research is quantitative and on the whole used controlled experiments to assess the impact of framed information on treatment choice, although several uncontrolled studies were also identified.

The studies examined the impact of both attribute and goal framing, with the impact of additional factors such as numeracy, involvement, age and cognitive impairment also being incorporated in a number of multi-factorial studies. These studies show the range of potential influences on how people perceive benefit information and the way it is

framed. However due to their small size, and often low quality design and reporting, they may not provide a definitive answer as to the impact of external factors, such as age and cognitive impairment, on understanding the benefits of treatments when framed in different ways.

The most striking finding was that contrary to the wider belief that framing impacts on behaviour, and to the findings of many of the individual research papers, it was shown that framing does not necessarily impact on behaviour. This also supports the theory that the framing of benefit information can impact upon patient understanding and behaviour. A systematic review did not find evidence that framing had any significant impact upon health consumers' behaviour. This review was of good quality and used robust methods to pool the findings of 35 randomised and quasi-randomised controlled trials. The review focused upon both risk of harm and risk of benefit communication, whereas the scoping review reported here focuses solely upon the communication of benefits. However it is relevant, as it shows how a meta-analysis of studies can improve the power of findings: it may change the view about the effects of framing which has possibly arisen from the findings of multiple, lower quality studies. When biased or poor quality studies are eliminated then the findings are contrary to the general belief that framing impacts upon patient choice. It is important to note that this review identified a great deal of heterogeneity among the research undertaken in this field.

To conclude, there is wide range of research into the effects of framing. The body of literature is varied and shows that different frames of health information can potentially impact upon understanding and behaviour. However, when the data from good quality randomised controlled trials are pooled the framing effect is not shown to have any impact upon health behaviour.

2.7.7 Evaluation of the quality of the research in the review

- **Scope and range of the methods**

The research undertaken into examining the effects of the presentation of benefit information in written health communications is large and heterogeneous. The body of research presented multiple methods, aims and outcomes and the types of format of benefit presentation were multiple and complex.

There were a range of different research designs. Several studies were small scale studies, examining the feasibility of presenting benefit information, e.g. Fuller et al

(2001 & 2002) who recruited n=50 and n=42 respectively. The weight of the findings of these studies needs to be taken into account, while they offer an insight into use of benefit information, it is possible that their findings are subject to Type-II statistical errors and that they might not be appropriately powered in order to derive statistically significant findings.

Several studies recruited large samples in a series of robust, well-described randomised trials. Gyrd-Hansen et al (2003) recruited n=3201 participants into an innovative study using a near full factorial design to explore different representations of ARR and RRR, and baseline risks. The series of studies undertaken by Tait et al (2010a, 2010b, 2010c), Zikmund-Fisher et al (2007) and Carling et al (2008, 2009, 2010) also show the strength of the research being undertaken in this area. These are large-scale randomised trials examining a variety of different types of benefit information, collecting good-quality data and drawing conclusions which are significant. The body of literature also includes several systematic reviews. In particular the Cochrane reviews undertaken by Akl (2011a & 2011b), which combine the findings of RCTs on both the presentation of summary statistics and the effects of framing, offer substantial contributions to the field.

- **Representativeness of scenarios used**

The majority of the research used **hypothetical scenarios** in which the benefit information was presented in the context of illness and treatment. The level of realism within these scenarios impacts upon the findings of the study upon the potential applicability of the findings in a wider setting.

The research included in this review used a number of different types of scenario. Ideally a study would recruit a real-life sample from the same group for whom the intervention is intended, and observe the impact on the actual decisions and behaviours made by the participants. Ideally the intervention would also be realistic and grounded in the evidence-base. Few studies achieved this. Some studies used simple scenarios based on fictitious illnesses and treatments. Several studies, whilst using robust methods were limited by their use of hypothetical scenarios. Often this research presented the benefits of a hypothetical drug, treatment for a hypothetical disease or the effects of a hypothetical screening programme.

For example, Zikmund-Fisher (2005) used an experiment where participants were randomised to view one of 4 survival graphs presenting different magnitudes of benefit

associated with a treatment for a hypothetical illness called Crawford's Disease (Zikmund-Fisher et al., 2005). Others presented scenarios about 'life threatening disease' (Malenka et al., 1993) a 'medical treatment' to prevent 'serious illness' (Gyrd-Hansen et al., 2003) or generic risks about cancer (Cuite et al., 2008). The benefits of using these 'generic' scenarios about risk is that they allow the researchers to present a number of different risk values that might not be measurable in real-life situations and test the impact of these on participants' attitudes and behaviours.

Kristiansen et al (2002) recruited a large sample of the Danish population to evaluate their preference to consent to a hypothetical drug that reduces the risk of heart attack. They presented a series of different magnitudes of benefit and evaluated a participant's intent to take the hypothetical medicine. The findings were striking as the number of participants consenting to take the medication remained the same for all of the different magnitudes of benefit. The study concluded that NNTs were not understood as they had little impact upon the proportions that consented to treatment. However, it is important to note the context in which the scenario was delivered. The hypothetical drug was used to treat a heart attack, an illness likely perceived as severe by patients. Also the benefits of the medicine were presented in isolation and no harm information was present. In a real life situation most participants would make a trade-off between the potential harms and benefits of their treatment and may not accept such a small magnitude of benefit as was found in this research. It is also possible that participants might not accept such small benefits as represented by the larger NNTs for illnesses perceived as less severe. This illustrates the limitations of using hypothetical scenarios and applying the findings of these studies to real-life situations. Such studies provide an insight into how benefit information might impact upon understanding on behaviours, but this insight is limited.

Bersellini et al (2006) and Garcia-Retamaro et al (2010) presented participants with fictitious scenarios which were realistic but used fictitious medicines and also lacked presenting associated harm information. Very few studies presented benefit information in the context of both benefits and harms. The exception is a series of studies undertaken by Tait et al (2010a) that explored how participants make risk and benefit trade-offs before making decisions about treatments (Tait et al., 2010a). There is a need for more research using real-life health scenarios in order to explore the authentic impact that benefit information might have.

The use of **hypothetical drugs** in scenarios was common although some studies presented real clinical trial data. Galesic et al (2009a) used a hypothetical statin

medicine as part of a comparison with other drugs but the benefits of the hypothetical statin were based on data generated from actual clinical trials (Galesic et al., 2009a). Hux and Naylor, (1995), presented participants with benefit data from the Helsinki Heart study in order to evaluate how three different formats of the same data impacted upon a participant's willingness to take the drug (Hux and Naylor, 1995, Frick et al., 1987).

Some studies used real-life situations to facilitate **hypothetical decision-making** about treatments. Others presented comparative benefit information for different interventions for example different treatments for symptomatic carotid stenosis (Bergus et al, 2002). A study which explored whether NNT expressions performed better than ARR and/or RRR expressions used generic scenarios and presented treatment benefits out of context. The findings showed that as a result of the hypothetical scenario, patients' personal involvement in the tasks was reduced. This might impact upon how the people process information. The study concluded that highly involved participants process information in a detailed and integrative way compared to those who are less involved, who process information more superficially (Sheridan et al., 2003). This emphasises the importance of undertaking research which uses a scenario relevant to the subject, and also leads us to consider the representativeness of the sample.

- **Representativeness of sample**

The representativeness of the sample recruited to a research study also could impact upon the generalisability of the findings. Several studies recruited patients and used scenarios, which were of high-relevance to the real-life situation of the participant. Bhandari et al (2003) recruited patients presenting at a fracture clinic into a study which assessed preference for treatment for hip fracture and presented 5 different types of benefit information. However, the sample was small and the study only assessed patient's preference for format, nevertheless, the use of real-life sample and scenario is a strength of this research. Sheridan et al (2003) also recruited patients from a hospital waiting room, however provided participants with a hypothetical scenario.

Malenka et al (1993), Hux et al (1995), Bergus et al (2002) and Galesic et al (2009) recruited participants who were either patients or those likely to make a similar treatment choice in the future. The findings of these studies have importance resulting from the participants' 'involvement' in the hypothetical decisions.

Several studies recruited samples that were representative of the general population. However some had flaws in their sampling strategy that led to the recruitment of an unrepresentative sample. Fagerlin et al (2007) recruited women from a hospital

cafeteria to test how providing comparative risk information impacts upon risk perceptions. They recruited a convenience sample which included a high proportion of health care professionals who may not be representative of the general population.

Galesic et al (2009), Cutie et al (2008), Schwartz et al (2009, 2007) and Gyrd-Hansen (2003) all employed recruitment strategies resulting in an above average highly-educated sample. The findings of their studies must be interpreted in light of this.

Studts et al (2005) recruited pre-clinical medical students to undertake an experiment where participants received one of four vignettes examining preferences on communicating the benefits of adjuvant chemotherapy. Although the findings are relevant, notably that the use of absolute survival benefit was preferred over negatively framed methods, it is important to note that these findings might be biased by the samples' higher numeracy and potential familiarity with different formats of risk and benefit presentation.

Non-representative samples were commonly used in experiments, such as those recruiting undergraduate students to research health conditions that were not common in the younger population. Price et al (2007), Timmerman et al (2008) and Studts et al (2005) all recruited undergraduates who often have higher numeracy skills than the general population (Price et al., 2007). Another challenge with using participants who are not representative of the population of interest is that they might not have the same 'involvement' that a patient with experience of the disease has. This has been shown to affect participants' interaction with decision-making and the processing of information (Rothman et al., 1993). It is important that in the context of research into medical treatments the most representative sample is the population likely to use the medical treatment and this population might not be demographically similar to the general population. Studies examining a disease that occurs predominantly in the older population should recruit representatively from the older population, for example the sample recruited by Natter et al (2005) had a mean age of 28.2. They asked participants to consider a scenario about 'flu vaccination and it is possible that the sample might not have involvement in the scenario and that this might impact upon the applicability of the findings.

Few studies adequately evaluated the impact of providing benefit information to actual **patients** in real-life scenarios. Bergus et al. (2002), and Bhandari et al. (2003) Galesic et al. (2009) all recruited patients and presented them with a scenario that was specific to the participants' condition. Whereas Hux and Naylor (1995), Goodyear-Smith et al.

(2008) and Malenka et al. (1993) recruited patients and presented them with scenarios which were hypothetical and unrelated to their condition.

Several studies recruited large and representative samples and presented scenarios which were realistic and had significant relevance to the sample. Tait et al (2010a, 2010b 2010c) undertook a series of large-scale studies evaluating the impact of providing parents with information about a clinical trial in order to examine decisions about enrolling a child in the trial.

To conclude, the methods used in much of the research in this field mean that the findings are potentially biased, mostly due to a tendency not to recruit representative samples, but also because of the problems inherent in using hypothetical scenarios as the setting for studies. Well-designed studies in this field used both a realistic scenario and also recruited a population which was representative of the target population. The findings of such studies are likely to be more generalisable. Caution should be used when applying the findings to different populations, especially when a sample has a high level of educational attainment.

2.7.8 Overall benefit scoping review findings

This review has shown the diversity and scope of research being undertaken into the effects of presenting benefit information to the general population. There is a great deal of breadth and range to the type of research being undertaken. There are a number of different methods that can be used and some of these formats have been more thoroughly researched than others.

It is apparent that there is a significant amount of research focussing on the feasibility of presenting different formats to patients, and there is some good quality evidence that patients can use different formats of benefit information, and find its inclusion in written health communication provides them with more detail about likely benefits. It is apparent that its inclusion is preferable to absence.

The research has shown that benefit information is complex, it can be challenging to present and difficult to interpret. Poorly designed benefit information is not valuable at conveying accurate treatment benefits.

There is a large amount of research of a good quality that shows how different formats can have different influences on patient perceptions of risk. For example it is well known that benefit information presented as an RRR can increase over-estimations of benefits and increase a participants intent-to-take a treatment, without improving their

understanding about what the information really means. It is apparent that techniques such as natural frequencies and ARRs tend to help patients make decisions about treatments that are in line with their values. For people to get the most out of the benefit information, it is therefore important for it to be presented in context. There is good evidence suggesting that the presentation of baseline risks can help improve accuracy of risk perception.

There is also a good deal of research that suggests the benefits of using graphical formats such as bar charts and icon arrays on improving the accuracy of risk estimation on patients perceptions (not presented in this review). These methods have been proved to be effective in some circumstances.

However it is also important to note that other areas are less well-researched. For example, there is some evidence recommending that NNTs be avoided as they are not easily interpreted by participants. However the research proposing these findings is flawed and did not present the NNTs in a context that was applicable in real life. There is a need for more good quality research, especially high quality RCTs, assessing the impact of providing different formats of numerical information on patient behaviour, for example.

It is also important to note that in some situations, where there is an absence of evidence, that this does not mean there is evidence of absence of effect. Formats where there is a lack of research, or where research has not shown positive effects may still be effective, it may be that design flaws or the size of research studies have not resulted in real positive effects being noted (Altman and Bland, 1995).

There is no definitive answer as to which type of format is better. Although it is apparent that different formats can have different impacts, so understanding the aim of the benefit information when choosing which format to use is important. Some formats, such as the RRR, can promote behaviour change.

There is also a need to understand more about how an individual's perspectives, values and circumstances can influence risk understanding. How the context in which people live with risks and benefits and how people can influence the risk in question impacts upon their perceptions of benefit information, and on their beliefs and behaviours (Edwards et al., 2003). More qualitative studies examining these concepts in detail would add valuable context to the body of literature.

The body of work is also lacking in research that has been undertaken in a naturalistic setting, with real-life patients being given actual benefit information and which assesses

the long-term and actual impact on behaviour. There is clearly a gap in the literature which assesses the feasibility of providing actual benefit information, which is relevant to a specific health condition to patients with that health condition and assessing the impact that it has.

There is also a need to undertake more research about the presentation of benefit information in context i.e. with the presentation of benefit information alongside the presentation of existing risks about treatments. Tait et al have undertaken some good-quality large-scale studies evaluating the impact of this on patient decision-making. More research on how patients make trade-offs between real life risks and benefits would add significantly to the literature (Tait et al., 2010a, Tait et al., 2010c, Tait et al., 2010b).

2.8 Application of the findings

2.8.1 Headline section

The idea of the use of a headline section in medicines information internationally has been receiving a higher profile in recent years (Medicines and Healthcare Products Regulatory Agency, 2005a, Food and Drug Administration, 2009). However, there has been very little research undertaken into how a headline section might impact upon a patient's knowledge, understanding and use of medicines information. Much of the research in this area has focussed upon 'warning' labels, incorporating research into signs, symbols and labels. The context of this research differs slightly from the aims of this review; as a result, the findings of reviews should be interpreted accordingly.

The evidence-base focussing specifically upon a summary of key information in a written document is almost non-existent and, before a decision is made to incorporate this adaptation into medicines information, there is a need for further research. In his 10 top tips on writing medicines information, Dickinson and co-authors suggest "Now ask the experts: patients" (Dickinson et al., 2001). Clearly there is a need to undertake relevant research with patients in a naturalistic setting to assess how they use and understand information provided in a headline section in written medicines information. This is essential to assess the utility of such a technique and to ensure it aids patients with finding and understanding key information about their medicines, rather than hindering them (Hartley, 2004).

Key findings and application:

- No evidence was identified that confirms that a headline section might be detrimental to the reader, encouraging them to skip over a boxed section in a body of text. It is unclear whether a headline section in a PIL has the potential to be detrimental to a reader.
- There is no evidence to suggest that a particular format of headline section is optimal.
- As a result the type of headline section identified by the MHRA will be considered for use in this research.(Medicines and Healthcare Products Regulatory Agency, 2005a)

2.8.2 Benefit information

There is a large and heterogeneous body of research exploring the potential impact of including information about the benefits of treatments in written health information. The findings are equivocal and the evidence suggests no clear format which is best suited to use in a PIL. The review of the literature revealed a number of key findings which will be useful to guide the development of benefit statements to be used in exemplar leaflets in the following stages of research in this thesis.

The addition of a textual statement about the effectiveness of a medicine can enhance a reader's preference for information and understanding about the benefits of a treatment in context and would be a feasible addition to a PIL (Bersellini and Berry, 2007b, Bersellini and Berry, 2007a, Vander Stichele et al., 2002).

The presentation of numerical information about the benefits of treatments provokes varied responses. RRRs in particular can be misleading and persuasive, leading people to make decisions that might not be line with their values (Carling et al., 2009). The review has also shown the necessity of providing baseline information when presenting numerical information (Sheridan et al., 2003, Fagerlin et al., 2007, Natter and Berry, 2005)

It has also shown the potential for natural frequencies to communicate the benefits of medicine (Akl et al., 2011a). Graphical formats of benefit communication, such as icon arrays and bar charts, also have great potential and have been shown to improve risk perception and understanding of medicines. However, their use in a regulated patient information leaflet is limited due to the space required to adequately communicate

graphics. (Space is at a premium in a PIL). There is no clear evidence that framing impacts upon patient understanding or behaviour. (Akl et al., 2011b).

Key findings and application:

- The use of an RRR format is not recommended.
- The use of a textual statement has been shown to improve risk perception.
- The use of a natural frequency has been shown to be useful
- There is limited research into the impact of NNTs, although some findings suggest this format might be difficult for some people to understand. More research would be valuable.
- There is no clear evidence that framing impacts on patient understanding or behaviour and as a result a combined frame will be presented.

Chapter 3:

Focus Group Study

Chapter 3 Focus groups (Study 2)

Patient perspectives on the inclusion of headline section and information about benefits in a patient information leaflet

3.1 Introduction

The two scoping literature reviews (chapter 2) identified several potential approaches to the inclusion of a headline section and information about benefits in a regulated PIL. This chapter describes how these approaches were used to develop PILs. which were then used as stimulus materials in focus groups to explore the perspectives of real-life users of medicines about the inclusion of a headline section and information about benefits.

The chapter is presented in several sections:

Firstly the methods of the study will be described and the justification for the use of these methods explained*. [3.2 Methods, 3.3 Recruitment, 3.4 Stimulus materials,3.5 Data analysis]*

Two sections that follow describe, respectively, the findings for the **headline** section and the **benefit** information strands of the study. This includes the presentation of data collected during the focus groups, which will be used to inform the findings of the study and provide context about the perspectives of the participants on the two interventions included in the leaflet. *[3.6 Study findings, 3.7 Headline discussion, 3.8 Benefit information]*

Finally there will be a discussion about the results of the study which will be placed in the context of existing literature. Consideration will also be given to how the findings can be applied to the next stage of the research in order to further explore the impact of a headline section and information about the benefits of medicines in a PIL. *[3.9 Discussion, 3.10 Conclusion]*

3.1.1 Research aims and objectives

Headline section aims

The study aimed to:

1) Identify preferences and suggestions for presenting a headline section in regulated PILs.
2) Explore how the inclusion of a headline section in a PIL impacts upon knowledge and satisfaction with medicines, and potential medicine-taking behaviour.

Six objectives specific to the headline section were identified to guide the design and conduct of the study:

- Identify the range of opinions on the inclusion of a headline section in a PIL.
- Identify the range of preferences for different formats of a headline section in a PIL.
- Map the range of factors that affect preference for headline section in a PIL.
- Identify the impact that the inclusion of a headline section has on people's understanding of, and satisfaction with, their medicines and medicines information.
- Describe the potential impact on medicine-taking behaviour.

Benefit information aims:

The study aimed to:

3) Identify preferences and suggestions for presenting benefit information in regulated PILs.
4) Explore how the provision of benefit information in a PIL impacts upon knowledge and satisfaction with medicines, and potential medicine-taking behaviour.

Six objectives specific to benefit information were identified to guide the design and conduct of the study:

- Identify the range of opinions on the inclusion of benefit information in a PIL.
- Identify the range of preferences for different formats of benefit information in a PIL.
- Map the range of factors that affect preference for benefit information in a PIL.

- Identify the impact that benefit information has on people's understanding of, and satisfaction with, their medicines and medicines information.
- Describe the potential impact on medicine-taking behaviour.

3.2 Methods: headline and benefit.

3.2.1 Methodology

This is a qualitative research study which uses focus groups as a data collection method. It applies a generic qualitative research approach, employing both descriptive and interpretive techniques to explore the opinions of users of medicines about suggested changes to the leaflets provided with medicines. A generic approach is described as one which *"seeks to discover and understand a phenomenon, a process, or the perspectives and worldviews of the people involved"* (Caelli et al., 2003).

A qualitative approach is essential in order to explore and understand differing patient perspectives on a headline section and information about benefits in PILs, which can then be used to inform further leaflet development in the later stages of the research. There are a range of qualitative approaches which could be used to inform the methods for this study - approaches which are more or less suited to different epistemological perspectives and different aims.

Alternative approaches considered include **grounded theory** (Glaser and Strauss, 1967), which is an inductive qualitative method designed to generate theory about a specific topic where little is known about it. A key feature of this approach is its iterative process, theoretical sampling and system of analysis (Lingard et al., 2008). Other interpretive approaches include **phenomenology**, an approach designed to describe the common meaning for lived experiences of a concept or phenomenon, and **ethnography**, which focuses on understanding culture. An ethnographic approach tends to examine a large group of individuals sharing a common culture (Creswell, 2013).

These methodologies have well-established strengths but are not appropriate for this study. Cultural roles no doubt impact upon medicine-taking and access to medicines information but this research does not intend to explore that aspect in detail - therefore an ethnographic approach is not suitable. Likewise, the methods of grounded theory are not appropriate to the aims of this study which are, initially, simply to understand in more detail medicine-users' preferences and opinions on the interventions of interest.

The aims of the initial focus groups are to test preferences for content and format of the leaflet; therefore a generic qualitative approach is best suited to this goal.

Generic qualitative research, also referred to as qualitative description, is a pragmatic method which is compatible with the use of questions such as “why”, “how” and “what”, which qualitative research examines. Sandelowski summarises qualitative description as research which offers a comprehensive summary of an event in the everyday terms of those events (Sandelowski, 2000). This approach tends to be the least theoretical on the spectrum of qualitative methodologies and has been criticised for its lack of theoretical position. It has also been criticised for being less interpretive than methods which describe an event in terms of a conceptual, philosophical or other highly abstract framework (Thorne, 2008). However, Sandelowski (2000, 2010) refutes this view, claiming that qualitative description produces findings which are ‘closer’ to the data than those produced by grounded theory or phenomenological research, as the method is less transformative. The aim of qualitative description is to present the facts of the case, a comprehensive summary of an event, in everyday language (Sandelowski, 2000).

Qualitative description is an appropriate method as it is both pragmatic and meets the aims of the study (which are ultimately practical as opposed to theoretical). While it has been criticised as being the least theoretical approach, it is not atheoretical and the use of theory can be woven into the methods to provide breadth and depth to the findings (Sandelowski, 2010). This approach assumes an ‘a priori’ understanding of the subject and uses the expert knowledge of the researcher, and the research team, to set priorities and develop the research questions and topic guide in a way that other more theoretical approaches might not. Again this is something that reflects the practical aims of developing recommendations for a regulated PIL, which is the intention of this body of research.

3.2.2 Data collection methods

Focus groups are an appropriate method for data collection in the context of this study, as they can collect large amounts of data and facilitate an environment which allows for the sharing of different perspectives. They also encourage group discussion and debate about stimulus materials, such as the exemplar leaflets, which may be less dynamic in an individual interview (Kitzinger, 1995, Geis et al., 1986, Holstein and Gubrium, 1995).

A topic guide was used to stimulate discussion during the focus groups. The questions were developed around the central topics of the research study and used a modified ‘knowledge, attitudes and beliefs’ framework to explore the different perspectives on the

changes to the PILs. With regards to attitudes towards the interventions, there was a specific focus on patient satisfaction (Ajzen, 1991) (Appendix 5).

3.2.3 Research Ethics consideration

Research ethics approval was obtained from School of Healthcare Research Ethics Committee, University of Leeds on 26 April 2012 (SHREC/RP/271).

3.3 Recruitment

Participants were recruited from fliers placed in community pharmacies and distributed amongst community elderly action groups that were within travelling distance of the University of Leeds. Approximately 1000 flyers were distributed across Leeds (See appendix 4). A further e-mail flier was sent to the members of the University of Leeds, School of Healthcare service user group. The fliers stated that interested participants should contact the researcher and an email address and telephone number was enclosed.

Participants were evaluated against the inclusion criteria, using brief questions about medicines use, educational attainment and whether they were a practising healthcare professional with expertise in medicines information; then allocated to appropriate groups accordingly. The initial contact also provided an opportunity to discuss or provide further information over the phone or via e-mail.

The sample was a convenience sample, with the inclusion criteria set to recruit a group of participants who were typical of the population of medicine-users. A research pack was sent to interested participants comprising a confirmation letter (which also provided instructions on how to read the different leaflets), a patient information leaflet about the research and 3 exemplar PILs. Participants were advised to read the leaflets before attending the focus groups, although it was stated that they need not read the whole leaflet, just familiarise themselves with it. (Appendices 6&7)

Inclusion criteria

- Aged over 50 years
- Current prescription for at least one medicine
- Able to read a patient information leaflet written in English.

Exclusion criteria

- Current prescription for sumatriptan and simvastatin (the medicines used to develop the leaflets), as they may have prior knowledge about the medicines, which could impact on their perceptions of the benefit information. If a participant was prescribed one of these two medicines, they were allocated into a focus group for the alternative medicine (i.e. a participant with a prescription for sumatriptan was eligible for inclusion in the group receiving leaflets based on simvastatin, and vice versa).
- Employed in a job that involved providing medicines information to patients.
- Visual impairment that prevents them from reading a standard leaflet.

3.3.1 Setting

Focus groups were held in a meeting room at the University of Leeds. Six focus groups were undertaken during June and July 2012, with between 6-9 participants recruited to each group. In total 42 participants were recruited, a sample size which facilitated a variety of perspectives and experiences, without the groups being too large to manage and without the themes that arose from the groups becoming too repetitive.

The focus groups were divided so that 3 groups received exemplar leaflets for Janatriptan (n=23) and 3 focus groups received them for Rebastatin (n=20). RD and an additional moderator ran all the groups. The groups were held at the University of Leeds and lasted between 1 hour 30 minutes and 2 hours. The groups were held at various times to accommodate participants' schedules.

A brief PowerPoint presentation was used to emphasise the focus of the discussion i.e. either on the headline or the benefits information. The slides included:

- the percentage and natural frequency benefit information from the exemplar leaflets.
- the positive and negatively framed statements - in order to generate discussion about preference for different framings of information. The statements were labelled 'positive' and 'negative' and referred to as such during the focus groups in order to highlight the difference between the statements in a way which was easy for the participants to refer to.

Groups were run by RD and a moderator. RD presented the questions from the topic guide, facilitated the discussion and kept the groups to time. Each focus group was run in a similar order. The topic guide questions and the benefit statements were presented

in the same order throughout. The moderator made notes of topics and concepts being discussed and observed the level of participation from the group.

Participants were provided with written information about the study prior to their involvement in the focus group and were advised that they were free to leave the group at any point. Consent was obtained prior to commencement of the group discussion.

3.3.2 Participants

58 potential study participants contacted the researcher. 16 were excluded due to being unable to attend the groups, because they were a practising healthcare professional or because, after receiving further information about the study, they declined to be involved. The final sample comprised 42 participants, of whom 29 were females, and they had an age range of 50-89.

Table 7: Participant characteristics.

Category	Sub-category	FG1	FG2	FG3	FG4	FG5	FG6	Total
N		7	8	6	6	9	6	**42**
Women		3	5	5	5	7	4	**29**
Age range		56-78	51-70	54-63	57-64	50-81	58-89	**50-89**
Education	No qualifications	-	-	-	1	-	-	**1**
	Foundation	-	-	1	-	-	3	**4**
	Intermediate	2	-	-	1	3	1	**7**
	Advanced	5	2	4	3	3	-	**17**
	Higher	-	6	1	1	3	2	**13**
Ethnic group	White British	6	8	6	6	9	2	**36**
	British Asian	1	-	-	-	-	1	**2**
	British Caribbean	-	-	-	-	-	1	**1**
	British Other	-	-	-	-	-	2	**3**
Items of medicine	1-5	6	7	6	5	6	3	**33**
	6-10	-	1	-	-	2	2	**5**
	11-15	1	-	-	-	1	1	**3**
	No data	-	-	-	1	-		**1**
Exemplar medicine		JANA	REBA	JANA	REBA	JANA	REBA	**-**

3.4 Stimulus materials

In total 6 leaflets were designed, based on 2 different medicines;

- Simvastatin - given the hypothetical name Rebastatin
- Sumatriptan - given the hypothetical name Janatriptan

The headline and benefit information are shown in Figures 7-10, the full leaflets are shown in appendix 9.

The leaflets were as follows:

[1] Rebastatin: Typical
[2] Rebastatin: Headline
[3] Rebastain: Benefits
[4] Janatriptan: Typical
[5] Janatriptan: Headline
[6] Janatriptan: Benefits

Each focus group considered either Rebastatin or Janatriptan, hence each participant viewed only 3 leaflets.

The **typical** leaflets were designed to resemble typical patient information currently provided with medicines in the UK. The **headline** section leaflets contained a summary of key information about the medicine. The **benefit** sections comprised 4 different benefit statements which were presented as a series of flaps, with a different colour used to highlight each benefit section.

The section below describes the justification for the choice of design of the interventions and the justifications for choosing the medicines for which the leaflets were designed.

3.4.1 Choosing the medicine

Leaflets were designed based on two different medicines used for different conditions:

1) Sumatriptan – used for the symptomatic conditions of migraine or cluster headache.
2) Simvastatin – used for the asymptomatic conditions of hypercholesterolaemia, hyperlipidemaemia and the prevention of cardiovascular events.

Medicines used for different treatment goals were chosen specifically to facilitate a deeper level of enquiry about how perspectives on the interventions may vary depending upon the purpose of the medicine. It has been shown that people have

different perceptions about the severity of different illnesses and this may impact upon the balance of risk and benefit that patients will accept with their medicines (Simes and Coates, 2001, Leventhal et al., 1998).

Previous research exploring the inclusion of benefit information in a PIL for a commonly prescribed heart medicine found the numerical benefit information to be unwelcome and something which evoked strong responses from participants recruited to a similar focus group study (Hamrosi et al., 2012). The numerical benefit information provided to the participants in that study was an NNT presented as:

If 100 people took this medicine for 2 years

- 3 of them will be saved from having a heart attack
- 1 of them will be saved from having a stroke

One of the findings from that study was participants were surprised that the level of benefit was as 'low' as 1 - 3 in 100. This aims of this study are to explore whether similar responses to numerical information are evoked with medicines that have higher magnitudes of benefit.

It was also decided to choose medicines for long-term conditions, the rationale being that these are the most commonly prescribed, they consume most of the national drug budget and are more likely to be associated with problems such as non-adherence. Advice was sought from experts in prescribing and medicine management, including a GP (n=1), pharmacists (n=5) and a nurse prescriber (n=1), on which medicines would be most appropriate for the research. Advice was also sought from an experienced patient advocate (GD) on the potential issues that might arise from choosing different types of medicine.

It was agreed that any medicines chosen had to meet the following criteria:

- Have commonly acknowledged safety issues (data provided from the MHRA on adverse drug reporting was used a criteria to measure this).
- Have data available for risks and benefits.
- Be commonly prescribed in a population that can be pragmatically recruited to a research study.

Medicines excluded from consideration included:

- Medicines with multiple indications. Development of the benefit statements is complex and the addition of several benefit statements for different indications

was challenging for this exploratory work. Therefore the use of a medicine with few indications, ideally one, was appropriate.

- Medicines with complex instructions for use; it was considered that such instructions have the potential to lead the participants away from the focus of discussion about the benefits.

The medicines were given hypothetical names, **Janatriptin** and **Rebastatin**, to ensure that they could not be confused with currently available medicines. The leaflets also contained a highlighted section which stated that these leaflets were for research purposes only.

3.4.2 Designing the headline section

The scoping literature review (See chapter 2) was designed to provide the rationale for developing the headline sections used here. However, the review found no clear evidence for the best way of presenting such summary information. As a result, the headline sections were developed based on that used by the MHRA in their publication 'Always Read the Leaflet' (Medicines and Healthcare Products Regulatory Agency, 2005a).

The MHRA criteria are given in full in figure 5. The key points relevant to the current study are:

- Concise, key information.
- Information on safe and appropriate use.
- Presented at the beginning of the leaflet.

- Concise key information on the safe and appropriate use of a product
- A focus on information that the patient must be aware of for safe and effective medicine use.
- Headline information at the beginning, presented to maximise visibility and likelihood of being read. This might include highlighting the text or using a larger font size.
- Information presented as a short series of bullet points – in most cases 2 - 6 points should suffice; however, there is no "standard" length with discretion needed in deciding the number and type of headlines. There may be some simple products for which no headlines would be necessary
- Only the key messages on safe and appropriate use of the product. As a general principle, the section should be kept short in order that patients do not rely on it as a substitute for reading the main body of the PIL.
- The most essential messages, bearing in mind the product and its therapeutic context. Typically these may relate to:
    - why the patient should take the product;
    - the maximum dose or duration of treatment;
    - potential side effects/withdrawal reactions (symptoms to look out for, especially for common or serious side effects);
    - contraindications;
    - important drug interactions;
    - circumstances in which the drug should be stopped;
    - what to do if the medicine doesn't work; or
    - where to find further information.
- "Positive" information on the anticipated benefit of taking the medication should be included (usually as the first bullet point) - to provide balance and context for the "negative" information referring to possible adverse events. Positive information should be limited to short factual statements stating the licensed indication (eg "Your doctor has prescribed [PRODUCT] because it is a treatment for X). Specific efficacy data or other product claims should not be included.
- A standard form of wording indicating the patient should read the rest of the leaflet. The date of the latest revision of the leaflet should be stated, so that long-term users will be aware when there is a need to re-read the PIL.
- Consistency across all products containing a particular drug substance and/or drug class is encouraged.(Medicines and Healthcare Products Regulatory Agency, 2005a)

Figure 4: MHRA proposals for headline sections in PILs

Both headline sections used in the study complied with these proposals. Both leaflets presented the headline section at the beginning of the leaflet. The headline was highlighted using a grey shaded box. Six short, bullet-pointed pieces of key information about the safe and effective use of the medicine were presented. The headline section contained a brief textual statement about the benefits associated with the medicine.

Underneath the headline was a statement advising that the user read the remainder of the leaflet.

In Always Read the Leaflet, the MHRA presented an exemplar headline section for Carbamazepine in a box with an outline. Expert opinion on the presentation of summary information in a box within a body of text suggests caution when using this technique as it might lead to the reader skipping over the boxed information and ignoring it, although the literature review in Chapter 2 did not identify any research which confirmed this theory (Hartley, 2004). A decision was therefore made to present the headline section in a grey shaded box, rather than a boxed outline, placed prominently at the top of the PIL. The use of textual signposts in the headline followed the same format as those used in Always Read the Leaflet.

The key messages included in the headline were agreed by the pharmacist members of the research team (TR and JM).

3.4.3 **Designing the benefit information**

The findings of the scoping literature review (chapter 2) did not show any particular method of benefit presentation to be superior and a decision was made to present participants with a number of different formats. Absolute risk formats were used rather than relative risk reduction statistics, in line with the findings of the scoping review.

The formats chosen were highlighted in the scoping literature review as those that had positively impacted upon patient preference and understanding in comparison to other formats. Natural frequencies and absolute risk reductions have been shown to facilitate understanding of numerical data and increased satisfaction with information (Carling et al., 2009, Carling et al., 2010, Tait et al., 2010a). Textual statements were identified as adding value to the information about medicines provided in a PIL and improved understanding about medicines and satisfaction with the information (Bersellini and Berry, 2007a, Bersellini and Berry, 2007b).

A number needed to treat (NNT) statistic was also chosen. Research into the NNT has shown that it is frequently misinterpreted; however the research in this area is limited and further research of its potential in a naturalistic setting would be welcome (Sheridan et al., 2003, Sarfati et al., 1998, Kristiansen et al., 2002).

As a result the following statements were created:

1) A textual statement of the rationale and effectiveness.

2) One using percentages to describe the ARR (presented using a combined frame).
3) One using a natural frequency to describe the ARR (presented using a combined frame).
4) One using a Number Needed to Treat expression.

The use of graphical formats was discounted for practical reasons, despite evidence that they can aid understanding. In the context of a PIL it is difficult to incorporate their use, as to be able to accurately display such information requires space. This is at a premium on a PIL. Also well-designed graphics tend to rely on the use of colour, which might not be possible in all PILs.

3.4.4 Source of benefit information

Several data sources were considered for generating the numerical data in the benefit statements. The 'gold standard' for studies into the effectiveness of medicines is a systematic review of trials with meta-analysis. Consequently if a Cochrane systematic review exists on the chosen medicines, then data would be used from this source.

Sumatriptan

Data were derived from a Cochrane systematic review on the effectiveness of Sumatriptan (oral route of administration) for acute migraine attacks in adults (Derry et al., 2012).

The Cochrane review presented multiple outcomes for the effectiveness of sumatriptan. Headache relief at 2 hours was chosen as the relevant outcome, after discussion with the same experts as above. Using this outcome generated an NNT with a denominator of 4 (4 people need treating for 1 to benefit). This was deemed sufficiently different from the denominator for simvastatin of 20.

Simvastatin

A Cochrane systematic review was available, but it combined data from different types of statin and included trials on primary and secondary prevention (Ward et al., 2007). As PILs are medicine-specific it is essential that data are medicine-specific, and not an aggregate of information from a group of medicines. NICE guidelines on lipid modification were also considered, however they also presented combined data on the benefits of different statins.

As a result, a single large randomised placebo-controlled trial of cholesterol-lowering with Simvastatin in secondary prevention was chosen: the Heart Protection Study

(2002) (Heart Protection Study Collaborative Group, 2002).This was an independently funded study which recruited over 20,000 participants to explore the effectiveness of simvastatin compared to placebo.

One of the key outcomes measured by the Heart Protection Study was the reduction in major vascular events, specifically major coronary event, any stroke or revascularisation. After discussion with experts in prescribing and medicine management, including a GP (n=1), pharmacists (n=5) and a nurse prescriber (n=1), it was decided that these events would be those that patients would want to know about when making decisions about their treatment.

3.4.5 Creating the benefit statements

The benefit expressions were derived using a risk generator, which calculates formats of risk/benefit by comparing the outcomes of different treatment effects in clinical trials (Spiegelhalter, 2012). The results were checked with pharmacists with expertise in research and medicines management (RK and DA) for accuracy. With regards to the format of the NNT statistic, there was no evidence in the published research to suggest whether to present the numerator or denominator first in the benefit statement. However, the majority of the research on NNTs presents the denominator first (Carling et al., 2009, Carling et al., 2008, Sheridan et al., 2003, Bhandari and Tornetta, 2004, Studts et al., 2005, Sarfati et al., 1998, Hux and Naylor, 1995, Edwards and Elwyn, 1999). This format is also reflective of the wording used in the natural frequency statements. Therefore the denominator was presented first in the benefit statements in order to provide consistency.

Several statements were generated and there followed several rounds of amendments where they were revised until they were readable, consistent and understandable. A consensus agreement was made on the statements amongst RD, DKR, PK and JM.

3.4.6 Production of leaflets

The leaflets were produced to imitate standard leaflets. Three leaflets were developed for each medicine:

1) **Usual** leaflet, which contained the information that would usually be included in a PIL.
2) **Headline** leaflet. This leaflet contained a grey shaded box containing key information about the medicine. The box was entitled ‘Important things you should know about XXX’ (Figure 6&7).

3) **Benefit** leaflet. This leaflet contained the four benefit statements shaded in different colours. This was to facilitate ease of discussion with participants who would be unfamiliar with the technical terms used for each type of statement in the literature. They could therefore refer to the ‘orange’ or ‘blue’ statement, for example. The statements were presented in a series of flaps that overlaid each other and opened up in a booklet style, so only one statement could be read at a time (Figure 9&10).

Important things that you need to know about Janatriptan

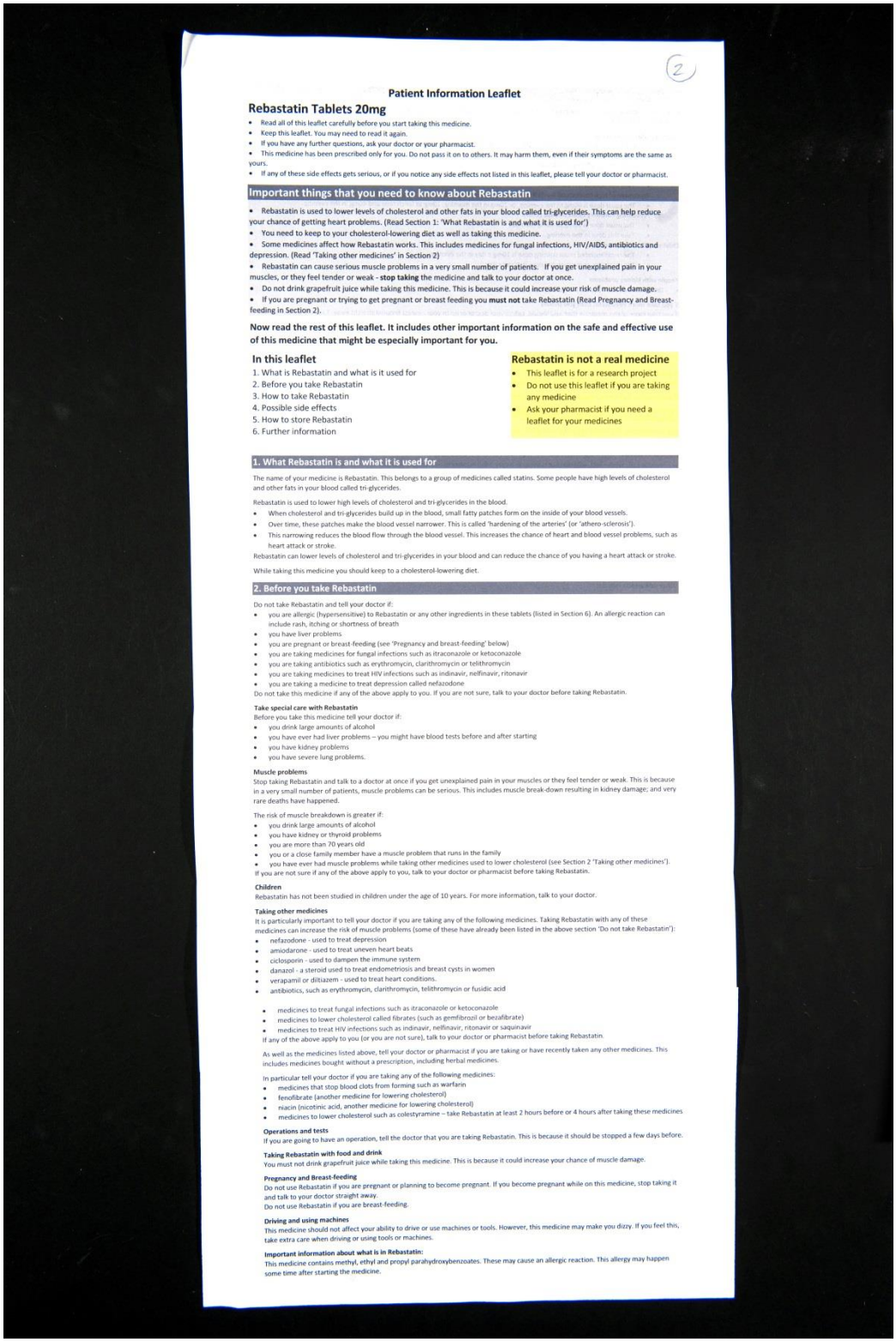
- Janatriptan is used to treat migraine – only use if your doctor has confirmed you have migraine attacks.
- Janatriptan only works when a migraine attack has started. It will not stop you from getting an attack.
- Do not take Janatriptan if you have ever had heart, circulation, or blood pressure problems, or have had a stroke (Read Section 2: Before you take Janatriptan)
- Do not take Janatriptan at the same time as other migraine medicines. Also, some other medicines affect Janatriptan. This includes medicines for depression and some antibiotics (Read 'Taking other medicines' in Section 2)
- Janatriptan may harm the unborn baby. Talk to your doctor before taking if you are pregnant.
- After taking Janatriptan you may feel chest pain or pressure for a short time. If this feeling is very bad, or does not go away, talk to a doctor straight away.

Figure 5: Example of the headline section used: Janatriptan.

Important things that you need to know about Rebastatin

- Rebastatin is used to lower levels of cholesterol and other fats in your blood called tri-glycerides. This can help reduce your chance of getting heart problems. (Read Section 1: 'What Rebastatin is and what it is used for')
- You need to keep to your cholesterol-lowering diet as well as taking this medicine.
- Some medicines affect how Rebastatin works. This includes medicines for fungal infections, HIV/AIDS, antibiotics and depression. (Read 'Taking other medicines' in Section 2)
- Rebastatin can cause serious muscle problems in a very small number of patients. If you get unexplained pain in your muscles, or they feel tender or weak - **stop taking** the medicine and talk to your doctor at once.
- Do not drink grapefruit juice while taking this medicine. This is because it could increase your risk of muscle damage.
- If you are pregnant or trying to get pregnant or breast feeding you **must not** take Rebastatin (Read Pregnancy and Breast-feeding in Section 2).

Figure 6: Example of the headline section used: Rebastatin.



Patient Information Leaflet

Rebastatin Tablets 20mg

- Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This medicine has been prescribed only for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of these side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Important things that you need to know about Rebastatin

- Rebastatin is used to lower levels of cholesterol and other fats in your blood called tri-glycerides. This can help reduce your chance of getting heart problems. (Read Section 1: 'What Rebastatin is and what it is used for')
- You need to keep to your cholesterol-lowering diet as well as taking this medicine.
- Some medicines affect how Rebastatin works. This includes medicines for fungal infections, HIV/AIDS, antibiotics and depression. (Read 'Taking other medicines' in Section 2)
- Rebastatin can cause serious muscle problems in a very small number of patients. If you get unexplained pain in your muscles, or they feel tender or weak – **stop taking** the medicine and talk to your doctor at once.
- Do not drink grapefruit juice while taking this medicine. This is because it could increase your risk of muscle damage.
- If you are pregnant or trying to get pregnant or breast feeding you **must not** take Rebastatin (Read Pregnancy and Breast-feeding in Section 2).

Now read the rest of this leaflet. It includes other important information on the safe and effective use of this medicine that might be especially important for you.

In this leaflet

1. What is Rebastatin and what is it used for
2. Before you take Rebastatin
3. How to take Rebastatin
4. Possible side effects
5. How to store Rebastatin
6. Further information

Rebastatin is not a real medicine

- This leaflet is for a research project
- Do not use this leaflet if you are taking any medicine
- Ask your pharmacist if you need a leaflet for your medicines

1. What Rebastatin is and what it is used for

The name of your medicine is Rebastatin. This belongs to a group of medicines called statins. Some people have high levels of cholesterol and other fats in your blood called tri-glycerides.

Rebastatin is used to lower high levels of cholesterol and tri-glycerides in the blood.

- When cholesterol and tri-glycerides build up in the blood, small fatty patches form on the inside of your blood vessels.
- Over time, these patches make the blood vessel narrower. This is called 'hardening of the arteries' (or 'athero-sclerosis').
- This narrowing reduces the blood flow through the blood vessel. This increases the chance of heart and blood vessel problems, such as heart attack or stroke.

Rebastatin can lower levels of cholesterol and tri-glycerides in your blood and can reduce the chance of you having a heart attack or stroke.

While taking this medicine you should keep to a cholesterol-lowering diet.

2. Before you take Rebastatin

Do not take Rebastatin and tell your doctor if:

- you are allergic (hypersensitive) to Rebastatin or any other ingredients in these tablets (listed in Section 6). An allergic reaction can include rash, itching or shortness of breath
- you have liver problems
- you are pregnant or breast-feeding (see 'Pregnancy and breast-feeding' below)
- you are taking medicines for fungal infections such as itraconazole or ketoconazole
- you are taking antibiotics such as erythromycin, clarithromycin or telithromycin
- you are taking medicines to treat HIV infections such as indinavir, nelfinavir, ritonavir
- you are taking a medicine to treat depression called nefazodone

Do not take this medicine if any of the above apply to you. If you are not sure, talk to your doctor before taking Rebastatin.

Take special care with Rebastatin

Before you take this medicine tell your doctor if:

- you drink large amounts of alcohol
- you have ever had liver problems – you might have blood tests before and after starting
- you have kidney problems
- you have severe lung problems.

Muscle problems

Stop taking Rebastatin and talk to a doctor at once if you get unexplained pain in your muscles or they feel tender or weak. This is because in a very small number of patients, muscle problems can be serious. This includes muscle break-down resulting in kidney damage; and very rare deaths have happened.

The risk of muscle breakdown is greater if:

- you drink large amounts of alcohol
- you have kidney or thyroid problems
- you are more than 70 years old
- you or a close family member have a muscle problem that runs in the family
- you have ever had muscle problems while taking other medicines used to lower cholesterol (see Section 2 'Taking other medicines').

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking Rebastatin.

Children

Rebastatin has not been studied in children under the age of 10 years. For more information, talk to your doctor.

Taking other medicines

It is particularly important to tell your doctor if you are taking any of the following medicines. Taking Rebastatin with any of these medicines can increase the risk of muscle problems (some of these have already been listed in the above section 'Do not take Rebastatin'):

- nefazodone - used to treat depression
- amiodarone - used to treat uneven heart beats
- ciclosporin - used to dampen the immune system
- danazol - a steroid used to treat endometriosis and breast cysts in women
- verapamil or diltiazem - used to treat heart conditions.
- antibiotics, such as erythromycin, clarithromycin, telithromycin or fusidic acid

- medicines to treat fungal infections such as itraconazole or ketoconazole
- medicines to lower cholesterol called fibrates (such as gemfibrozil or bezafibrate)
- medicines to treat HIV infections such as indinavir, nelfinavir, ritonavir or saquinavir

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking Rebastatin.

As well as the medicines listed above, tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines bought without a prescription, including herbal medicines.

In particular tell your doctor if you are taking any of the following medicines:

- medicines that stop blood clots from forming such as warfarin
- fenofibrate (another medicine for lowering cholesterol)
- niacin (nicotinic acid, another medicine for lowering cholesterol)
- medicines to lower cholesterol such as colestyramine – take Rebastatin at least 2 hours before or 4 hours after taking these medicines

Operations and tests

If you are going to have an operation, tell the doctor that you are taking Rebastatin. This is because it should be stopped a few days before.

Taking Rebastatin with food and drink

You must not drink grapefruit juice while taking this medicine. This is because it could increase your chance of muscle damage.

Pregnancy and Breast-feeding

Do not use Rebastatin if you are pregnant or planning to become pregnant. If you become pregnant while on this medicine, stop taking it and talk to your doctor straight away.
Do not use Rebastatin if you are breast-feeding.

Driving and using machines

This medicine should not affect your ability to drive or use machines or tools. However, this medicine may make you dizzy. If you feel this, take extra care when driving or using tools or machines.

Important information about what is in Rebastatin:

This medicine contains methyl, ethyl and propyl parahydroxybenzoates. These may cause an allergic reaction. This allergy may happen some time after starting the medicine.

Figure 7: Example of the headline section in situ in leaflet.

PURPLE:

Janatriptan reduces the swelling of blood vessels in the brain and can improve your chance of having a less severe migraine headache after 2 hours.

BLUE:

The chance of having a less severe migraine headache after 2 hours is 32%. This becomes 57% for people who take Janatriptan.

This means that the chance of not having a less severe migraine after 2 hours is 68%. This becomes 43% for people who take Janatriptan.

ORANGE:

In 100 people like you, 32 will have a less severe migraine headache after 2 hours. This becomes 57 in 100 of those people who take Janatriptan.

This means that in 100 people like you, 68 will not have a less severe migraine headache after 2 hours. This becomes 43 in 100 of those people who take Janatriptan.

GREEN:

If 4 people like you take Janatriptan, 1 of them will have a less severe migraine headache after 2 hours.

Figure 8: The four benefit statements - Janatriptan.

PURPLE:

Rebastatin can lower levels of cholesterol and tri-glycerides in your blood and can reduce the chance of you having a heart attack or stroke.

BLUE:

The chance of not having a heart attack or stroke over the next 5 years is 75%. This becomes 80% for people who take Rebastatin.

This means that the chance of having a heart attack or stroke over the next five years is 25%. This becomes 20% for people who take Rebastatin.

ORANGE:

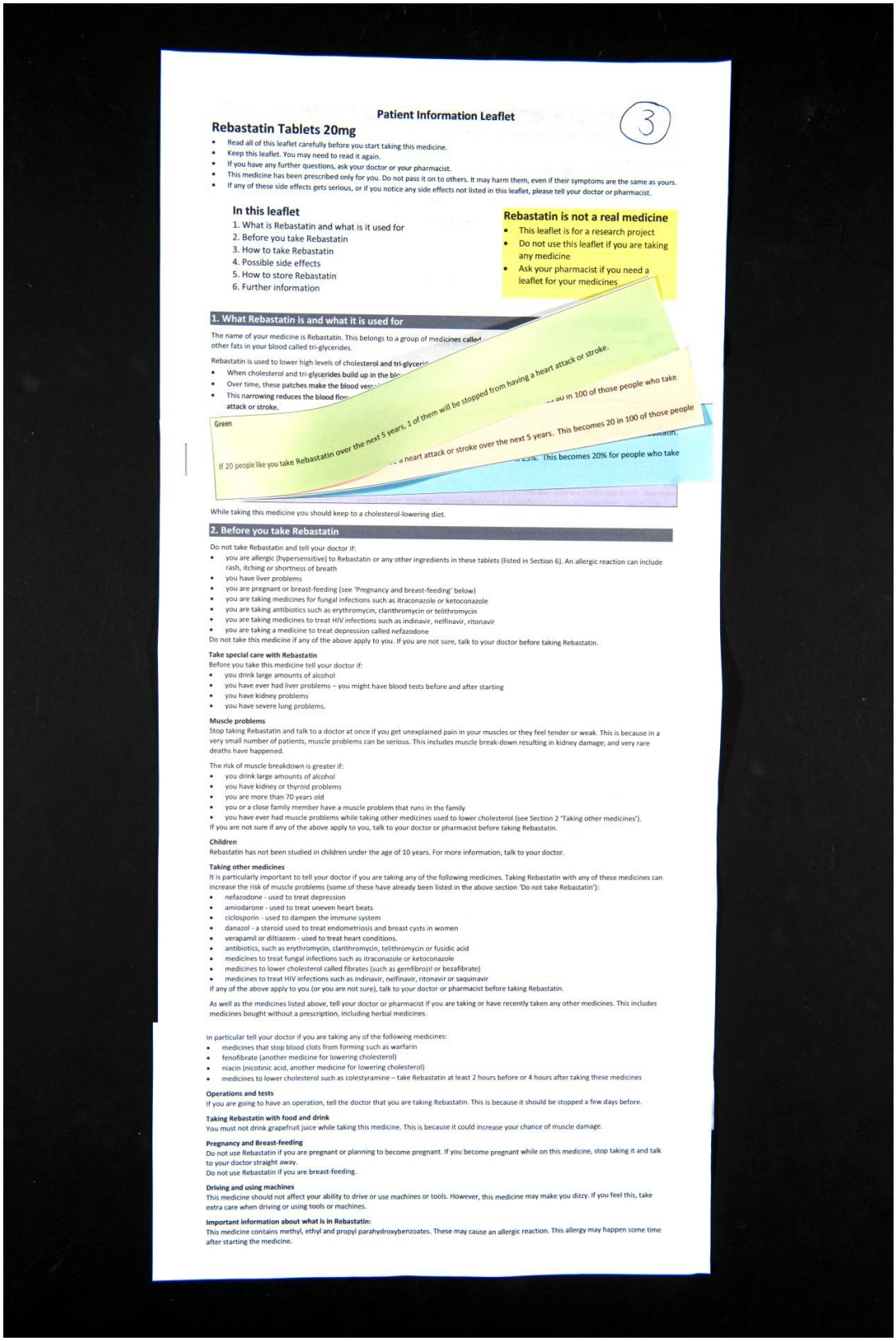
In 100 people like you, 75 will not have a heart attack or stroke over the next 5 years. This becomes 80 in 100 of those people who take Rebastatin.

This means that in 100 people like you, 25 will have a heart attack or stroke over the next 5 years. This becomes 20 in a 100 of those people who take Rebastatin.

GREEN:

If 20 people like you take Rebastatin over the next 5 years, 1 of them will be stopped from having a heart attack or stroke.

Figure 9: The four benefit statements - Rebastatin.



Patient Information Leaflet

3

Rebastatin Tablets 20mg

- Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This medicine has been prescribed only for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of these side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet

1. What is Rebastatin and what is it used for
2. Before you take Rebastatin
3. How to take Rebastatin
4. Possible side effects
5. How to store Rebastatin
6. Further information

Rebastatin is not a real medicine

- This leaflet is for a research project
- Do not use this leaflet if you are taking any medicine
- Ask your pharmacist if you need a leaflet for your medicines

1. What Rebastatin is and what it is used for

The name of your medicine is Rebastatin. This belongs to a group of medicines called
other fats in your blood called tri-glycerides.

Rebastatin is used to lower high levels of cholesterol and tri-glyceri
- When cholesterol and tri-glycerides build up in the bl
- Over time, these patches make the blood ves
- This narrowing reduces the blood flo
attack or stroke.

Green

If 20 people like you take Rebastatin over the next 5 years, 1 of them will be stopped from having a heart attack or stroke.

ou in 100 of those people who take

a heart attack or stroke over the next 5 years. This becomes 20 in 100 of those people

This becomes 20% for people who take

While taking this medicine you should keep to a cholesterol-lowering diet.

2. Before you take Rebastatin

Do not take Rebastatin and tell your doctor if:
- you are allergic (hypersensitive) to Rebastatin or any other ingredients in these tablets (listed in Section 6). An allergic reaction can include rash, itching or shortness of breath
- you have liver problems
- you are pregnant or breast-feeding (see 'Pregnancy and breast-feeding' below)
- you are taking medicines for fungal infections such as itraconazole or ketoconazole
- you are taking antibiotics such as erythromycin, clarithromycin or telithromycin
- you are taking medicines to treat HIV infections such as indinavir, nelfinavir, ritonavir
- you are taking a medicine to treat depression called nefazodone

Do not take this medicine if any of the above apply to you. If you are not sure, talk to your doctor before taking Rebastatin.

Take special care with Rebastatin
Before you take this medicine tell your doctor if:
- you drink large amounts of alcohol
- you have ever had liver problems – you might have blood tests before and after starting
- you have kidney problems
- you have severe lung problems.

Muscle problems
Stop taking Rebastatin and talk to a doctor at once if you get unexplained pain in your muscles or they feel tender or weak. This is because in a very small number of patients, muscle problems can be serious. This includes muscle break-down resulting in kidney damage; and very rare deaths have happened.

The risk of muscle breakdown is greater if:
- you drink large amounts of alcohol
- you have kidney or thyroid problems
- you are more than 70 years old
- you or a close family member have a muscle problem that runs in the family
- you have ever had muscle problems while taking other medicines used to lower cholesterol (see Section 2 'Taking other medicines').

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking Rebastatin.

Children
Rebastatin has not been studied in children under the age of 10 years. For more information, talk to your doctor.

Taking other medicines
It is particularly important to tell your doctor if you are taking any of the following medicines. Taking Rebastatin with any of these medicines can increase the risk of muscle problems (some of these have already been listed in the above section 'Do not take Rebastatin'):
- nefazodone - used to treat depression
- amiodarone - used to treat uneven heart beats
- ciclosporin - used to dampen the immune system
- danazol - a steroid used to treat endometriosis and breast cysts in women
- verapamil or diltiazem - used to treat heart conditions.
- antibiotics, such as erythromycin, clarithromycin, telithromycin or fusidic acid
- medicines to treat fungal infections such as itraconazole or ketoconazole
- medicines to lower cholesterol called fibrates (such as gemfibrozil or bezafibrate)
- medicines to treat HIV infections such as indinavir, nelfinavir, ritonavir or saquinavir

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking Rebastatin.

As well as the medicines listed above, tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines bought without a prescription, including herbal medicines.

In particular tell your doctor if you are taking any of the following medicines:
- medicines that stop blood clots from forming such as warfarin
- fenofibrate (another medicine for lowering cholesterol)
- niacin (nicotinic acid, another medicine for lowering cholesterol)
- medicines to lower cholesterol such as colestyramine – take Rebastatin at least 2 hours before or 4 hours after taking these medicines

Operations and tests
If you are going to have an operation, tell the doctor that you are taking Rebastatin. This is because it should be stopped a few days before.

Taking Rebastatin with food and drink
You must not drink grapefruit juice while taking this medicine. This is because it could increase your chance of muscle damage.

Pregnancy and Breast-feeding
Do not use Rebastatin if you are pregnant or planning to become pregnant. If you become pregnant while on this medicine, stop taking it and talk to your doctor straight away.
Do not use Rebastatin if you are breast-feeding.

Driving and using machines
This medicine should not affect your ability to drive or use machines or tools. However, this medicine may make you dizzy. If you feel this, take extra care when driving or using tools or machines.

Important information about what is in Rebastatin:
This medicine contains methyl, ethyl and propyl parahydroxybenzoates. These may cause an allergic reaction. This allergy may happen some time after starting the medicine.

Figure 10: Example of benefit statements in situ in leaflet.

3.5 Data analysis

The focus groups were audio-taped and 3 were transcribed by the researcher (RD) and 3 by an external company. RD and the moderator of each focus group met after each group to discuss the outcomes from the groups and consider dominant themes and striking perspectives. As a result, field notes were prepared to support the data analysis.

The general methodological approach to the study was described in chapter 3.2.1; what follows is a brief description of the approach used for data analysis. The **framework analysis** approach was used to analyse the data in this study. Data analysis in qualitative descriptive studies tends to use a form of **content analysis** and framework analysis is a well-described framework which can be applied to the content of depth descriptions collected through methods such as focus groups or interviews (Creswell, 2013).

Other methods, such as grounded theory, were considered. Grounded theory is characterised by a process where data collection and analysis occur simultaneously, with the aim being to use what is uncovered in the interviews to build upon during further interviews. This is particularly useful when very little is known about a subject (Glaser and Strauss, 1967). Framework analysis does not have an underlying epistemological grounding in the same way as grounded theory, but is instead a practical response to the challenge of undertaking qualitative research with specific outcomes in a short time scale. (Lacey and Luff, 2007) It is pertinent to the underlying intentions of this study, which are based in applied health research. The aim of this enquiry is not necessarily to uncover a 'new' theory but instead to generate new information and incorporate that with knowledge already acquired, to respond to objectives driven by policy on medicines information.

Framework analysis is well-suited to the pragmatic aims of this study. Its roots are in applied policy research and the approach is particularly appropriate for projects with explicit aims, such as this one. This method is being increasingly used in applied health research due to its systematic approach, which allows the researcher to undertake a meticulous approach to qualitative analysis leaving an effective and transparent audit trail (Smith and Firth, 2011). One criticism of the 'generic' qualitative descriptive approach is that it is not thorough and that its methods are not always adequately described (Caelli et al., 2003). The use of the framework approach addresses this issue

as one of the strengths of framework analysis is that it is systematic and leaves a clear data trail, which facilitates rigour (Spencer et al., 2003).

This method is effective for analysing cross-sectional descriptive data, enabling different aspects of the phenomena of interest to be captured (Smith and Firth, 2011). It is a thematic approach, which is considered less in-depth than grounded theory. However it usually provides richer findings than content analysis. Using the framework approach enables the researcher to develop a framework and analyse various aspects of the captured phenomena across the entire framework. This facilitates the production of an emergent account of the data which develops from a basic thematic description of the phenomena to a deeper description which allows for the creation of themes and typologies and can explore relationships across the range of interviews or groups.

The following phases were undertaken:

a) Familiarisation with the data

The audio-recordings were listened to and the transcripts and field notes were read several times, although were not double-checked for accuracy by other members of the research team. Emerging themes were considered and discussed with the research team.

b) Identifying a thematic framework

A thematic framework was developed, which is a list of concepts or themes that can be applied in order to organise or code the data into initial themes. The initial coding framework was developed from familiarisation with one focus group. Each line of the focus group was considered and initial thoughts on its meaning, were noted (appendix 10).

These initial themes were then refined and grouped into a thematic framework, which contained 9 substantive themes with a number of sub-themes. RD developed the initial framework and applied it to 1 focus group initially. Another researcher (JM) independently used the framework to code the same focus group as a reliability check. RD and JM compared the similarity in coding and any discrepancies or disagreements were resolved through discussion and consensus. Two further researchers (TR and PK) checked the applied framework to sections of the same focus group to assess its usability and relevance.

There was consensus among the researchers concerning the thematic framework developed for the headline section. There was less unanimity in applying the codes

associated with the benefit information; as a result some amendments were made to clarify definitions of codes. Comments from all members were taken into account, to ensure the framework was agreed.

c) Indexing

The thematic framework was applied to all the focus groups and used to code the data. An initial check of a segment of coding of an interview by JM confirmed unanimity in its application.

d) Charting

The data were then sorted according to each theme. This allowed the researcher to focus on the distinctions and details within each theme. The data were then summarised into a thematic chart where a matrix for each substantive theme was developed with sub-categories heading each column. The individual participants and their comments were charted across the rows. The aim of this process is to summarise the data, while retaining the original meaning in a format which allows for easy referencing between different cases (appendix 12).

e) Mapping and interpretation.

There followed a process of mapping and interpretation where the different cases were compared across the matrix, to develop a descriptive account of participants' opinions. There also followed a deeper, multidimensional analysis of the data where themes were described and grouped according to similarities and differences.

Figure 11: An example of the analysis exercise undertaken to develop the categories and sub-categories.

Typologies were developed across the cases, resulting from a cross-case analysis of the charts, with attention being paid to any deviant cases. The initial codes were grouped and refined until a clear and organised group of categories and sub-categories emerged. See appendix 16 for the refinement and emergence of the main categories and typologies.

An example of a chart was checked by another member of the research team (JM) who had also moderated the focus groups. JM was provided with an example of the data trail from interview to coding to charting through to the process of mapping and interpretation. The different stages of mapping and interpretation were discussed and the emerging categories agreed by consensus.

3.6 Study findings: Headline section

Overall there was a great deal of consensus within and amongst the different groups on the subject of the inclusion of a headline section in a patient information leaflet. The majority of the participants in all groups felt that a headline section would make for a positive addition to a PIL and, although a small number voiced concerns about the headline, all but one expressed a preference for the leaflet containing the headline section.

The findings were grouped into categories and sub-categories that related to the initial research questions that focused on opinions on the headline section in a PIL and how this might impact upon patients' satisfaction and understanding of their medicines. The key findings are given below under the following headings:

- Noticing the headline
- Engaging with the headline
- Influence of the headline
- Desirable features
- Format

3.6.1 Noticing the headline

- ***The headline was noticeable***

The preliminary information given to the participants drew their attention to the headline section. This means it was difficult to evaluate how noticeable participants found the headline section. However, most participants reported that they felt the headline section was something that drew their attention.

"I thought it was excellent. It leapt out and the white font on the grey background leapt out and was in your face and the fact that the paragraph had a grey background to it as well...I think your eyes are drawn to it." (F, 61, FG2, REBA)

Several features aided participants in noticing the section. The position of the headline at the beginning of the leaflet was identified as contributing to it being noticeable.

"I like it because it's right at the front, it's not at the back, you notice it straight away, it's like, you know, this is it, read this first because if you read it and then you get down there and you think, urgh, because it's repeating itself so if you've got it there it's... you'll read that first." (F, 62, FG4, REBA)

"Exactly, and it's near the beginning, so you don't have to wade through." (*F, 58, FG6, REBA)*

It was felt that the beginning of the leaflet was an important place because it enabled the reader to access important information immediately.

"I think it makes good use of the beginning of the leaflet. I think it is a good place for it. Because that's not immediately apparent in the first leaflet [usual leaflet], that that's the very beginning, or near the very beginning. Because the very beginning of the information leaflet is an important place and it should be giving you the stuff that you really want to know immediately there. I think it was well-positioned and it does function." (M, 60, FG3, JANA)

- ***It appeared 'important'***

The choice of wording, in particular the heading 'Important things...' was also viewed as something that drew some participants' attention.

"When I see 'important things', I would read it, just that word alone would draw me towards, to read this part. Not at the moment but when I see 'important things', you know, automatically I will want to read It". (F, 69, FG6, REBA)

- ***The shading is 'eye-catching'***

Several participants reported that the grey shaded box drew their attention and helped them notice the information:

"I think the tint makes you feel it's important to read, it's catching your eye. Otherwise it's all just the same thing."(M, 64, FG1, JANA)

However, there was some discussion in the groups about the choice of colour for the tint, with some participants concerned that the choice of black font on a grey tint might reduce the readability of the text.

"In another leaflet you might use a different coloured tint altogether that made it a little bit more legible." (F, 68, FG1, JANA)

There were frequent discussions in several groups about a similar feature on the leaflet, which was an artefact of the research process. This was the yellow highlighted section that stated 'This leaflet is for research purposes'. It was common for participants to prefer the yellow tinted box to the grey colour chosen for the headline section. Despite this attraction to the yellow highlighting, participants were aware of the potential limitations of using colour in leaflet and some expressed concerns about cost as well as readability for visually-impaired populations, such as those with colour blindness and older people. One participant spoke of having a problem with her vision and how she had found the shaded section easy to read as it helped it stand out.

> *"I find the grey box very useful because I don't actually see white, I see a shade so that being shaded makes it stand out a bit more, yeah. That definitely drew my attention straightaway." (F, 67, FG5, JANA)*

Only one participant expressed concerns about how noticeable the headline section was, as she thought it was a typing or printing error:

> *"I looked at it purely because I thought that had been some typing error or photocopying error. The grey didn't stand out for any other reason, so that was the reason I looked at it. I wouldn't say I was particularly impressed with it. The font was slightly larger than the font on the leaflet in that area, but it didn't attract me. It certainly didn't make me look at that bit more than the first one, except that at first I thought it was a printing error." (F, 56, FG3, JANA)*

However, other participants in the same focus group felt that even if the reader initially thought the shading was an error it had still drawn their attention and that it would help them engage better with the information.

3.6.2 Engaging with the headline

- ***Current leaflets are challenging to engage with***

One key finding that emerged was the difficulty that participants had in engaging with and understanding current PILs, which they felt were unappealing, too technical and generally quite a challenge to read.

> *"I always read, but I do find it far, far too difficult and too much information" (F, 70, FG2, REBA)*

> *"This (leaflet) is a very long piece of paper and it would put most of us senior citizens off" (F, 69, FG, REBA)*

Patients found them time consuming to read and the information difficult to navigate. It was apparent that several participants undertook different behaviours to help them manage the volume of information in a leaflet. This included circling and highlighting the

text, ‘skimming’ through the leaflet and picking out information that was perceived to be relevant. These behaviours were aimed at making it easier to obtain relevant and important information.

“I read them. They can get complicated. I tend to make notes if it’s of reference to me, you know, circle things that I’m also taking.” (M, 61, FG4, REBA)

- ***Reduces the challenge of reading the leaflet***

As a result, for several participants the headline section was a welcome addition to the leaflet, as they felt the summary aided them in trying to make sense of the information provided.

“I think it’s recognition that the whole of the leaflet is quite an arduous read that you have to plough through it. So I feel they are offering some new major points, important points, right up there. It almost shows a bit of respect for the patient having to read this, because you might need a summary. It doesn’t mean that you don’t read the rest of the leaflet, because you do! It highlights the important points. That’s what it says it is doing, and as far as I can see, that’s what it does.” (M, 60, FG4, JANA)

The inclusion of the headline section appeared to ease the challenge of accessing relevant information in a document that patients felt was difficult and technical. It lessened the cognitive burden apparent for many patients that can result from an overload of information and so stopped the leaflet feeling quite so daunting:

“I think that’s a brilliant idea, so I mean if you don’t want to go through the daunting task of reading the whole leaflet, it draws your attention to that which means that that is the most, what she says, important things.” (F,62, FG4, REBA)

“I think that it’s quite clear and less intimidating than some of the more detailed ***stuff you get later.” (M, 64, FG5, JANA)***

- ***“It’s more user-friendly” (F, 70, FG2, REBA)***

Several participants also felt that the headline section was a technique that responded to how arduous some people find the task of reading the leaflets and finding relevant information about their medicines. The headline provided a useful summary that patients reported as easing the burden of reading what is perceived as a challenging and boring piece of technical writing. It was viewed as more user-friendly:

“ I preferred it to the first one because it’s a bit of a summary and you need a bit of a summary at the top if you are just having a bit of a quick read” (F, 54, FG3, JANA)

3.6.3 **The influence of the headline section**

Participants reported that the headline section had the potential to impact positively upon both their satisfaction and understanding with the information they received, but also potentially upon their medicine-taking behaviour.

- ***The influence upon patient satisfaction with medicines information***

Participants reported they were satisfied with the contribution the headline section made to the leaflet:

> *"I think it's very good because it's bringing the main, the most important things…so even if you don't see the rest of it you are reading the most important things" (F, 57, FG4, REBA)*

> *"The box is brilliant" (F, 63, FG4 REBA)*

There was a good deal of enthusiasm about the inclusion of the headline section and all participants except one said they preferred the leaflet with the headline section. The headline was viewed as concise, informative and a positive addition to the leaflets.

> *"Yes, it's very short and sweet. You can read it and understand it". (P5, F, 68, FG6, REBA)*

- ***The influence on knowledge and understanding about medicines.***

The headline section was viewed as a technique that had the potential to improve a reader's ability to understand more about his or her medicines.

> *"I think it would encourage more people to read the highlighted section and if you made that section good enough and accurate enough and short enough and clear enough, they would pick up the gist of it very quickly through that highlighted section."(M, 63, FG1, JANA)*

Current leaflets were viewed as lengthy and impenetrable whereas a positive attribute of the headline was that the information was presented in smaller, bite-size chunks, which several participants felt, might help them to retain information.

> *"I think that having it précis so it's something that relates to you very quickly and which tempts you to go on and read a bit more about it, providing then you don't have to go through the whole leaflet to get to it. I think you would be very tempted to read that section." (M, 56, FG3, JANA)*

> *"It was a little list of do's and don'ts that you can cross reference with the leaflet. Even if you can't be bothered to read what is written in the rest of the leaflet, you can follow that grey box and you'll be OK." (M, 65, FG2 REBA)*

- ***The influence on health behaviours***

There was no evidence that the headline section would impact upon the medicine-taking behaviours of any of the participants, nor was there any evidence that it would significantly impact upon informed decision-making, i.e. encouraging participants to make decisions that were in line with their values. However, it was apparent that the headline section had the **potential** to influence attitudes and behaviours towards the use of medicines information. Throughout the focus groups, both positive and negative repercussions were discussed in response to the provision of information containing a headline.

a) Encouraging the non-reader

The headline was viewed as something that might encourage people who were usually reluctant to read their leaflets, or who found the information difficult to process, to read more about their medicines in the first instance. Some participants who stated they did not always read their leaflets reported that they would be keener to read the headline section.

> *"I think what I would do; I would scan it (the headline section). I wouldn't read all of it, but I would scan it… would think 'right, that's not relevant for me, not relevant for me'. But yes, I would actually read it." (F, 70, FG5, JANA)*

Some participants still reported that they would read it especially if the prescription was new.

> *"I think I'd be more likely to read it earlier on." (M, 59, FG 2, REBA)*

b) Discouraging the reluctant reader

A small number voiced concerns that the headline section might actively discourage them from reading the rest of the leaflet:

> *"Personally for me, I think I'd read less of the leaflet, because those things down there aren't relevant to me, so I wouldn't read them, unless it was the first time and if it was the first time then I would probably read them because I do tend to read everything the first time" (F,56, FG 3, JANA).*
>
> *"The only thing is, that some, who would not ordinarily, or who might not read the leaflet if they think that's the most important thing, will they think the rest doesn't matter? It's quite possible." (M, 89, FG1, JANA)*

One participant considered that this decision was the prerogative of the reader, who needs to take responsibility of her own medicine-information needs.

"I think it's very good because it's bringing the main, the most important things so even if you don't see the rest of it you're reading the most important things. But then, as I say you cannot spoon-feed everyone. People are adults, they have to take responsibility" (F, 57, FG 4 REBA)

c) Overall impact

Concerns were expressed that the headline section would not engage all users of medicines and that it had the potential to discourage further reading of the leaflet. However, participants acknowledged the challenge in communicating about medicines effectively and noted that although many users of medicines were unwilling or unable to engage, the headline section might benefit more people than it would impact on negatively. The communication of medicines information was frequently viewed as a two-way process between the sender and the receiver; participants felt that there was responsibility on the receivers' part to engage in this process.

On balance, it was considered that the inclusion of the headline section was still beneficial as it may encourage those who wouldn't usually read a leaflet to read the important points.

"If you did see the summary that might be all that you would read. I'm the sort of person who would read it anyway. But I feel that some people, who might not read a leaflet, might not read that and go any further, but as you say, it does seem that it's the important points and these are the bits that we need to tell them and I think it's a good thing." (M,51, FG 2, REBA)

Other concerns included that the headline section was not very influential and that it might not contribute to significant changes in behaviours that promote and support the safe and effective taking of medicines. However, again it was accepted that the headline section was an improvement to what was available already and, while it might not have a substantial impact on the safe and effective taking of medicines (although this was not assessed during this study), it may help people to better engage with their medicines information and inform them about important aspects:

"I think, particularly in elderly people who may have sight problems or who may not feel comfortable reading, and I think they may feel comfortable in the knowledge that they may not have to wade through the leaflet. But it might not change what they do…but they might have more knowledge than they would otherwise." (F, 61, FG 2, REBA)

Despite some minor concerns about the headline section discouraging the reading of the rest of the leaflet, most participants felt that the headline was a concise and

informative précis. They expressed the view that it treated them with respect, helped them to engage with their medicines information, encouraged a better understanding of medicines and had the potential to encourage some readers to at least engage with a small, but important part of the leaflet.

> *"What I could picture somebody doing is cutting that out and sticking it on their notice board or sticking it on their pillbox, something like that. Because that's a real memory aid…that's it all in a bullet point! And then they have got a full copy, because they have probably got more than one of these, sitting in the back of a drawer somewhere. And every other one, they just bin." (M, 65, FG 2 REBA)*

3.6.4 Desirable features of a headline section

- ***The content of the headline section***

Many of the participants appeared satisfied with the content of the headline as presented. They felt it was concise, informative and reflected what they wanted to know about their medicines:

> *"I prefer this one as well (Headline leaflet) because it is everything about the medicine in a nutshell, there and then." (F, 69, FG6, REBA)*
>
> *"Also, what it contained. I felt it was very, very helpful and it referred to other things within the further content of the leaflet and you could follow that up if you wanted to. I thought that was really good." (F, 61, FG2, REBA)*

When asked about their preference for the type of information that should be included in a headline, it was apparent that safety concerns were a high priority. Participants wanted to know about important, pertinent issues with their medicines, especially issues that they felt might be potentially harmful:

> *"I preferred it (the headline leaflet) to the first one because I think it's a bit of summary and you need a bit of a summary at the top so if you are just having a bit of quick read...it should have the main things, the most dangerous things...If you take it with this, then you will die!" Those sort of things. Then if you need to find out a bit more you can read the rest of the blurb underneath it. But I think a summary with the vital facts is really useful." (F, 54, FG3, JANA)*

Some of the issues commonly reported as desirable in a headline section included drug interactions, contraindications, side-effects, allergies, how much and when to take, where to find further information, what to do if you have a problem.

It was commonly reported that it was useful for the headline section to contain some information about what the medicine is for. This information appeared to help provide context to both the medicine and the information provided in the headline and enable the individual to apply the information to their own situation.

"And I love the fact that it tells you what it's for. You know, the first point is that it is for migraines. Because I was given lots of things for chemotherapy and I didn't know what they were for and I was trying to look at them and see because I didn't know. I wanted to see which were steroids and which were...because I didn't want to get them all mixed up. And it's easier if it's very obvious on them." (F, 54, FG3, JANA)

While there was a clear tendency for participants to want their attention drawn to key safety messages, there was some conflict on how this should be achieved. For some participants the headline section was the ideal opportunity to provide 'in your face' warnings about the potential danger of the medicine.

"To me the issue is, rather than having this (refers to headline). It's nice, but it's verbose. It still takes some reading. But to have that 'take care' or 'danger if', in black and white, so it's really in your face...It needs to frighten you...'danger if' and at the bottom 'get back in touch with your doctor'" (M, 56, FG1, JANA)

Some older participants found this approach to be concerning and something that could potentially discourage them from taking their medicines.

"I'd find that frightening...the old people that I am living with, if they saw 'danger' they would get frightened and, like my friend, just throw their tablets away. (F, 78, FG1, JANA)

The need to strike a balance between informing about potential harms without being too alarmist was noted.

- ***Concerns about repetition***

Another area where a need for balance was identified concerned the amount of repetition in the leaflets. A small, but vocal minority in FG1 disliked the amount of repetition.

"I agree with you in so far as the information is included word for word and line for line in the shaded section to the section which is headed in this leaflet ... I think we are in danger of making the leaflet bigger again by putting that section in, when the information is already there. I would have thought they could condense the information and have a new heading for it and that new heading would be 'important things that you need to know about JANA and what it is used for' to combine the two rather than, you've got it there and you've got it here, you can just rule them 2 out and put a combined new paragraph in, that's my thought on it." (M, 63, FG1 ,JANA)

The concern about repetition stimulated some debate about the role of the headline in FG1, which was not apparent in the other focus groups. There was conflict about the amount of repetition, in particular what constituted too much and what was in fact a necessary emphasis on key information.

One participant noted the need to strike a balance to ensure the headline section functions in providing and reinforcing clear and concise essential information, but keeps superfluous repetition to a minimum:

"If you cut out all the repetition then it could become confusing. But you need to watch that you don't repeat things that don't need repeating and there are a lot of superfluous bits that you could cut down on and still make it clear." (F, 68, FF 1, JANA)

3.6.5 The format of the leaflet

- ***"If they look good it might encourage you to read them." (M, 60, FG4, JANA)***

The headline format chosen was popular; participants felt it was well-set out and noticeable. The headline appeared to achieve its objectives but was viewed as functional, basic and visually unattractive.

> *"If they look good it might encourage you to read them. And this (the headline section) is almost industrial grey and it has a very fine print and a whole list of things that are very uninviting" (M, 60, FG3, JANA)*

It was apparent that the users of medicines desired information that was more attractive and aesthetic, but which remained functional:

> *"The other thing that bothers me, they are all the same the leaflets. Not one contains any icons, any pictures, any logos, any exclamation marks, just to make it [a] more attractive and [b] more pleasant to read. You don't need a lot, just little logos, icons which will help. All you have got is thousands of words, all mingling into the other" (M, 76, FG1, JANA).*

Many suggestions were made as to the type of techniques that might help and such suggestions varied. Using a coloured headline was a popular suggestion, as well as the use of bold font, a large font size, logos and icons, underlining, italics, upper-case lettering and the use of a border (rather than a shaded box). There were many such suggestions but, at the same time, it was clear that participants were cautious about using too many techniques, preferring to 'keep things simple'. They also expressed a desire for 'uniformity' of the leaflets and for the leaflets to be aesthetically pleasing.

- ***Sign-posting***

One final recommendation about the headline section referred to the issue of sign-posting, to allow the reader to cross-reference within the leaflet. This issue was only raised in one group where some participants reported difficulties in using the headline to find the more detailed (maybe better) information that was further down in the leaflet.

"I think it's quite useful to have that there and I do think that something like that might be a bit better in being a bit bigger and then having your cross-referencing. So you have your important information you've got it and if you read this bit alone you've got more information, but if you want more you know where to find it..." (F, 68, FG1, JANA)

3.7 Headline discussion

The aim of this qualitative study was to examine the potential impact of providing a headline (or summary) section in a regulated PIL on the satisfaction, knowledge and potential medicine-taking behaviour of medicine-users. The findings are supportive of the inclusion of a headline section in a regulated PIL and include suggestions for improvements made by participants.

The headline section, presented in this research, as a summary of key points of information about a medicine in a grey shaded box, was seen as a valuable addition by almost all participants. There was very little dissent or conflict expressed about the inclusion of the headline section.

The headline section was viewed as noticeable, something that drew the eye and appealing. A key finding was how daunting reading an existing leaflet was perceived to be. This is something that has been noted in previous research, including a systematic review which identified how patients felt there was a significant gap between patient information leaflets and information that patients would value (Raynor et al., 2007). Despite improvements to leaflets produced since the review, possibly resulting from guidelines which aim to improve the readability of PILs (European Commission, 2009), it appears that patients still perceive shortcomings. Patients still view the information leaflet as technical documents that are difficult to read and use.

3.7.1 Key Finding: The headline section reduced the burden patients felt in finding important and relevant information

The headline section was viewed as a potential solution to the daunting prospect of reading existing leaflets. Participants felt it responded to the arduous and challenging task they had themselves of summarising the key, important facts about their medicines. They felt the inclusion of the headline section treated them with respect and lightened the load of retrieving important information, in comparison with existing leaflets.

Cognitive load theory could be used to explain participants' acceptance and high levels of satisfaction with the headline section. This theory describes how cognitive resources are focused and used during learning and attempts to provide a framework to illustrate how cognitive processes and instructional design are linked (Chandler and Sweller, 1991, Sweller and Chandler, 1991). According to the theory, complex instructions are better understood when design is focused on reducing the cognitive load placed upon the reader when engaging with them.

The theory assumes that an individual's cognitive load may vary due to both intrinsic and extraneous factors. The intrinsic load refers to the inherent difficulty of the information content. Medicines leaflets are inherently complex, they can include difficult concepts, and this cannot always be altered because of the legal framework. However, according to cognitive load theory, the use of good instructional design, which pays attention to the different factors which impact upon understanding, can change the extraneous cognitive load placed by the materials onto the reader. It is feasible that the headline section works to reduce the extraneous load, which aids understanding and increases the satisfaction the participants experienced after receiving a leaflet with a headline section (Paas et al., 2003, Sweller and Chandler, 1991).

The theory describes several different instructional effects which can be used to reduce extraneous cognitive load. Some of these effects are relevant to the headline section and it is probable that its use contributes to understanding and satisfaction in the following ways:

(a) It is plausible that the inclusion of the headline section in a large body of text contributes to the **redundancy effect**, which occurs when unnecessary information is presented. A common complaint about the leaflets in general was the amount of information they contained that participants felt was not relevant to them. The headline section potentially reduces the superfluous information patients wrestle with when they first encounter a leaflet and helps prioritise key issues and facilitates understanding.

(b) Participants reported using several coping techniques to manage the amount of information provided in a PIL. For example skimming the leaflet, or picking out the important parts. It was apparent that, for the participants, the key information about the medicine was scattered amongst the leaflet, and their attention was split by searching amongst the different sections to find the information relevant to them. This could potentially increase the chance of a **split-attention effect** occurring, which according to cognitive load theory can cause illegibility. Reducing the split-attention effect by

consolidating the essential information might potentially increase legibility of the leaflet. (Cooper, 1998, Paas et al., 2003)

(c) Cognitive Load Theory also supports the theory that '**chunking information'** together minimises extraneous load and increases the legibility of an instructional document (Cooper, 1998). The aim of the headline section is to consolidate key information on the safe and effective use of medicines and the findings support the theory that chunking of information is beneficial to readers.

3.7.2 Key Finding: Patients noticed and engaged with the headline section

Most participants noticed the inclusion of the headline information, even if (in one case) it was because they felt a mistake had been made during the printing. Most participants felt the headline section drew their eye and provided them with important information they needed to know. Participants spoke highly of the headline section, often stating that they could see the difference between the headline leaflet and the usual leaflet immediately and that their initial reaction was that the difference was an improvement.

While this was commonly reported, and something that participants were enthusiastic about, it is important to note that the ability of the participants to notice the headline was not tested. The headline leaflet was provided with instructions on how to find and use the headline section, which would impact on perceptions of noticeability. In a natural setting it is possible that the findings might be different.

3.7.3 Key finding: Good design is essential

Participants valued well-designed leaflets which looked attractive and were well set out. Current leaflets were perceived to have significant failings attributed to poor design. They were viewed as boring and complicated and did not encourage patient engagement. The groups had several ideas about improvements, which included the increased use of colours and symbols to help make the leaflets more aesthetically pleasing. A common concern was the size of the font, and this has been noted in previous research (Raynor et al., 2007).

The headline section was viewed as an improvement to the leaflet, although it was apparent that a segment of the groups found it to be similar to the current leaflets in its lack of appeal. A general recommendation is to improve the aesthetic of the leaflets and

pay attention to good design. If a headline section is to be included, attention should be paid to ensure it is aesthetically pleasing, yet remains functional and usable.

There is little research in this field that focuses specifically upon the use of summary sections, such as a headline section, in medicines information. The use of techniques such as boxes and outlines have been suggested to be problematic in instructional design generally, because they can separate the information from the main body of text and this can impact negatively upon a reader's comprehension (See chapter 2). Hartley suggests that there is little evidence for these concerns, but their use remains controversial (Hartley, 2004).

3.7.4 Key findings: What information is important?

The headline sections for both Janatripatan and Rebastatin were seen as having a good balance of information. Section 4.5.2 describes the list of key information identified by the MHRA as important to consider for inclusion in a headline section. The same types of information were identified as important in the focus groups. There were few deviations from this list, and the list of key issues did not differ significantly in any of the groups.

The issue of the sign-posting of the information contained in the headline was raised during one focus group. Several participants stated that they desired each piece of key information in the headline section to be more effectively cross-referenced, so they could find it more easily in the main text. This group received the leaflet for Janatriptan, which contained 2 textual sign-posts in the headline section which directed the reader to the section of the leaflet where additional information could be found; however it did not appear to be commonly noticed in the focus groups. The issue of sign-posting is important. The reader should be able to find important information about his or her medicines with ease and attention should be paid to ensure that the headline section facilitates this.

3.8 Study findings: Benefit information

It was apparent that for most participants the benefit information presented in the focus groups provoked a range of strong responses. The individual responses were often varied and fluid, changing throughout the course of the focus groups as participants engaged with the information and shared and explored new perspectives. This meant that for some participants, their initial responses transformed as they developed a new

understanding. However, frequently participant's initial responses were often very pervasive and did not appear to change when the participants were asked again about their preferences at the end of the focus groups.

Four main categories were identified which map the range of responses about the benefit information, they are as follows:

1. Initial reactions to general benefit information
2. Preference for the inclusion of benefit information and preference for format.
3. Barriers to engaging with benefit information
4. The impact of the benefit information

The first category of findings aims to present the participants' perspectives based on their initial 'gut' feelings and reactions. There follows a category that describes the preference for the different formats of benefit information and maps the range of response about each statement. Category 3 presents the multiple barriers to engaging with the benefit information and explores how this might impact upon decision-making about medicines. The final category explores the impact of the benefit information on understanding and knowledge and explores how patients reported this might impact upon their future medicine-taking behaviour.

3.8.1 Initial reactions to general benefit information

There was a range in terms of participants' ability to understand the information within the groups. It was apparent that the benefit information provoked varied initial, gut reactions, ranging from acceptance to hostility. The strongest negative reactions were reserved for the numerical data in particular, and where possible the reactions described are differentiated between the textual and the numerical format. Four different types of participant initial response to the benefit information were identified.

- ***Non-engagement***

One type of response noted from several participants was that of non-engagement, where the participant did not like, nor wish, to engage with the benefit information. (This was particularly evident when numerical benefit statements were discussed). Textual benefit information was tolerated, but viewed as unnecessary or superfluous. This response was characterised by a lack of interest through to a strong dislike for the benefit information.

These participants frequently stated that they would do what the doctor advised and that they did not wish to engage with the benefit information. They did not appear to be active participants in decision-making, preferring to take without question medicines

that the doctor prescribed. However when questioned on their understanding of the information, they did seem potentially able to understand the benefit information and could express opinions on the different formats when asked to do so. However, the benefit information was not welcomed in a PIL. These views tended to be immovable and fixed.

- ***Non-understanding***

The information presented was challenging for most participants and many struggled to understand it. However, there was a small group who did not appear to understand the information at all. It was very difficult to gauge the opinions of this group on the different formats and often when questioned about a preference for format, or on how the information might impact on them, they would answer with a vague question about medicines information in general.

> *"I liked the purple [textual] because it was a nice soothing colour, it reminded me of lavender" (F, 54, FG3, JANA)*

Their opinion again tended to be immovable and fixed, with a lack of interest in the inclusion of benefit information (particularly in numerical form) in a PIL.

- ***Positive appreciators***

A small number of participants expressed a positive response about the inclusion of benefit information. This group appeared to understand the information and welcomed its inclusion in a PIL whole-heartedly. For this group, the information led them to feel they were being treated with respect and enabled them to make choices about their medicines. The positive appreciators' opinions were subject to change when discussing preference for format, but they remained positive about the inclusion of the benefit information itself.

- ***The concerned majority***

The majority of participants found the benefit information very challenging to interpret, irrespective of format. For this group the benefit information induced a number of emotional responses. These responses were often fluid and changed through the course of the focus groups as the participants had the opportunity to talk about the benefit information and explore different perspectives and contexts. This group was not homogenous but incorporated a number of different initial reactions to the benefit information, which were often emotional. Several different types of initial response were noted:

a) Surprise at the poor benefits

It was common for participants to express shock and surprise at what they perceived to be poor benefits of the medicines. The benefit information was viewed as negative and participants were genuinely surprised at how few would benefit from taking the medicines. The likelihood that people would benefit from taking the medicines was not as good as they expected.

A few participants expressed their opinions on what a good benefit would be, suggesting that many may over-estimate how likely their current treatments are to benefit them.

> *"It was a surprise, but I wasn't surprised at how many people benefited. It was how many didn't. And I just presumed, maybe because I've never had a migraine, but that these medicines, say maybe 90% did benefit the patient." (F,56 FG3, JANA)*
>
> *"19 out of 20 is good pill." (M, 89, FG6, REBA)*

There were no differences in perspective for either of the medicine groups. Both medicines were perceived to have poor benefits and were not as good as expected.

b) Fear and nihilism

The benefit information had a very unsettling effect on many of the concerned majority. Several people were upset about the inclusion of the 'numerical' benefit information: they reported being frightened by the numbers and found this information depressing. The inclusion of the numerical benefit information appeared to shake these participants' faith in their medicines.

> *"If your doctor is prescribing you medicine then you trust your doctor. That they are prescribing the right medicine and you have a kind of belief system that if he is prescribing that then it's going to be better and if, for some reason, something happens then you go and speak to your doctor. But I think it [the numerical formats] takes away that belief that you're going to get better if you start seeing these numbers. So, the medicine might not work as well because you've already in your mind said as well." (F, 58, FG6, REBA)*

A large concern some participants held was that this information would remove faith in medicines so much that the medicine would no longer work. They believed that negative thoughts about the medicine would impact negatively on effectiveness.

There was turmoil for some participants as they tried to come to terms with the revelation that the medicines were not as effective as expected. People either expressed a loss of faith in their medicines or lost value in the information they were given, declaring it meaningless and questioning the point in taking their medicines. This

was an emotive and upsetting process and characterised by high states of anxiety, concern and nihilism, as the meaning and hope that the medicine once represented, dissipated, leaving fear and confusion.

> *"I just thought this is preposterous! A friend of mine is actually in this situation and I was telling her about this and she said 'That's what's on mine and I absolutely give up'. It made her so depressed and she just thought 'What's the point in taking this if I've only got this chance?' And I know my brother would think 'why bother?' And it's almost like playing God to say, because there is no guarantee that anybody's not going to have a miracle cure. So, no. I thought they [the benefit statements] were quite crazy." (F, 70, FG2 REBA)*

c) Denial of the 'facts'

After the initial response of fear and nihilism there occasionally came a second response which saw the veracity of the benefit information being disputed. Participants appeared to try and deny the 'facts'. Some wished to ignore the information entirely and did not want to see it included in a PIL.

> *"To me there is no help in at all in the information it's giving me. It's very negative and I don't want to know about it." (M, 89, FG6, REBA)*

Others disputed the accuracy of the information. It was common for participants to express a mistrust of statistics and to question the trustworthiness of how the numbers had been generated.

> *"People who know the statistics though, they say 'the old "lies, damned lies and statistics."' Can you trust them though? Do you know the parameters? It can be meaningless." (F, 69, FG2, REBA)*

The use of statistics and numbers in wider society, particularly in advertising, appeared to bolster the suspicion of the use of statistics, as people were aware of the ways in which 'bad science' has been used to advertise beauty products, supermarket deals and broadband speeds. The applicability of the statistics to the individual's situation was often deeply debated.

> *"Well, they can only give averages can't they? They test on a thousand people…and then they get averages from that and there will always be exceptions." (F, 54, FG3, JANA)*
>
> *"It's such a generalisation all of this, because nobody can tell you what's going to happen to everybody." (F, 70, FG2, REBA)*

A suggestion to overcome this mistrust was to include the source of the information in the leaflet with the benefit information.

"You could even say 'clinical trials have shown that', because people then know that's what this is and it's not something that has just come out of the GP's head" (F, 61, FG2, REBA).

These feelings of statistical mistrust were not universal, with other participants trusting the source of information and accepting the information given:

"I would make the assumption from any information given that these numbers, which are included in this leaflet that they haven't been plucked out of the air. That there are clinical reasons behind it. So it doesn't worry me. And I wouldn't nit-pick bits off it" (F, 59, FG2, REBA)

Some participants voiced concerns that the other participants were downplaying the relevance and meaning of the information because the information provoked feelings of discomfort. Two participants in particular were dissident voices, speaking against their fellow participants and questioning their haste to dismiss the reliability and meaning of the numerical information.

"But it's obviously not meaningless. It may not mean what you want it to mean, but it means something" (M, 69, FG2, REBA)

There was a definite conflict about which type of benefit information is valued and despite this denial of the 'facts', it was apparent that the participants still wanted benefit information in their patient information leaflets. They just didn't want the (poor) benefit information provided in the study.

"There does seem to be a bit of a difference between everybody's view of choosing the purple [textual], but what comes out in the discussion is that we want to know the facts. Is that a fair comment?" (M, 60, FG3, JANA)

3.8.2 Preference for and the influence of the format of benefit information

- **Textual benefit information**

There was a good deal of enthusiasm for the textual benefit information; its inclusion in a PIL was popular in the focus groups. It was almost always preferred to the original leaflet, without such information. Participants found the textual benefit information to be very informative:

"If [you] do get migraines you need to understand what was happening. I need to know what's happening and what will improve it. That would help me having that information." (F, 54, FG3, JANA)

One participant felt the textual information reinforced the GP's decision to prescribe the medicine:

"I think the doctor is prescribing this tablet...The doctor's going to guess. He has an array of tablets so he has to decide. If he decides on this one, I think at the same time as prescribing he'll say, "this may help you, it may not, but try it" and I think with that information, and backed up by the purple [textual], we won't lose anything." (M, 76, FG1, JANA)

The textual information was always viewed as the most positive and hopeful of the different benefit statements:

"If I was glimpsing at the leaflet, I'd want to see the purple one that gives you confidence in taking it." (F, 52, FG2, REBA)

"I've got here, the mauve one [textual]. It's the best. Keep it clear and simple and optimistic." (F, 69, FG2, REBA)

It was also preferable because it was viewed as simple, but this was in comparison to the numerical formats, which were viewed as complex and tricky to understand.

"The simplest way of giving information is the purple one [textual]; there is no need for a calculator." (M,64, FG1, JANA)

However, a small group of participants noted that the purple information was often quite vague, and while it included further information about how the medicine would benefit the patient, it was vague about the likelihood and more information was required for a patient to understand this in context.

"I didn't like the purple [textual] because it was a bit too vague." (F, 79, FG4, REBA)

So for some participants, after initially preferring the textual information, when they later assessed how their understanding had been affected by the various statements, it became apparent that the textual statement did not inform very much. These participants began to feel that they needed information added to the textual statement to understand more about how likely the medicine would be to help them. There was a constant conflict between simple information and information that put the benefits into perspective. For some participants a compromise was to incorporate numerical information into the textual statement.

"If you're going to try and simplify it, why don't you just use the purple one [textual]...then on the back you put all the positive statements like you've got on the orange [natural frequency]." (M, 64, FG5, JANA)

For one participant it became apparent that the textual information, which was her preferred format initially, had misled her. During a discussion about using the benefit information to inform a decision on purchasing an OTC medicine, she acknowledged that she would be more likely to purchase a medicine that included a textual benefit statement and would not choose one that contained a NNT statement, even though she

could now see that the medicines had the same benefits. For some it appeared that the textual statement offered an illusion of benefit, which was removed when the numerical information was considered alongside it.

Other concerns about the textual information included that it was repetitive and that the information provided was already mostly included in the leaflet and that in total it was just too much information.

There were a few suggestions on improvements that could be made to the textual statement. For example changing the wording of the benefit statement so it contained the word 'may' instead of 'can' to convey the uncertainty that participants experienced when reading the numerical information, but without resorting to the 'frightening' numbers.

- **Percentages**

On the whole the percentage format was viewed as complicated. People found it 'mathematically confusing' and muddling. Many participants were inexperienced with using numbers and did not find the percentage format intuitive. For those who were familiar with using numerical data, such as in their working life, the percentage format was more popular.

> *"It might be an age thing that, I don't know. I'm a teacher but we're probably all quite au fait with percentages, so we don't mind them" (F, 50, FG5, JANA)*

Where people were able to engage with and understand the percentage information it was apparent that it helped to put the benefit information into perspective and provided some comparative information about those who didn't take the medicines. As a result people could make an informed decision about how likely the medicine was to benefit them:

> *"When I first read the sentence and it said in '100 people like you', I thought it meant taking the tablets, 'people like you', that's the first thing I thought. So I got really confused when I got to the second sentence I thought 'it doesn't mean that!' I had to read that again. It means people with migraines; it'll get better in 32% of people anyway, on its own'" (F, 68, FG1, JANA)*

However, it was apparent that for some participants this comparative information was confusing and difficult to interpret. Occasionally participants struggled to understand the relevance of providing this baseline information, as this extended excerpt from the first focus group shows:

> *"Participant 5: Why do we want to know that people who don't take the tablet? Why do I want to know the results of people who don't take the tablet? It's not important to me, if somebody is not taking the tablet. It's not important to me...the*

only thing that is important to me is 57% of people of people who take this tablet are better off…

Participant 6: They're not, that's exactly what they are not! Only 25 are better, not 57, because 32 will get better anyway…

Participant 2: The numbers are semantic, let's say 57% are better if they take the tablet, then you don't need to know how many people are better off if they don't take the tablet

Participant 6: But you do need to know

Participant 2: But let's say that 57% are better off and you don't need to know how many people are better off if they don't take the tablet...Say 57% are better off if they do take and actually 93% are better off if you don't. Now do you want to know about it?

Participant 5: No, all I want to know is...

Participant 2: But I've just told you that 93% of the people will be better off if they don't take the tablet

Participant 5: Awwwww!

Participant 2: So you do want to know about it?

Participant 5: No, no, no, no!

Participant 6: But you do if 32 are going to get better anyway why would you take the tablet?

Participant 5: To improve your chances

Participant 6: But by only 25%

Participant 5: But it doesn't matter!

Participant 2: You need to know

Participant 5: No you don't need to know the %, but you don't! What you need to know is that you are better off taking the tablet than not taking the tablet. That's all you need to know. The percentage doesn't matter!" (M, 56, F, 68 & M, 76 in FG1, JANA)

The percentage also proved a challenge for one participant who, although they understood the information, had concerns that the reader would intuitively try and make the percentage figures add up to 100%, which would cause confusion:

Participant 7: But you know what I mean, I'm looking for things… if you are going to have percentages you are going to look for things that add up to 100%

Participant 6: but the 32 ain't in the 57%…

Participant 7: yes, I know… but you've got to go digging to get to that. I'd be thinking 32, 89, where's the other 11!" (M, 63 & F, 68, FG1)

It was therefore apparent that for some participants the percentage information had the potential to mislead by encouraging misinterpretations of the benefit data due to mistakes in making calculations using the data provided.

- **Natural frequencies**

The natural frequency format did not seem to provoke such extreme reactions in comparison with the other numerical formats. For many, the removal of the percentage made the statement instantly easier to read and it was generally viewed as understandable and user-friendly. Participants tended to have fewer objections to the inclusion of the natural frequency.

> *"And it's better, just taking away the percentage sort of thing, it does make it a bit easier to read." (F, 63, FG3, JANA)*

However, there were still concerns about this format. Some found it challenging to interpret and it was viewed as quite wordy. The first sentence in particular was viewed as tricky to understand. The phrase 'in 100 people like you' appeared to provoke a negative response as people questioned 'who are people like me?' It was common for participants to question whether the 'people like me' were similar in age, ethnicity and gender to them. There were occasionally concerns about the relevance of the numbers to the participants' personal situations.

- **NNTs**

NNTs were viewed as comparatively easy to read, especially in light of some of the other formats. Many of the participants felt they were quite simple to understand. However the message they gave was viewed very negatively and it was apparent that the benefits were surprising. These views were held regardless of the type of medicine.

> *"The [NNT], it's not terribly positive is it! But it's easy to understand." (F, 54, FG3, JANA)*

The NNT was viewed as straight to the point and, by some people, quite honest.

> *"The green one is almost like a television advert. "If 20 people like you...this will not..." It's really direct and it's just like something you would get on the television basically, that has got the limited time and space to say it, so basically it just throws the punch straightaway and gets the point home." (F, 57, FG4, REBA)*

For some participants it appeared to convey a sense of accuracy and the small numbers it presented were easy to relate to.

> *"I suppose it's narrowing down to a small group of people and you think, "there's something here" One of us would have less of a migraine if I take this tablet and I think I'd like to be that one please." (F, 50, FG5, JANA)*

It did appear to make people more aware about the benefits of their medicines, but this awareness was not always welcomed:

> *"I found the [NNT] a bit depressing 'Oh it will only improve 1 in 20 in 5 years', well I wouldn't bother." (F, 70, FG2, REBA)*

Frequently the NNT caused confusion about what happened to the other 3, or other 19, patients. This was disconcerting and unsettling for those participants and fed into the feelings of fear and nihilism that were identified. For some participants it appeared to stimulate them to reject the medicine.

One lone participant felt that the NNT was presented in a way that was too positive. He felt that the information could put a greater emphasis on the uncertainty associated with the treatment:

> *"I'd say it even stronger, I'd put in front of it 'most people do not benefit from taking this medicine, in fact most do not, but a large minority of people do benefit from taking this medicine' and then put the 4 people like you taking the drug, 1 will benefit. So you have 1 vote for the NNT." (M, 60, FG3, JANA)*

- **Framing**

The majority of the participants preferred the information when presented in a positive frame. The negative frame contained a double negative, which the participants found challenging to read.

> *"The one with the double negative, I was going backwards and forwards trying to figure out that!" (M, 56, FG1, JANA)*

The combined frame was also viewed as challenging to read:

> *"Yes, you cannot present both because it gets confusing. Like in my situation [making a choice about chemotherapy] with that doctor where he was getting confused between people living and people dying or getting better and we were going around in circles" F, 54, FG3, JANA)*

Overall, participants felt that it was important to put the benefit information in a positive frame, because the benefit information was supposed to be positive.

> *"You are trying to focus on the positive benefits of the medicine, so I think the statement needs to be positive" (F, 57, FG4, REBA)*

- **Alternative formats**

A few participants suggested alternative formats that they thought they might prefer to see in a PIL. The most popular suggestion was the inclusion of a graphical format or chart, although several members of the groups voiced concerns that they would not understand the graphs. These members tended to be older group members.

It was apparent that a few members of the focus groups mentally converted the benefit data into a relative risk format. It appeared they felt this gave them the biggest benefits and was preferable to the small benefits they perceived in the other formats:

> *"I think the purple if it can be altered to say JANA can improve your chances by 25% of having less of migraine after 2 hours is the simplest way of doing it. I think*

this 1 in 4, 1 of them, it sounds as though you have got very little chance! Well it's a bit negative; if it can improve your chances by 25% it's more positive." (M, 76, FG1, JANA)

One final suggestion was to present the benefit information in a similar way to how the side-effect information is presented (which is a form of natural frequency), so the methods of data presentation are uniform.

"When they do the side effects they say may affect up to 1 in 10 people, may affect up to 1 in 100 people. So they are using these rough figures and there's nothing to stop them using these rough figures there." (M, 56, FG1 JANA)

3.8.3 Barriers to engaging with benefit information

There were several barriers which prevented or limited a participant's willingness to engage with the benefit information. A lack of willingness then influenced people's ability to make informed decisions about their medicines. The following influencing factors were identified from the data:

- ***It's complex***

A common complaint about the benefit information was that it was complex and very hard to understand. People found it 'muddling' and 'mathematically confusing'. It was viewed as hard to interpret and too complicated. A problem, methodological in origin, was the presentation of the all benefit statements in one leaflet. This led to some participants trying, and struggling, to understand the different methods used to calculate each statement and finding the maths overwhelming. Many understood the general idea that the figures presented were different statistical representations of the same data, but couldn't work out the maths to get from the percentage to the NNT, for example. This led to some distraction and frustration with the numerical statements. All in all the biggest complaint about the numerical benefit statements was that they were simply too difficult to understand. Some participants could not comprehend their meaning at all.

Conversely, some participants understood the benefit information well, and there were occasions when these participants would explain the different calculations of benefits to their fellow participants with confidence and ease. Surprisingly, these participants were not always receptive to the inclusion of benefit information in PILs and the complexity of the information was not the only factor that influenced whether people would engage with it.

- ***The unsettling nature of chance and uncertainty***

While some participants could comprehend the chance that the medicine would benefit them with relative ease, for others this was a challenging concept. Participants wanted more certainty than the benefit information, particularly the numerical information, could offer.

"I would rather have a sentence that said it will always work." (F, 68, FG1, JANA)

The uncertainty about the effects of the medicine was very unsettling. People were worried that they would not be the one who was saved and found it difficult to understand how the medicine would benefit them individually. Occasionally this stimulated a desire for more information, in order to put this uncertainty into context. However, this in turn provoked concerns about being overburdening with information and it was challenging to find a balance that suited the needs of all the participants.

- ***"It puts people off!"***

As a result of this uncertainty and unease there were also concerns that the information would only serve to put people off reading the information or would encourage them to make bad (uninformed) decisions that might impact upon their medicine-taking.

"Participant 7: you don't [need the benefit information], because it just puts people off...

Participant 6: And 25% wouldn't take it." (M, 63 and F, 68 FG1, JANA)

On the whole, concerns about people being 'put off' from reading their leaflets, or taking medicines were about how this information might impact on others, such as friends and families. Participants in the focus groups felt they would see their GP before making decisions about taking a medicine.

- ***Passive decision-making and the advice of the GP.***

"I'd just do what the doctor says." (F, 81, FG5, JANA)

A big influencing factor on whether people wished to engage with the benefit information was how strongly people valued their GP's advice. There was a range of preferences for their relationship with GPs, with some participants seeing themselves as bearing the main responsibility for medicine-taking decisions and others preferring a more paternalistic relationship with their GP, where they follow the GP's advice with little questioning. It was apparent that the GP's recommendations about taking a prescribed medicine impacted significantly on a decision to take a medicine and that for

many these appeared to overrule any thoughts on effectiveness that arose from the interpretation of the benefit information.

> *"The numerical information allows you to make an informed decision. It gives you the facts and the figures. But you wouldn't stop taking a drug without seeing a doctor would you?" (M, 51, FG2 REBA)*

Some participants were incredulous at the suggestion that they might use the benefit information to help them make decisions about their medicine. Many participants, particularly older participants who received prescriptions for larger numbers of medicines, did not appear open to shared decision-making or engagement with the benefit information at all. Instead they took a passive role and relied on the GP to make decisions on their behalf.

> *"It's your doctor's job to tell you what is right." (F, 74, FG5, JANA)*

A negative impact of providing the benefit information was that on occasions it undermined the faith people had in their medicine, and also the trust in their GP.

> *"The blue one, I would question why the doctor even give it to me in the first place because it only becomes 80%. There's only 5% difference between the ones who don't and do. So, what's the point in taking this medicine in the first place? I looked at all these different colours it was too confusing. It didn't really add anything in the information that I would really want to know, because the one where it says about the purple one 'it can lower and it can do this'...well, the doctor wouldn't give it if it wasn't supposed to do what he wanted it to do." (F, 58, FG6, REBA)*

This was a very troubling and alarming situation for the participants to find themselves in and often reinforced the feelings of fear and nihilism that they had reported initially.

> *"The green one, it set my heart pumping fast because it says one of them you stop having a heart attack. I thought, well...are we 1 in 19 that can have a heart attack? I don't think, probably the wording, but I wouldn't give anybody this information, that 1 out of 20 it stops heart attacks. What of the other 19 that it states what happens? Does that mean it won't work for us? It's a concern for me. I feel that way and it will set me with negative thoughts." (F, 69, FG6, JANA)*

A very troubling concern was that the numerical benefit information, which was frequently perceived as negative, would impact on the values people placed on their medicines, and therefore upon the effectiveness of the medicine. A deeper concern was that this would encourage patients to give up on the hope that their medicines would help.

> *"You want to think that you're not going to be the other three that it doesn't have an effect on. But now you have got this seed planted it might not work. Whereas, if you didn't have the information...Then it's like the placebo, but the other way round." (F, 56, FG3 JANA)*

The final barrier to engagement with the benefit information in order to facilitate decision-making appeared to be a sense of inertia that was generated alongside the prescription for a medicine. A few participants stated that if they had received a prescription for a medicine (or in the case of an OTC medicine, purchased a box) they would take the medicine anyway, regardless of their interpretation of benefit information.

> *"Well if I'd been prescribed it anyway then surely the fact that I've been prescribed it and I've gone and got it means that I'm gonna take it, I'm not being facetious but I mean surely you're making that decision, you've made that decision anyway before you even get to reading the leaflet." (F, 57, FG4, REBA)*

This raised some questions about whether the leaflet was the right place for this information as some participants stated they wanted to have this information before they received a medicine, so they could make a decision. Others felt that benefit information was something that their GP should impart.

Only one felt that the leaflet was the perfect place for this information.

> *"I think that seems like a good reason to come clean. To put it in the patient information leaflet, because you know, that's what it is: An information leaflet, it is not advertising. I think that the patient deserves to be treated with enough respect to have this information, and to be able to understand this information. I didn't know either how few people would benefit from this medicine." (M, 60, FG4, JANA)*

- ***Personal experiences***

Previous experiences with medicines appeared important in decision-making and could be a barrier to a person's willingness to engage with the benefit information. Participants appeared more comfortable in making decisions which were familiar to them in some way. For example, decision-making might be influenced partially by their previous experience in taking a medicine or by their friends and family's experiences.

> *"I've never had any adverse effects...I think if you have had adverse effects your opinion, your thoughts on it would be very different. I don't have any adverse effects so I find it difficult to say 'well, I wouldn't do this and I wouldn't do that." (F, 74, FG4, JANA)*

> *"I would also watch out for friends and colleagues who've taken statins in the past, I don't know how many years, and presumably they haven't all survived or haven't all been killed by heart attack so I would watch out for that." (M, 69, FG2, REBA)*

It was apparent that there was an emotional context to decision making that participants prioritised.

- ***How high are the stakes?***

The seriousness of the illness was something that was identified as an influencing factor on whether participants wanted this information in the first place, and also on whether the participants felt the benefit information could help them in making decisions about their medicines. Some participants were more receptive to receiving benefit information if their illness was perceived as life threatening.

> *"This is looking at a migraine treatment rather than a cancer treatment. It's very different. I would respond differently to statistics about a migraine treatment and statistics about a life or death situation, potentially." (F, 56, FG3, JANA)*

One participant (FG3) in particular talked poignantly about receiving benefit information when she was offered chemotherapy for breast cancer. However, another in the same group who also had experience of cancer stated she did not necessarily want to receive the benefit information.

The severity of the illness might also be something that would impact upon decision-making more than the benefit information. Despite the poor perceived benefits of the Janatriptan medicine, some participants often stated that they would still take the medicine if they were desperate.

> *"I'm fortunate I don't suffer with migraine, but the people that do, you know, who I know suffer from it, you feel they'd do anything because of the pain and if you went to the doctor and they said, "look, it only works in a quarter of the cases," I think I would still have a go at it because I'd be searching for anything that would relieve the pain." (M, 67, FG5, JANA)*

It is also interesting to note that discussion about the severity of illness did not appear to differ between the two groups for the medicine types. There was no immediate difference in opinions from the groups for the statin medicine and the group for the migraine medicine. These differences were drawn out when a disease such as cancer was talked about.

- ***The context of the decision***

The context of the decision could also be a barrier to engaging with the benefit information. Participants often found it easier to comprehend the utility of the benefit information when presented with a scenario where they had to make decisions between two medicines which might be purchased over the counter, as opposed to a medicine that had been prescribed by a GP.

> *"I think if it was an over-the-counter medicine, and you can buy medicines in supermarkets now. I think people need to know that you could take this and get benefit but people need to know that you could get no benefit and I think you*

need to know that. I think if you get it is a prescription then your GP should give you some guidance and he should know you and as to whether it could help you, but I think if you're buying it and it is a drug that is going on general release in the supermarket, and I think in that case then the information has to be given and they should be given in more bullet points and it has to be more dot, dot, dot or people don't read it." (F, 63, FG3, JANA)

- ***Loss of hope***

Hope was frequently identified as a motivating factor that impacted upon medicine-taking. Medicines provided hope that the patient would recover from an illness or symptoms. It appeared that the provision of numerical benefit information took away that hope.

"I like my hope. I must have this idea that most medicines are going to help me and they are not going to hurt me. They've got to be positive and doing some good. I think that is not going to be 100%, it might be 1%. It's got to be doing some good or I wouldn't be taking it." (F, 56, FG3, JANA)

As a result this often discouraged the participants from either wanting the benefit information, or from taking the medicines.

"So when you are giving me very little hope and telling me this is what is going to happen to me I don't want to know." (M, 56, FG1, JANA)

"They [benefit statements] weren't of any interest to me because I'm a very positive person and if my doctor has prescribed the medicine for me I hope it will work. I don't want to know who it didn't work for or who it did or what percentage of people. It would make me more poorly, yes, that is my feelings about it." (F, 69, FG6, REBA)

The numerical information was generally found to be lacking in hope. What participants tended to want was benefit information that was more optimistic, more encouraging and more positive. Often this was the textual format of benefit information.

"Keep it clear and simple and optimistic." (F, 69, FG2, REBA)

"Participant: I like number three with the purple statement.

Interviewer: Do you think that's encouraging?

Participant: Yes I do think people need encouraging." (F, 52, FG2, REBA)

The information has to be able to instil confidence in the patient:

"I think that is a keyword, confidence. You have got to have confidence in your GP. I need to have confidence in the medicines and the leaflets. To me they should confirm that confidence that your GP has given to you to take them and they should give you warnings if you are feeling unwell when taking this. And to

me this is too much! It should be short, sharp, to the point, the positives!" (F, 52, FG2, REBA)

In order to make the benefit information more encouraging participants would occasionally reword and recalculate the information to make it sound more positive and encouraging to them. Sometimes they would recalculate the percentage to make the benefits sound larger or occasionally insert words such as 'greatly' or 'increases' instead of 'this becomes', in order to put a positive spin on the benefits. The lack of 'positive spin' appeared disheartening:

"It is a positive benefit even though it's not a big figure. But it wouldn't stop me taking them. It doesn't exactly put a positive spin on them." (M, 51, FG2, REBA)

There were a few participants who were exceptions to the general feeling that the benefit information was negative, often these were a lone voice in the groups. For these participants the benefit information truly was benefit information, which gave them hope and encouraged them to take their medicines optimally:

"I was really happy to see something positive about the medicine. I've never been a medicine taker; I've never liked taking medicines. When I was given tablets for my blood pressure I was absolutely mortified. I was really fighting not to take them. So for me, to see something positive about why I am taking the medicine helped me...a little...not a lot. Because when I read the leaflet I think 'urgh!' but there is a reason as to why I will benefit from it. Comforting I guess." (F, 59, FG2, REBA)

3.8.4 The impact of the benefit information

- ***Developing understanding and knowledge***

It was apparent that some groups did not engage with, nor understand, the information sufficiently for them to develop any further knowledge or understanding of their medicines. Sometimes the benefit information was disorientating and unsettling. In some people it stimulated reactions of shock and disbelief and their initial reaction was to reject the information. However, there was a group of participants who, once they had expressed their shock, disbelief and concerns about the medicines, appeared then to develop a better understanding of the numerical information and this translated into a deeper awareness about their medicines:

"I like the orange one first [natural frequency] and the green [NNT] second. You like to know what you are taking and what's going to happen." (F, 68, FG6, REBA)

Even though the information was at times alarming, some participants still valued its inclusion.

"It would frighten me, but it would make me more aware." (F, 53, FG4, REBA)

It was apparent that the benefit information did help some participants understand more about the benefits of their medicines (although this was not always welcomed). This was especially apparent when participants compared the different statements with each other, particularly comparing the textual statement with a numerical one:

"I'm kind of a sock-it-to-me person and if I got the purple I know that I would have to do work. I would zoom in onto 'can' improve your chance and I'd need to get some harder information…If the information was there in the first place I would feel the information leaflet was treating me with respect and was saving me a lot of hassle in the first place." (M,60, FG3, JANA)

Several of the participants did develop a deeper understanding of the benefits and how they would impact upon them. In particular they learned that the benefits were smaller than expected and this offered them a new perspective on their medicines and potentially impacted upon the choices they might make. Often in the groups there were interesting exchanges as the meaning of the information became clearer during discussion:

"Interviewer: If you had to make a decision between 2 medicines, so suppose you had another migraine medicine, do you think having this numerical information might help?

Participant 1: Oh yes! It would do, especially if they were a different price as well.

Particpant2: And if one had a better success rate…but obviously no one would buy the other medicine would they?

Participant 1: Well, they would have to improve it wouldn't they!

Participant 2: They would, wouldn't they? You think you are getting the best don't you, but that's not always the case is it?

Participant 6: Would that mean that you would not buy the green, you wouldn't buy the green but you would buy the purple?

Participant 1: Yes, that would make a difference to me.

Interviewer: Because the purple might not be as good as the green and they've not told you?

Participant 1: And it sounds so positive.

Participant 2: It's not actually until you start talking about it that you begin to realise...it's not as easy as just producing a leaflet." (F, 54, F, 56 & M, 60, FG3, JANA)

Despite initial reservations about the benefit information it was apparent that the information made an impact on some participants' understanding of the benefits of their medicines. This knowledge provoked concern, although it was frequently felt that the information should be provided as a general principle:

"This is about the general principle of people being given the information so they can make the decision, because even if things are prescribed, we as individuals make the decision to take that medicine or not, and I think that the more information you have helps you make an informed decision." (F, 68, FG1, JANA)

- ***Making choices and decisions about medicines***

Despite the multiple barriers to engaging with the information, having 'some' benefit information available was viewed as important. It was reported that the benefit information had the potential to influence choices about medicines, even though the information caused considerable conflict. For some participants it was an enabling, empowering force that encouraged them to weigh up the pros and cons of their medicines, although this was not universal amongst participants.

- **Encouraging active decision-making**

The benefit information was identified as helpful in supporting people to make judgements about their medicines. This was particularly distinct where participants were already active decision-makers.

"Basically it gives you something to work on, it brings in real statistics and things you can actually relate to and you can make judgements. It helps you make the judgement yourself. It's presenting you the facts as opposed to just statements and claims. I mean, they are very important to know facts. Because so many companies, medical companies make claims about things and then years down the line those claims are all undone and it's disproving and whatever. But if you've got facts, proven facts and figures, then I think it makes it more credible to you and you can make a more reasoned judgement about it, basically make your own decision without accepting that they say this is the best and whatever, you can actually decide yourself how good you think it is" (F, 57, FG4, REBA)

The provision of benefit information encouraged several participants to state that they would consider seeking additional advice from their GP or pharmacist about the medicines in order to understand more about the benefits of taking the medicine.

"If people are on a lot of medication and they don't know whether they should take another tablet, and if they know they'll get better without taking the tablets, it may make them change their mind and say 'I'm not going to take it because the chances aren't increased that much'. So I think, for some people, that information is very relevant" (F, 68, FG1, REBA)

So while the information was frequently viewed as surprising and shocking, it did appear to stimulate the need for additional information about medicines from some participants. This was apparent even for those who did not like, nor believe the information was relevant.

In focus group 6, one participant was particularly vociferous about his dislike of the benefit information in all formats. However, the information provoked a response from

him. It made him aware that the medicine (Rebastatin) was not as effective as he had expected and this caused him to reflect on his medicine-taking behaviour. He decided he might choose not to take a medicine with such poor benefits and would seek advice from his GP. It was not an uncommon response for participants to report that they would alter their information-seeking behaviour after reading the benefit information. This participant's response was deeply emotional, but other responses were more positive. In particular the benefit information often stimulated the weighing up of the risks and benefits of a treatment and the consideration of making trade-offs.

- **Weighing up the risks and benefits**

The benefit information did appear to stimulate a risk-benefit analysis where the potential side effects were considered alongside the benefits of the medicine.

> *"Well, initially I went for the purple [textual] but I have had second thought about that and am trying to understand why. I think I'd like to know how much better the chance I've got, and I'm a figures person anyway, so I think I will go for the first sentence of the blue [percentage] because that seems to be quite simple and you can see that 32% get better without taking this tablet, so I'd be looking at the side effects and thinking 'is that migraine really that bad, do I really want these side-effects when 32% get better anyway? Maybe I'll live with it.' The other one doesn't really tell me how much better, it doesn't give me anything to compare it with. So now that I've read it…When I first read it I thought [the textual] that's quite simple, that's better. For the most people, well…it probably is better. But now I want to know how much better." (F, 68, FG1,JANA)*

This was not always a comfortable process, and provoked concern in some participants, especially in light of the unexpectedly low level of benefits.

> *"I think, to me, there's more of a concern of all the different, possible side effects you can have. To me, I feel worse when I read all the things you can have because I look and say "well, if these are the things I could possibly have, does that outweigh what this pill is actually going to do for me?" So that makes me nervous." (F, 58, FG6, REBA)*

It was also noted that the benefit information might not initially provoke the weighing up of the risks and benefits prior to the initial decision to take a medicine, but it was important information that might help to influence long-term decisions:

> *"If I was suffering a side-effect, all of a sudden it would become really important to me" (M, 64, FG5, JANA)*

Often this was a process that was very personal and dependent upon multiple factors that included an understanding of the facts that were presented, but also reflected on the individual's personal values and experiences.

3.9 Discussion

The aims of this qualitative research study were to provide further insight into the provision of benefit information in a PIL and to explore how the benefit information might impact upon knowledge, satisfaction and behaviour. A further objective was to identify preferences and suggestions for presenting 'benefit information' in a regulated PIL. Our findings show a significant range of opinions on the inclusion of benefit information.

It was apparent that many participants welcomed the inclusion of positive information about the benefits of their medicines in a PIL when presented in a textual format. Participants wanted more information about how their medicines worked and how likely they were to benefit from taking them. However, the inclusion of numerical benefit information was more divisive. Some participants welcomed the provision of 'facts' about their medicines. For others the numerical information was difficult to understand and there was a great deal of shock at the perceived low benefits which appeared to cause turmoil and distress in some participants. Several key findings were drawn from the focus groups.

3.9.1 Key finding: Numerical benefit information is difficult to understand

Effectively communicating risk and benefit information is a challenge. People might not possess adequate numeracy skills to interpret data accurately and some statistical formats have been shown to be misleading, persuading people to make decisions about treatments that are not well-informed (Gigerenzer and Edwards, 2003, Akl et al., 2011a). The benefit statements used in the exemplar leaflets did not use summary statistics shown to be persuasive, such as relative risk formats. Both the natural frequency and percentage formats used absolute numbers in order to promote understanding and reduce the risk of patients being misled or unfavourably influenced (Bhandari and Tornetta, 2004, Malenka et al., 1993, Gigerenzer, 2002). However, a curious finding was that occasionally the participants converted the numerical statements into a relative risk. This appeared to be done to enhance the benefits of the treatment and make the benefits appear bigger, and more positive. This mirrors the findings of other studies which suggest that relative risk formats can be easily understandable, but can mislead patients who perceive bigger benefits of treatments with the absence of absolute risk information (Carling et al., 2008, Carling et al., 2009, Carling et al., 2010).

Misinterpretation of the data and confusion about its meaning was common and many participants struggled to understand the numerical benefit statements in any format. Providing comparative information has been shown to enhance understanding of risk-benefit probabilities. Gigerenzer and Edwards (2003) recommend the use of a reference class when giving probability and frequency information (Fagerlin et al., 2007, Gigerenzer and Edwards, 2003). This information was provided in the percentage and natural frequency formats, with the reference class being the number of people who would suffer a side-effect without the treatment. However, several participants found the provision of this comparative information confusing and could not understand its relevance.

However, for some participants the provision of the reference class appeared to help clarify the information and promoted an understanding of benefit of the treatment in context. The findings from this study suggest that while the provision of a reference class can help reduce misunderstanding of probability information, this is not the case for everyone and some people struggled to comprehend the meaning of such numerical formats.

No numerical format was preferred above all others, nor identified as the easiest to understand; one limitation of the research is that the participants' understanding of the formats was not formally tested. A range of opinions were expressed about the different formats, and individual experiences, of medicine-taking were influential. Familiarity with the format appeared to influence preferences; however it is important to note that preference has not been found to be indicative of the performance of different numerical formats in conveying understanding.

Natural frequencies were often identified as understandable. This echoes the findings in the wider research literature that natural frequencies can aid understanding and foster insight into numeracy (Galesic et al., 2009b, Gigerenzer et al., 2007). Their use is promising in the context of medicines information and they appeared here to generate less nihilism and concern than percentage formats or NNTs. However, it was apparent that they were not understood by all, they often caused confusion and the wording of the natural frequency was not always popular. Occasionally it provoked a negative response. Numerical information about the harms of medicines (side-effect information) in legislated PILs is currently provided in the form of a natural frequency.

The NNT statements were generally viewed by the participants as the simplest numerical format to understand. The research literature on NNTs has mixed findings,

with some evidence showing that they can be easily understood, although this research often focuses on understanding among healthcare professionals (Rajkumar et al., 1996, Riegelman and Schroth, 1993). Other research has shown that lay people find it difficult to interpret NNTs; that they can lead to misinterpretation; and that NNTs lack contextual information which can moderate reactions to small but important benefits (Kristiansen et al., 2002, Hamrosi et al., 2012). The biggest challenge with the NNTs shown in the current study is that the information they conveyed was perceived to be very negative.

There is a need for more research into this area, in order to measure which formats promote accurate understanding of treatment benefits and to examine whether different formats of numerical information influence decision-making and medicine-taking in participants who receive numerical benefit information in their medicines information.

3.9.2 Key finding: Patients frequently over-estimate the benefits

It was apparent that over-estimations of benefit were common. Participants were shocked by the perceived low benefits of the treatments and reported that they expected benefits to be much higher. Hamrosi et al (2012) found similar views and reported that when participants were shown an NNT stating "if 100 people took the medicine then 1 would be prevented from having a heart attack and 3 from having a stroke", participants expected benefits of at least 50 in 100 experiencing beneficial treatment effects. We found that participants also expected higher level of benefit and they reported expectations of treatment benefits such as 90% of those taking the medicine experiencing a benefit or 19 in 20 benefiting. These differences in expectation of benefit between these studies could be attributed to the adjustment heuristic, which anchors people to a specific figure (in this case the NNTs used in each study). As the NNTs varied, with lower benefits in the Hamrosi et al (2012) study, the participants adjust their expectations from the initial anchor which results in differences in their final expectations (Tversky and Kahneman, 1974). In this study, where the benefits were higher, it seems that the participants expected treatment benefits that were higher still.

The expectation of better benefits was apparent regardless of whether the participants received a leaflet with a higher or a lower NNT. So the groups receiving leaflets for Janatriptan, where the benefits were reported as "4 people need to take the medicine for 1 person to benefit" also perceived the benefits as very poor and were surprised at the low numbers who benefited (this was regardless of format). This was a surprising finding, as it was expected that there might be more satisfaction with the benefit information when larger benefits were presented. It is possible that the severity of the

condition the medicine is used to treat impacted upon perceptions of, and expectations, of benefit.

Janatriptan was portrayed as a medicine used to treat migraine, a debilitating but not life-threatening condition, whereas the portrayed purpose Rebastatin is the prevention of heart attack or stroke, which are both life-threatening conditions. It is possible that as a result of the difference in health outcomes, patients will cope and react differently with the threats they pose (Leventhal et al., 1998, Cameron and Leventhal, 2003). For an illness perceived as less of a threat, such as migraine, the participants may make different trade-offs, expecting bigger benefits and fewer side effects. Whereas, when the threat is more severe, for example a heart attack, the participants may accept smaller benefits and, possibly more side-effects, in the hope that they will be the one to be saved. This phenomenon has been observed in studies of people making decisions about whether to accept chemotherapy treatment for cancer. It has been noted that cancer patients are frequently more willing to risk the adverse effects of chemotherapy for a smaller benefit due to the social and emotional context of a life-threatening disease and because of the high values they place on the potential beneficial outcomes of the medicines, which can ultimately save their life (Matsuyama et al., 2006, O'Connor, 1989).

This is another area that would warrant more research in order to develop a deeper understanding of the reasons why patients tend to over-estimate the benefits of their medicines and to development of strategies to help people understand medicines in context. These needs to be considered in light of the feelings of nihilism and fear that were evoked when participants read the numerical benefit statements in the exemplar leaflets. In addition, an understanding of how benefit information is perceived alongside side-effect information, for a range of conditions, will provide insight into the best methods of supporting patients with making decisions about their medicines.

3.9.3 **Key finding: Textual information is preferred, but numerical information can help with judgements**

There is evidence that good quality textual benefit information can support patients to make better judgments about their medicines (Bersellini and Berry, 2007b, Bersellini and Berry, 2007a). However, in the absence of numerical information about how likely a medicine is to benefit the taker, it was apparent in these studies that participants found it difficult to weight up the advantages and disadvantages.

Participants in the current study frequently stated that they preferred the textual statement to numerical statements and it was apparent that some would make different decisions about taking the same medicine depending upon whether the benefits were presented textually or numerically. They were more likely to choose a medicine after reading the textual benefits, which were viewed as encouraging, and stated they would not take a medicine when the same benefits were represented in a numerical format. The numerical format aided some participants to gain a deeper insight into how likely the medicines were to work for them. This suggests a greater susceptibility for over-estimation of benefit with an exclusively textual statement.

Criticisms of the textual statement were that it was vague and lacking in context. However, the textual format was very popular, and participants felt the inclusion of additional information about how their medicines worked and how likely they were to benefit them was a step forward. There is need for more research into how a textual statement can be enhanced in order that it can provide good quality information and convey the uncertainty inherent in many medical treatments.

3.9.4 Key finding: Numerical benefit data can have an influence over understanding and potentially behaviour, regardless of whether it is desired

Regardless of its popularity, the numerical information frequently had an impact on many participants' satisfaction with medicines and medicines information, their level of understanding and their potential behaviour. Often this impact was unwelcome and many reported high levels of dissatisfaction and concern about the treatments presented. Clearly this is not ideal. One aim of providing factual information about medicines to patients is to help with informed decision-making where "a reasoned choice is made by a reasonable individual using relevant information about the advantages and disadvantages of all the possible courses of action, in accord with the individual's beliefs" (Bekker et al., 1999).

It was apparent that the provision of numerical benefit information caused significant anxiety and dissatisfaction among many participants. Moderate levels of anxiety have been shown to be helpful in promoting good decision-making, as it encourages people to explore all their options. However, high levels of affect are associated with the increased use of a heuristic, or rule of thumb, to make a decision, as opposed to reasoned judgement (Bekker et al., 1999, Loewenstein and Lerner, 2003, Tversky and Kahneman, 1974). This is particularly influential when people are weighing up the risks

and benefits of different hazards. It is possible that the provision of numerical information about the low perceived benefits, combined with a high perceived threat of side effects (which is a common concern with medicines) (Raynor et al., 2007) increased the anxiety people experienced and impacted upon their abilities to make reasoned judgements.

More research is required to understand how the provision of benefit information in patient information leaflets impacts upon decision-making and whether it leads to people either making reasoned judgements or increasing the likelihood that they will rely upon an affect heuristic to make a decision.

3.9.5 Key finding: A positive frame is valued

It is well known that the way that information is framed can influence decisions, especially when these decisions involve risks and benefits. This is known as the framing effect and is an example of how cognitive biases towards choices can influence decisions (Tversky and Kahneman, 1981). The benefit information in this scenario was presented as a combined frame in an attempt to avoid unduly influencing decision-making about medicines. However, the combined frame was viewed as challenging to read, and was quite cumbersome when compared to either a frame that was exclusively positive or negative. The presentation of the numerical information in a positive frame was clearly preferred by the majority of participants. It also appears that this was more easily understood. This preference for a positive frame reflects the participants' desire to have information that is optimistic and encourages medicine-taking.

This is an interesting finding, as the aim of the benefit information was not to promote 'adherence' to medicines by encouraging people to take them, but instead to provide more detailed information about medicines with the aim of enabling patients to make informed-decisions. It appears that some people value a more paternalistic approach to medicine-taking and see the medicines information leaflet as instructional documents, that tell you how to take medicines, rather than information sources that help with decision-making. Hamrosi et al (2012) also noted that participants did not want always benefit information to help empower them to make better decisions; instead it was desired because of a sense of 'knowing'.

So while the positive frame was preferred, caution must be applied when considering the framing of benefit information, as positive frames have been shown to be more persuasive than negative frames. However, in the context of a PIL it is important to note that the increased amount of information, as provided by the combined frame (which

was said to be cluttered and difficult to read), appeared to increase affect; as did the negative framed statement. As a result a positive frame appeared to be more effective in conveying the benefits of the treatments.

More research is required to evaluate the impact of different frames in patient information on a wider scale and to explore the development of a less cumbersome combined/neutral frame.

3.9.6 Key finding: Participants valued their GPs advice

It was apparent that the most trusted source of advice about medicines, and the biggest influence over decisions to take a medicine, was the GP. A concerning effect of the benefit information was that, for some participants, it appeared to shake their faith in their medicines and in turn their confidence and trust in their GPs.

Written information is frequently viewed as having a supportive role, with GPs providing a crucial role in providing education and information about medicines. It is important to ensure that any benefit information provided in a PIL does not undermine the confidence that a patient has in their GP, but is instead informative and an aid to decision-making. Many people stated an interest in having discussions about the benefits of their medicines, in particular the statistical benefits, with their GPs. Healthcare professionals should rise to the challenge of providing patients with this complex information in a format which suits the educational abilities of the individual and the desires of the individual while being mindful that not all patients want this information.

3.10 Conclusions

3.10.1 Headline section

The inclusion of a headline section in a PIL was welcomed by participants in a series of focus groups. The section was viewed as an adaptation that helped participants better engage with their leaflets and which responded to their perceptions of current patient information leaflets being arduous to read and complicated. Participants reported high levels of satisfaction with the inclusion of a headline section and felt that it had the potential to help them understand more about their medicines and influence the safe use of medicines. The users of medicines information value good design and desire leaflets, and the headline section, to be visually appealing and practical to use.

The impact on understanding and behaviour was not assessed directly by this research, but patients reported the potential for the headline to allow them to access more information with ease and to encourage them to read some of leaflet as opposed to none of the leaflet. Further research is required to assess the impact of the headline on understanding and behaviour.

There were some concerns about the headline section discouraging a reader from accessing information elsewhere in the leaflet, but many felt the headline had the potential to encourage someone who might not otherwise read the leaflet to read the highlighted key information. More research is required to assess whether the inclusion of a headline section in a PIL influences patients in finding information and/or understanding more about their medicines.

3.10.2 Benefit information

The provision of benefit information in PILs raises important questions about how the benefits of medicines are currently conveyed to patients. It is apparent from the participants in this study that over-estimations of the benefits of medicines are common and that patient expectations are not always in line with the realities of the health outcomes that medicines can provide. It is concerning that patients do not appear to have realistic expectations of the benefits of their treatments and that the provision of this factual information can cause anxiety and fear.

The findings of this study highlight several areas of conflict about the provision of benefit information, which are not easily resolved. The textual benefit information was preferred by the majority of participants but did not provide all of them with sufficient information to make informed decisions. The numerical benefit information often helped patients understand the limitations of their treatment and encouraged more reasoned decisions about whether to take a treatment. However it was viewed as unpopular and increased anxiety.

Presently there is a great deal of interest in improving risk-benefit communication based on the view that it is important that patients receive fair and unbiased information about medicines, so that they are aware of how likely their treatments are to benefit them. Currently this information is not necessarily received by patients in any standardised format, if at all. It is possible that the PIL, an instructional and factual document, and which is a legal requirement in the UK and European Union, is a good place for presenting standardised benefit information. For patients to make informed decisions

about their treatments it is vital that they receive facts so they can make decisions which are in line with their values and experiences (Department of Health, 2010, Bekker et al., 1999, Charles et al., 1997, Carling et al., 2009). Benefit information also allows patients to weigh-up the harms and benefits of treatments and provides communications that are balanced.

However, numerical benefit information is not useful for all participants. Several participants struggled to understand this information and could not apply the data to their situation in order to help make decisions. Some found its inclusion very off-putting and there is the potential that it might impact negatively on decision-making, leading patients to reject their medicines because of emotion rather than reasoned decision. One of the biggest concerns about providing the benefit information was its potential impact upon hope for recovery and faith in healthcare. The uncertainty that the benefit information conveyed was unsettling for some participants and generated feelings that medicines had little value or meaning. The benefit information also appeared to have the potential to undermine the confidence that participants had in their medicines and in their GP. This could suggest that a PIL is not the right place for benefit information of this kind.

The findings show no consistent approach to the appropriate presentation of benefit information, and this needs to be resolved before it is included in a PIL. There is the potential that improvement to textual benefit information could help inform patients about medicines without creating the unease that numerical data tends to provoke. However, there remains an ethical quandary about whether benefit information, especially in a numerical format, should be made available to patients; although with the increase in usage of web-based resources and the increase in open access journals containing trial data, it can be argued that this data is already freely available to the public. It is therefore essential that this information be well communicated in order to promote informed-decision making and help people take their medicines safely and effectively.

More research is required into understanding how this can be done without causing the anxiety that participants felt when faced with this surprising numerical data and without leading them to employ affect heuristics to interpret its meaning. Patients need to be able to have good quality factual information, whilst retaining their faith and trust in their GPs and in their medicines. Before steps are taken to incorporate benefit information in PILs more research is needed to resolve these issues.

3.11 Strengths and limitations of the methods

3.11.1 Headline section

The use of summary information, like headline sections, is currently being championed by medicines regulators such as the MHRA and the FDA, however there is very little research in this field which assesses the impact of the headline section. This research study contributes to the field, with an in-depth exploration of the impact of including a headline section in a PIL on patient satisfaction, knowledge and potential behaviour.

The research recruited a representative sample of active medicine-takers to examine their opinions on the inclusion of a headline section in regulated PIL. Although the study used a convenience sample, it covered a range of attributes including gender, age, medicine use and levels of education. The sample included a higher than average number of women, which is not unusual in health research. The participants were more highly-educated than the general population and therefore the sample potentially contained a high number of people with higher than average literacy skills. This could impact upon the applicability of the findings to populations with lower levels of education and more research in this population is required as a result.

Finally, while the research explores the potential impact of the headline on patient satisfaction, knowledge about medicines and medicine-taking behaviour, it was not designed to test any actual changes in understanding and behaviour. The actual impact on a patient's knowledge and understanding and on their medicine-taking behaviour is not known. More research designed to test this will be valuable.

3.11.2 Benefit information

This study is an exploration into the opinions of the users of medicines on the inclusion of benefit information in their medicines information. There has been little previous research in this field, with most research into the communication of treatment benefits focusing upon preference and understanding. Very little is known about the deeper impact of providing this information and the range of opinions and impact on the inclusion of benefit information in this context. This research contributes significantly to the field by providing a qualitative investigation into the presentation of benefit information in medicines information.

The strengths of this research are its inclusion of real-life users of medicines combined with the use of real clinical trial data to generate the benefit statements. Most research in this area has focused on exploring the preferences and understanding of non-representative samples, and has recruited samples who might not take medicines. A non-representative sample might not have the same deep involvement in making decisions about medicines, and as such the findings from these studies might not be applicable to real-life users. A significant amount of research in this area has used hypothetical treatments, which are not always based on real-life data, in order to explore understanding of numerical formats of treatment benefits. In this study, although the medicines were given hypothetical names, the benefit statements were based on actual clinical trial data. The findings of this study are generated from focus groups with actual users of medicines presented with benefit information of actual treatments and asked to consider how this information might influence them. The next step in undertaking research in this field might be to explore how this information impacts upon decisions; that is the decisions that are made by users of medicines making choices about actual treatments.

This study adds weight to the findings of Hamrosi et al (2012) by examining the impact of providing benefit information with higher levels of benefits in PILs for different conditions. As a result there is greater understanding about how people respond to different values of benefit information.

This study did not report any measures of understanding, such as literacy and numeracy, and it is possible that participants stated that they understood the information when they actually did not. This suggests the need for further research into how the different formats impact upon understanding and medicines beliefs. One objective of the research was to identify which type of format was preferred in a PIL. It was apparent that participants valued a textual format, but the textual format we provided was perceived as vague. It was apparent that many participants would make different decisions about their treatments when the information was presented numerically, as opposed to textually. It is possible that there is a need for a quantitative analysis into which formats best promote understanding when used in the context of a PIL.

The provision of the multiple formats of benefit information occasionally contributed to an additional challenge in interpreting the information. Many participants struggled to understand the formats and there was a sense of 'information overload' caused by reading, and trying to calculate how the different formats related to each other. Potentially this could lead to a sense of 'cognitive burden', where the inherent difficulty of the information places a burden on the patient which hinders their ability to engage with the information (Chandler and Sweller, 1991). This is something that would be reduced in a naturalistic setting, as only one format would be used in a PIL, and this additional burden was not observed in every participant. Several participants understood all the formats, and some did not understand any, and the presence of the multiple formats did not appear to make a difference to this. It is possible that the leaflet designed for the research caused increased difficulties in comprehension of the benefits that would not exist in a real-life PIL. The findings must be interpreted with this in mind.

The labelling of the framed statements as 'positive' or 'negative' may have influenced the participants in their preference of statement. Also, the use of the colours to highlight the different benefit statements may have had an influencing effect and be a possible confound (Elliot and Maier, 2014).

Finally, it is important to note that the participants in the sample were generally well-educated. A small number held professional qualifications and were familiar with statistical concepts. Their understanding of the numerical information is likely to be greater than the general population, and although the study recruited a mixed sample of education levels, it was apparent that many of the participants had very good numeracy skills. This will impact upon the generalisability of the findings.

3.12 Application of the findings

3.12.1 Headline section

The headline section was viewed as a positive inclusion within a patient information leaflet. The participants in the focus groups raised very few concerns about the inclusion of this adaptation in a PIL. The design of the headline section presented in the focus groups was largely viewed as favourable, although participants raised the need for better signposting.

The findings of these focus groups will be used to improve the design of the headline section and the next stage of the work reported in this thesis will involve the user-testing of this intervention in order to assess whether a headline section can help people find and understand key information about their medicines.

3.12.2 Benefit section

The inclusion of benefit information in a PIL is a complex topic and appears to provoke strong feelings in people, who frequently find it to be surprising and upsetting. The focus groups did not reveal a clear best format.

At this stage it would be difficult to measure whether participants can find and understand benefit information in a PIL, as there is still a great deal of uncertainty about which format is most effective at conveying the benefits of treatment whilst minimising any decisional conflict. As a result of this uncertainty and the evocation of negative emotional responses, it is also unclear whether a leaflet is an appropriate place for this information. Little is understood about how the actual users of medicines might respond if this information was provided about the medicines they are prescribed. More research into how benefit information impacts upon the knowledge, understanding and behaviour of the real-life users of medicines is needed.

Consequently, in terms of benefit information, the findings of the focus groups will be used in a number of ways:

- To develop the benefit statements further in light of the reported preference and understanding for format.
- To develop further research questions that explore the patient's understanding of the benefits of their medicines, in particular which explore participants' tendency to over-estimate the benefits of medicines.
- To understand in more detail the impact of providing benefit information to actual users of medicines, as opposed to a sample comprising those who are not required to make a real-life decision about medicine-taking.

As currently little is known about the provision of benefit information in regulated PILs, and participants appear unfamiliar with this concept, a more detailed investigation into the type of benefit information that is already available in PILs would be useful. This would improve our understanding of current benefit information, and allow the categorisation of the different types of benefit information currently provided to the users of medicines.

Chapter 4:
User-testing Study

Chapter 4 User-testing a headline section (Study 3)

Do patients use a 'Headline' section in a PIL to find key information about their medicines? The findings from a user-test study.

4.1 Introduction

The preceding chapter described the findings from Study 2, a focus group study which explored patient preferences for the inclusion and format of a headline section, and benefit information, in a regulated PIL. Participants reported very positive opinions on the inclusion of a headline section, believing it to be a valuable addition to a PIL. It was viewed as an adaptation which might help relieve the cognitive burden that current leaflets appear to place on patients and something that responds to their desire for well-designed, succinct information which captures the key facts about their medicines. (The findings from the benefit section were equivocal and as a result this study does not address the user-testing of benefit information, but focuses solely on the headline section).

Good quality written information is important for the safe and effective use of medicines and it is known that patients value good quality written medicines information to support their medicine-taking and want well designed patient information leaflets that meet their needs (Dickinson and Raynor, 2003, Grime et al., 2007). The headline section appears to respond to this need and the findings of study 2 are in line with the limited literature on this topic, supporting the view that a headline section has the potential to encourage readership of at least some parts of a leaflet, especially for those who might not otherwise read the entire leaflet.

A limitation of study 2 is that it did not evaluate whether a person could effectively use a headline section in practice. Currently little is known about the effectiveness of a headline section in a PIL and how people might use it. This chapter describes a user-testing study which aims to explore how people use a headline section. A previous user-testing study which compared patients' use of a leaflet with a headline section and one without did not show any difference in their ability to find and understand key information. This study did note that the headline section was valued as a positive inclusion to the leaflet by the research participants. It concluded with the need for further research in a more naturalistic setting to determine if the addition of a headline would encourage patients to read at least that section (Dolk et al., 2011). The current

study used a different medicine to that tested in the study by Dolk et al (2011), although the headline sections in both studies were based on the MHRA examples published in 'Always Read the Leaflet' (Medicines and Healthcare Products Regulatory Agency, 2005a). A key difference in the user testing process in the current study was that participants were not allowed to read the PIL immediately before the test took place (normal practice when undertaking testing of conventional PILs). This was because one of the limitations of that study identified by the authors was that allowing participants to read the PIL in advance allowed them to '*make a mental representation of its structure before answering the test questions which may have led to a reduction in the effect of the headline section*' (Dolk et al., 2011). The key differences in the methods and findings of Dolk et al and the current study will be discussed in more detail in the discussion section (chapter 7).

This chapter will describe the methods used and present findings from both the quantitative and qualitative elements of the user-test study. Finally the chapter will conclude with a discussion of the findings and consideration will be given to the wider application of a headline section in regulated PILs.

4.1.1 Aims and objectives

Aims

To explore how readers use a headline section in a PIL to find and understand key information about their medicines.

Objectives

- To use performance based user testing to evaluate how frequently participants use a headline section to locate key information about their medicines.
- To evaluate the frequency of use of textual and visual signposts in the headline section.
- To determine general views on the headline section and how it might be improved.

4.2 Methods

4.2.1 Methodology

User-testing employs both qualitative and quantitative methods to test whether key pieces of information in a written document can be easily found and understood. The choice of this method supports the pragmatic approach used to underpin this thesis; which is practical in its objectives and aims to develop recommendations on the best ways to design PILs containing a headline section which meet the needs both of the public and the standards set out by the appropriate regulatory bodies.

A pragmatic research approach suits this aim as it focuses on the outcomes of the research - meaning the actions and consequences of the inquiry take priority over the underlying epistemological foundations. This study reflects this perspective as it is less focused on one system or philosophy, but instead concentrates on using the using appropriate methods of data collection which best answer the research question and which can facilitate practical applications of the research for the future (Creswell, 2013).

The pragmatic approach may incorporate the use of multiple methods of appropriate data collection to best answer a research question and can therefore include both qualitative and quantitative techniques. User-testing is a method which employs both methods to test the readability of written information. It is currently the gold-standard method in performance-based testing for patient information leaflets to ensure they are legible, clear and easy to use (European Commision, 2009). In Europe PILs are under a legal obligation to be tested with the target patient group. Therefore it is expected that this method is appropriate to measure outcomes which are applicable to the real-world and thereby facilitate the production of a headline section that meets the requirements of European regulators of medicines.

The strengths of user-testing include that it recruits potential real-life users of medicines to test the information, and responds to the unpredictable ways that a reader might use a piece of information (Sless and Shrensky, 2007). This is rather than relying on other methods, such as readability formulae, which may test aspects of the ‘readability’ of written information, but do not test whether patients can actually find and use the information they need (Meade and Smith, 1991) (Raynor, 2008).

There is a growing body of literature using user-testing as a research method to improve the readability of other types of written healthcare information. User-testing has been shown to improve the readability of many health documents, ranging from patient

information leaflets, clinical trial patient information sheets (Knapp et al., 2009b) healthcare instruction booklets, (Brooke et al., 2012) (Knapp et al., 2010) and healthcare appointment patient information (Lasser et al., 2006).

4.2.2 Design

The process of user-testing consists of a number of steps:

- Firstly 12-15 key points of information from the leaflet are identified that are relevant to the medicine's safe and effective use.
- A questionnaire is developed that:

(a) Determines whether people can find and understand each piece of information (quantitative) and
(b) Gathers additional comments from the participants on the documentation being tested through a qualitative semi-structured second part of the interview.

- Rounds of 10 participants are recruited from the target population and interviewed using the questionnaire. The aim is for all participants to be able to find each piece of information, and be able to express it in their own words (Raynor et al., 2011, Dickinson et al., 2001).
- The results of both the quantitative and qualitative parts of the questionnaire are then examined to determine if there are faults within the document. If so, good practice in information writing and design are employed to rectify those faults and the revised document tested on another cohort of 10.

4.2.3 Training

Prior to commencement of the user-testing, the researcher undertook training at Luto Research, a University of Leeds spin-out company that provides user-testing services. She shadowed a trained user-tester and observed several user-testing interviews undertaken at the organisation. This enabled her to observe the way in which the questionnaire was administered and consider the role of the researcher when providing prompts to the participants. Insight was also gained from a Luto staff member with experience in questionnaire design for user testing.

4.2.4 Participants

20 participants were recruited to 2 rounds of user-testing (10 participants in each round). Participants were members of the public who had an expressed an interest in

participating in research and who had provided their details to Luto Research. A database search identified potential recruits who met the inclusion criteria.

Inclusion criteria:

- aged over 50
- had not previously taken part in a user-test

Exclusion criteria

- had received a prescription for the type of medicine on which the exemplar leaflet was based (a statin medicine)
- unable to read a PIL in English
- a healthcare professional or in a role where they provide information about medicines.

Potential participants were then contacted by the researcher by telephone, to confirm their eligibility. Spoken information about the research was provided and if they expressed interest in taking part, a date for interview was agreed and an information sheet about the study was posted to them.

The following demographic details were recorded:

- age
- highest level of educational attainment
- use of written documents as part of their work

Each round of participants was recruited to a similar profile of age, education and use of documents.

4.2.5 Materials

a) Patient Information Leaflet.

Choice of medicine for the leaflet

In Study 2, two exemplar PILs were studied, one for a 'statin' medicine to lower cholesterol, and one for a 'triptan' medicine for migraine. It was decided to undertaken user testing on the former, i.e. for the hypothetical medicine Rebastatin (based on the real-life medicine simvastatin). This was because simvastatin, which Rebastatin is based on, is commonly-prescribed. Also, the safe and effective use of simvastatin requires patients to be aware of several key issues such as adverse effects and dietary restrictions. This information is well-suited to the concept of a headline section.

Design of the headline section

The leaflet contained a headline section, presented as a grey shaded box. The section was inserted at the beginning of the leaflet, and contained 7 key points of information about the medicine. The headline section was titled, using a darker shade of grey, '*Important things you need to know about Rebastatin'* and the 7 pieces of key information were presented as bullet points.

The headline section was developed in accordance from guidance from the MHRA (Medicines and Healthcare Products Regulatory Agency, 2005b, Medicines and Healthcare Products Regulatory Agency, 2005a). Previous research into the use of a headline section (Dolk et al, 2011) was also utilised to develop the headline section in accordance with the evidence-base and with the findings of study 2 which suggested the following:

a) The grey-shaded box format was an acceptable presentation of a headline section and was viewed as noticeable.
b) A need for improved navigation through the leaflet, hence the development of graphical markers.
c) The nature of the points of the headline used during the study was acceptable and responded to participant desire for key information.

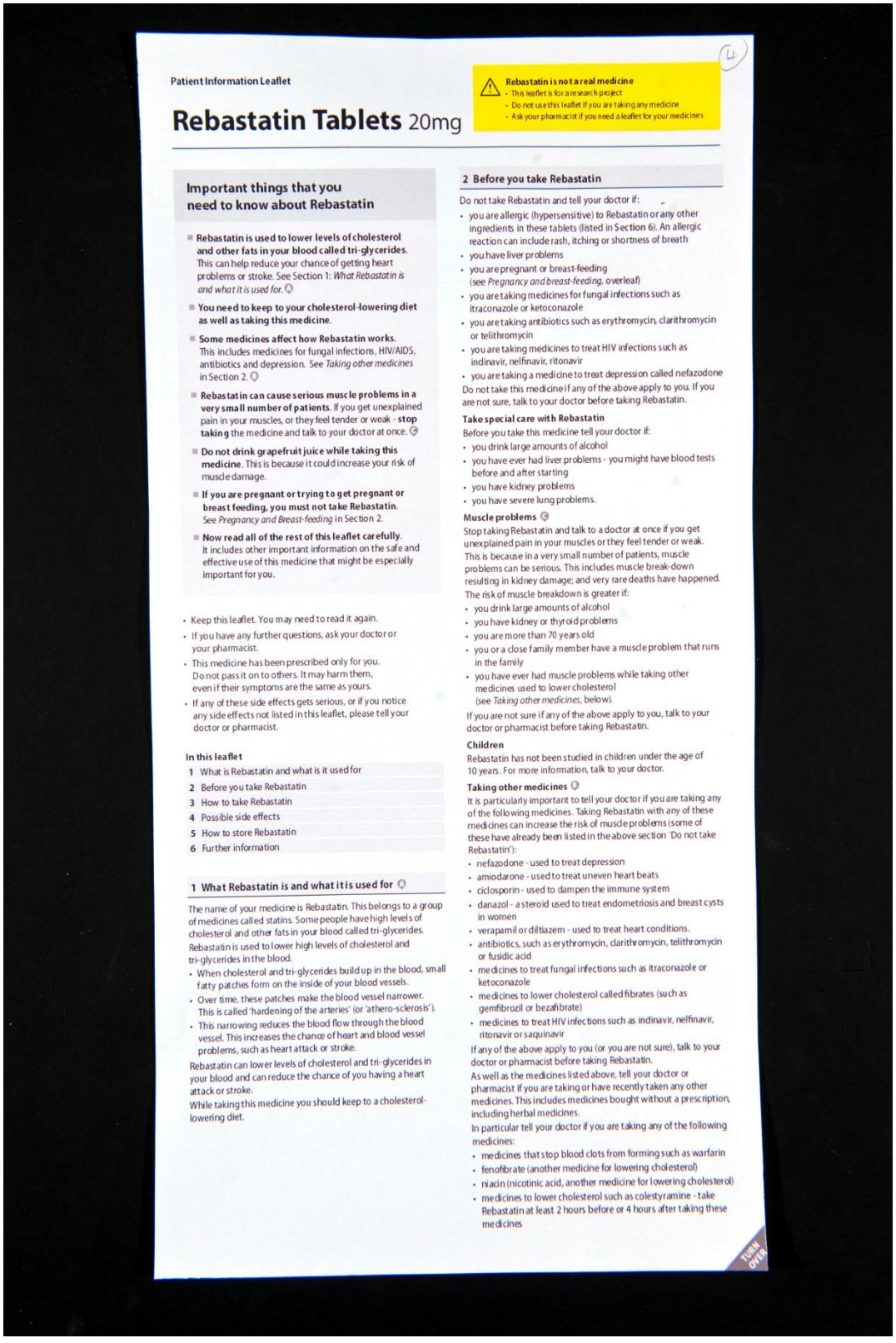
The exemplar leaflet was presented in a two column format and printed on 2 sides. The two column format is recommended by the MHRA as the short line length helps poorer readers (Medicines and Healthcare Products Regulatory Agency, 2012a).

A small icon in the bottom right hand corner instructed the reader to 'turn over' (figure 13). The layout and content of the leaflet followed guidance provided by the European Commission (European Commission, 2009) and the Co-ordination Group for Mutual Recognition and Decentralized Procedures – Human on the presentation of patient information leaflets (Co-ordination Group for Mutual Recognition and Decentralized Procedures - Human, 2011). The content was based on a standard leaflet for a simvastatin medicine and the key information included in the headline section was proposed by the pharmacist supervisors (DKR and JM). A graphic designer (BP) was consulted and he redesigned aspects of the headline section, in particular the signposting, according to the findings of the focus group work which underpinned this research. (Chapter 3)

Important things that you need to know about Rebastatin

- **Rebastatin is used to lower levels of cholesterol and other fats in your blood called tri-glycerides**. This can help reduce your chance of getting heart problems or stroke. See Section 1: *What Rebastatin is and what it is used for.* A
- **You need to keep to your cholesterol-lowering diet as well as taking this medicine**.
- **Some medicines affect how Rebastatin works**. This includes medicines for fungal infections, HIV/AIDS, antibiotics and depression. See *Taking other medicines* in Section 2. B
- **Rebastatin can cause serious muscle problems in a very small number of patients**. If you get unexplained pain in your muscles, or they feel tender or weak - **stop taking** the medicine and talk to your doctor at once. C
- **Do not drink grapefruit juice while taking this medicine**. This is because it could increase your risk of muscle damage.
- **If you are pregnant or trying to get pregnant or breast feeding, you must not take Rebastatin**. See *Pregnancy and Breast-feeding* in Section 2.
- **Now read all of the rest of this leaflet carefully**. It includes other important information on the safe and effective use of this medicine that might be especially important for you.

Figure 12: Headline section used in the leaflet.



Patient Information Leaflet

Rebastatin is not a real medicine
- This leaflet is for a research project
- Do not use this leaflet if you are taking any medicine
- Ask your pharmacist if you need a leaflet for your medicines

Rebastatin Tablets 20mg

Important things that you need to know about Rebastatin

- **Rebastatin is used to lower levels of cholesterol and other fats in your blood called tri-glycerides.** This can help reduce your chance of getting heart problems or stroke. See Section 1: *What Rebastatin is and what it is used for.*
- **You need to keep to your cholesterol-lowering diet as well as taking this medicine.**
- **Some medicines affect how Rebastatin works.** This includes medicines for fungal infections, HIV/AIDS, antibiotics and depression. See *Taking other medicines* in Section 2.
- **Rebastatin can cause serious muscle problems in a very small number of patients.** If you get unexplained pain in your muscles, or they feel tender or weak - **stop taking** the medicine and talk to your doctor at once.
- **Do not drink grapefruit juice while taking this medicine.** This is because it could increase your risk of muscle damage.
- **If you are pregnant or trying to get pregnant or breast feeding, you must not take Rebastatin.** See *Pregnancy and Breast-feeding* in Section 2.
- **Now read all of the rest of this leaflet carefully.** It includes other important information on the safe and effective use of this medicine that might be especially important for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This medicine has been prescribed only for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of these side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet

1 What is Rebastatin and what is it used for
2 Before you take Rebastatin
3 How to take Rebastatin
4 Possible side effects
5 How to store Rebastatin
6 Further information

1 What Rebastatin is and what it is used for

The name of your medicine is Rebastatin. This belongs to a group of medicines called statins. Some people have high levels of cholesterol and other fats in your blood called tri-glycerides. Rebastatin is used to lower high levels of cholesterol and tri-glycerides in the blood.

- When cholesterol and tri-glycerides build up in the blood, small fatty patches form on the inside of your blood vessels.
- Over time, these patches make the blood vessel narrower. This is called 'hardening of the arteries' (or 'athero-sclerosis').
- This narrowing reduces the blood flow through the blood vessel. This increases the chance of heart and blood vessel problems, such as heart attack or stroke.

Rebastatin can lower levels of cholesterol and tri-glycerides in your blood and can reduce the chance of you having a heart attack or stroke.
While taking this medicine you should keep to a cholesterol-lowering diet.

2 Before you take Rebastatin

Do not take Rebastatin and tell your doctor if:

- you are allergic (hypersensitive) to Rebastatin or any other ingredients in these tablets (listed in **Section 6**). An allergic reaction can include rash, itching or shortness of breath
- you have liver problems
- you are pregnant or breast-feeding (see *Pregnancy and breast-feeding*, overleaf)
- you are taking medicines for fungal infections such as itraconazole or ketoconazole
- you are taking antibiotics such as erythromycin, clarithromycin or telithromycin
- you are taking medicines to treat HIV infections such as indinavir, nelfinavir, ritonavir
- you are taking a medicine to treat depression called nefazodone

Do not take this medicine if any of the above apply to you. If you are not sure, talk to your doctor before taking Rebastatin.

Take special care with Rebastatin

Before you take this medicine tell your doctor if:

- you drink large amounts of alcohol
- you have ever had liver problems - you might have blood tests before and after starting
- you have kidney problems
- you have severe lung problems.

Muscle problems

Stop taking Rebastatin and talk to a doctor at once if you get unexplained pain in your muscles or they feel tender or weak. This is because in a very small number of patients, muscle problems can be serious. This includes muscle break-down resulting in kidney damage; and very rare deaths have happened.
The risk of muscle breakdown is greater if:

- you drink large amounts of alcohol
- you have kidney or thyroid problems
- you are more than 70 years old
- you or a close family member have a muscle problem that runs in the family
- you have ever had muscle problems while taking other medicines used to lower cholesterol (see *Taking other medicines*, below).

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking Rebastatin.

Children

Rebastatin has not been studied in children under the age of 10 years. For more information, talk to your doctor.

Taking other medicines

It is particularly important to tell your doctor if you are taking any of the following medicines. Taking Rebastatin with any of these medicines can increase the risk of muscle problems (some of these have already been listed in the above section 'Do not take Rebastatin'):

- nefazodone - used to treat depression
- amiodarone - used to treat uneven heart beats
- ciclosporin - used to dampen the immune system
- danazol - a steroid used to treat endometriosis and breast cysts in women
- verapamil or diltiazem - used to treat heart conditions.
- antibiotics, such as erythromycin, clarithromycin, telithromycin or fusidic acid
- medicines to treat fungal infections such as itraconazole or ketoconazole
- medicines to lower cholesterol called fibrates (such as gemfibrozil or bezafibrate)
- medicines to treat HIV infections such as indinavir, nelfinavir, ritonavir or saquinavir

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking Rebastatin.
As well as the medicines listed above, tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines bought without a prescription, including herbal medicines.
In particular tell your doctor if you are taking any of the following medicines:

- medicines that stop blood clots from forming such as warfarin
- fenofibrate (another medicine for lowering cholesterol)
- niacin (nicotinic acid, another medicine for lowering cholesterol)
- medicines to lower cholesterol such as colestyramine - take Rebastatin at least 2 hours before or 4 hours after taking these medicines

TURN OVER

Figure 13: Photograph of the headline section to show positioning in the leaflet.

Textual signposting

Where the headline section contained additional information which was expanded upon in the main body of the leaflet, there was a textual signpost directing the reader to the appropriate section of the leaflet where the additional information could be found, e.g. 'See Section 1: *What Rebastatin is used for?'* If the information provided in the headline was discrete and not elaborated upon elsewhere in the leaflet or if additional information was available in multiple places then a textual signpost was not included.

Graphical signposting

'Graphical markers', such as were included after the textual signpost for 3 of the key points. This was an additional signpost designed to direct the reader using a visual cue. These signposts were repeated in the body of the leaflet, where the appropriate information was to be found.

b) Questionnaire.

The purpose of the questionnaire was to:

- Test a participant's ability to find and understand 15 key pieces of information.
- Determine participants' general views on the document, and its positive and negative points.

User testing can be undertaken to assess the readability of all of a document, or just one part. The latter is referred to as a 'focus test'. However, it was decided not to 'focus test' the headline section because:

- We need to know if the addition of a headline section impinges on the effectiveness of the rest of the leaflet.
- Some of the points in the headline section are sign-posted to text in the main body of the leaflet.

Hence the questionnaire was developed to cover all aspects of the leaflet.

The questions are listed in Figure 14; and there were 6 questions related to information in the headline section. For 4 questions the answer could be found in its entirety in the headline section (questions 1, 3, 7 & 9). Two questions (questions 6 & 10) were devised to test whether the headline section would be used as a point of reference to find additional information elsewhere in the leaflet and whether the reader would use either the textual or visual signpost.

The user-test questions were presented in a different order to how the information appeared in the leaflet. This was to ensure that the participant had not learnt that the points of information in the questionnaire were sequential in terms of placement in the PIL.

For the second, qualitative, part of the interview a brief topic guide was prepared covering 6 points – see Figure 15.

	Question	Main leaflet section	Headline Section?	Textual signpost	Graphical signpost
1	What is Rebastatin used for?	1	Yes	n/a	n/a
2	What does the leaflet tell you to do before you start taking this medicine if you drink large amounts of alcohol?	2	No	No	No
3	Suppose you are pregnant, what information does the leaflet give about whether or not you can take this medicine?	1	Yes	Yes	No
4	What is the usual dose of Rebastatin for people with Coronary Heart Disease?	3	No	No	No
5	What group of medicines does this medicine belong to?	1	No	No	No
6	Imagine you are already taking Rebastatin and would like to take an antibiotic, what does the leaflet tell you to do?	2	Yes	Yes	Yes
7	How does Rebastatin affect your chance of having a heart attack?	1	Yes	n/a	n/a
8	How many people are likely to feel sick after taking this medicine?	4	No	No	No
9	Suppose you start to take Rebastatin, what information does the leaflet give about your diet?	1	Yes	No	No
10	Unexplained pain in your muscles can be a sign of muscle problems. What can happen if you get these muscle problems?	2/4	Yes	Yes	Yes
11	Suppose you forget to take Rebastatin and it is nearly time for your next dose, what does the leaflet tell you to do?	3	No	No	No
12	Imagine you are taking this medicine then you develop a rash, with weak legs, what does the leaflet tell you to do?	4	No	No	No
13	Why should you not drink grapefruit juice while taking this medicine?	2	Yes	No	No
14	Suppose you are already taking Rebastatin and you need to have an operation, what does the leaflet tell you to do?	2	No	No	No
15	Imagine you already have a kidney problem, what information does the leaflet give you about the dosage of the medicine?	3	No	No	No
Light grey shading refers to questions assessing use of headline Dark grey shading refers to questions assessing use of headline and signposting					

Figure 14: User-testing questionnaire.

The questionnaire was initially piloted with 2 participants to evaluate the usability of the questionnaire in a test scenario. The characteristics of the participants are reported in table 7. Both the questionnaire and leaflet performed well and no significant issues were identified (appendix 17). However the order of the questions was changed to ensure a more even spread of the questions that focused on the headline section throughout the questionnaire.

4.2.6 **Procedure**

Interviews were conducted in an interview room with the researcher (RD). The participant was welcomed into the room and the aims and procedures of the research discussed and written consent obtained. The participant was then provided with the exemplar PIL and the user-test began immediately. The researcher administered the questionnaire, asking each question in the order specified in figure 14. The participant was able to refer to the leaflet as required throughout the user-test. The user-test was timed and audio-recorded (with permission).

The researcher recorded the following outcomes:

- Whether the participant could find and understand the answers to the question. (Using a dichotomous score of yes/no).
- The time taken to locate the answers.
- The number of prompts required to help clarify the question. (Prompts include rephrasing or restating the question). The same prompts were used for each user test. For example, if a participant responded with a partial answer, the question “Does the leaflet provide any additional information?” would be used to prompt a more complete response.
- The location in the PIL from where the answer was found. In particular, it was noted whether the answer to the question was found from the headline section. If the location where the information was found was not obvious to the interviewer, she asked the participant to point it out on the PIL.
- Whether the participant used the textual or graphical signpost. (This was evaluated through observation and questioning if necessary).

Following the user-test questions general qualitative questions were asked in order to explore perceptions of the headline section.

- What is your impression of the leaflet in general?
- What did you think about the 'important things' section at the beginning of the leaflet?
- Most leaflets don't, at the moment, have this 'important things' section – would you like them to have such a section, or do you prefer leaflets as they are? Can you tell me why you would prefer/ not prefer an 'important things section'?
- Can you recommend any improvements to this section?
- Do you think you would do anything differently if your leaflets came with this section? *Prompt: might you just read this section?*
- What did you think about the way you were sometimes directed in the 'Important things' section to further information in the main leaflet/

Figure 15: Qualitative questions.

4.2.7 Data analysis

Data analysis comprised of two distinct phases, that relating to quantitative data and that relating to qualitative data.

Quantitative

The performance of the leaflet was measured in the following ways:

1) The total number of answers that were found or not found, was recorded.
2) If answers to questions were found and understood by 80% or less of participants, this was taken as an indication that there was an issue which might need to be resolved. This is in accordance with the threshold recommended in EU legislation on the testing of medicine leaflets.
3) Whether the information was located in the headline section was recorded for each question (where relevant). This enabled the researcher to compare and contrast the use of the headline section use across the questions.
4) The number of opportunities to use the headline section and number of times the answer was located in the headline was recorded.
5) Whether a signpost was used was noted for each question where this was relevant.

Qualitative

The qualitative data were analysed using content analysis. The interviews were listened to and transcribed verbatim by RD. A process of familiarisation followed where the interviews were listened to again, the transcripts re-read and notes made. The data was then charted according to participants' responses by question (appendix 18). This enabled the researcher to explore any common responses and explore the data according to participant response and characteristics.

A process of mapping and interpretation was undertaken. Each response was summarised and the summaries grouped into corresponding themes. The themes were grouped into coherent categories and sub-categories. Appendix 19 shows part of this process.

4.2.8 Research ethics

The research was approved by the University of Leeds, School of Healthcare Research Ethics Committee (SHREC RP/271).

4.3 Quantitative results

20 participants were recruited and formed 2 rounds of 10. Their characteristics are reported in table 8.

Table 8: Participant characteristics

Category	Sub-category	Pilot (n=2)	Round 1 (n=10)	Round 2 (n=10)
Women		2	7	6
Age	50-59	1	5	4
	60-69	1	3	4
	70+	0	2	2
Education*	1	1	5	2
	2	0	3	6
	3	1	2	2
Literature use**	Lit	2	5	5
	No Lit	0	5	5

*1=attended school, 2 = attended college or further education, 3= graduate level education

** Lit = regularly uses written documents as part of work. No lit = does not regularly use of written documents as part of work, or are currently not working or are retired.

4.3.1 General performance of the PIL

Overall the leaflet performed well. The data collected in round 1 identified 2 problematic questions. These questions were:

[1] **What does the leaflet tell you to do before you start taking this medicine if you drink large amounts of alcohol?** Found 7/10 and understood 7/10

[2] **Imagine you are already taking Rebastatin and would like to take an antibiotic, what does the leaflet tell you to do?** Found 8/10 and understood 7/10

As the issues identified with the questions were not related to the use of the headline section, a decision was made not to make changes in between the rounds as changes would not impact upon the use of the headline section.

In round two at least 80% of the participants found and understood all the information. (Which is in accordance with the threshold recommended in EU legislation on the testing of medicine leaflets) (European Commission, 2009). No significant problems with the leaflet were identified.

As a result of this the presentation and analysis of the results will focus on those questions relating to information found in the headline section.

4.3.2 Using the headline section

The following questions related to the headline section:

(a) Self-contained pieces of text which are replicated in the main body, with no additional information there

1] What is Rebastatin used for?

2] Suppose you are pregnant, what information does the leaflet give you about whether or not you can take this medicine?

7] How does Rebastatin affect your chance of having a heart attack?

8] Suppose you start to take Rebastatin, what information does the leaflet give about your diet?

13] Why should you not drink grapefruit juice while taking this medicine?

(b) Piece of text which is expanded upon in the main body of the leaflet

6] Imagine you are already taking Rebastatin and would like to take an antibiotic, what does the leaflet tell you to do?

10] Unexplained pain in your muscles can be a sign of muscle problems. What can happen if you get these muscle problems?

It was apparent that the headline section was used by the participants, although it was not used all time. When the data were collated a range of frequencies of headline use was identified, depending upon question type.

Table 9 shows the scoring for the questions which assessed the frequency of use for the headline section, whilst table 10 shows the scoring for the use of the signposts. The findings were as follows:

Table 9: Frequency of use of the headline section

Round	Headline		Q1	Q3	Q6	Q7	Q9	Q10	Q13
1	Headline used?	Yes	8	2	0	2	7	0	8
		No	2	8	10	8	3	10	2
2	Headline used	Yes	10	4	0	3	4	0	7
		No	0	6	10	7	6	10	3

Light grey shading refers to questions assessing use of headline

Dark grey shading refers to questions assessing use of headline and signposting

Question 1:

- **What is Rebastatin used for?**

The headline was most frequently used for question 1. This was the first question and the majority of the participants looked immediately at the beginning of the leaflet in the headline section. (18/20, 90%)

Question 6 and 10:

- **Imagine you are already taking Rebastatin and would like to take an antibiotic, what does the leaflet tell you to do?**
- **Unexplained pain in your muscles can be a sign of muscle problems. What can happen if you get these muscle problems?**

These questions tested the frequency of use of the headline as a tool for directing the reader to related information included elsewhere in the leaflet.

While the participants could not locate the complete answer to these questions in the headline, it could be used as a tool to direct the reader to the relevant information that was in the main body of text. It was observed that the headline section was not used as a prompt in locating the answers for either of these questions. Instead participants used the main body of the leaflet where this information was repeated, often several times for each question, to retrieve the correct answers. For both questions, the answers were

predominantly found in Section 2: Before you take Rebastatin. Although for question 10 the answer was occasionally (n=4) found in Section 4: Possible side effects.

The headline section was used infrequently for the remaining questions (Q3, 7, 9, 13). If the information was self-contained in the headline section, then there appeared to be a greater chance that the headline would be used to locate it. For example, both Q9 and Q13 had answers that were found either in the headline or in only one other place in the leaflet. Neither of these pieces of information could be easily found under a logical heading elsewhere in the leaflet. For example information about Pregnancy could be found under a sub-heading: **Pregnancy and Breastfeeding**, which was highlighted in bold. The answers to these 2 questions were contained within larger bodies of text and were often isolated (i.e. not surrounded by relevant information as they were stand-alone statements). For question 9 the headline was used 11/20 times (55%) and for question 13 the headline was used to locate the answer 15/20 times (75%).

Question 3, which referred to whether the medicine could be taken during pregnancy, was found 6/20 (30%) in the headline. Information about pregnancy was available in 2 places in Section 2.

And finally, question 7, which was located in two places in the leaflet, but presented in the headline alongside other information about the uses of the medicine. This headline was used to locate this information 5/20 (25%).

To conclude, there were 140 opportunities for the reader the use the headline section find or assist with the location of important information. The headline was used, in total, for 55/140 opportunities (39%).

4.3.3 Use of the signpost

Two questions, Q6 and Q10, were designed to test whether participants used the signposts by being designed so that the participant could find a partial reference to the answer in the headline, but to find the full answer they needed to use the signpost to find the answer elsewhere in the leaflet. The headline was not used to retrieve the answers to these questions. However, it was observed that some of the participants noticed and used the textual signpost for some of the other questions when the headline section was used. 1 participant reported they had used the textual signpost on question 1 and 4 participants reported usage of the signpost on question 4. One participant stated they had noticed the signpost during their qualitative interview but there was no evidence it was used.

Table 10: Frequency of use of the signposting (both textual and graphical)

Round	Textual (T)or graphical (G)	Score	Q1	Q3	Q6	Q7	Q9	Q10	Q13
1	Signpost noticed	Yes	1 (T)	-	NO	-	-	NO	-
		No	-	-	NA	-	-	NA	-
2	Signpost noticed	Yes	-	4 (T)	NO	1 (G)	-	NO	-
		No	-	-	NA	-	-	NA	-

Light grey shading refers to questions assessing use of headline

Dark grey shading refers to questions assessing use of headline and signposting *

T = Textual signpost, G=Graphical signpost.

4.4 Qualitative results

Overall the majority of the participants described the headline section as a valuable inclusion in a PIL. Only one participant did not voice positive views.

4.4.1 Helping people engage with information

The headline section was viewed as a useful tool to assist the reader to engage with information; however a small number of participants stated they either did not see the headline section initially or at all:

> *"I didn't realise why that was there and I haven't really read that much. That's like the bullet points of what is going to be in the information leaflet." (P17, F, 60)*

Those that noticed the headline tended to view it as a useful aid in assisting the reader find key facts about the medicine. The highlighting of the section was viewed as helpful in emphasising the key information and bringing it to the reader's attention:

> *"I'd probably be more likely to read that bit because it is highlighted in bold and it appears to carry the most important type of information. " (P8, M, 56)*

It was also viewed as noticeable and helpful because of its prominent position, at the beginning of the leaflet:

"I think you are right to put it first because that's the most important things." (P10, F, 63)

Usual leaflets were viewed as long and difficult to retrieve information from:

"I think it's a good idea because quite often you look at a leaflet and you think there is an awful lot of information and you think, I'll read it when I need to, and that's the last you see of it." (P3, F, 63)

The headline was viewed as a tool which aided the reader to locate important information from a mass of information, that might not all have the same relevance (or be as important):

"Well, it brings you to important facts straight away, rather than trying to find individual facts throughout the leaflet. You can go straight to that and the most important parts of the document." (P9, M, 50)

It was viewed by some as essential in helping patients find information quickly. Speed of retrieval of important information was viewed as important for many participants and some held the view that they could obtain key information by glancing at their leaflets, rather than having to search though for specific points:

"I think from a glance at the front you can identify if you are going to fall into any categories where this might be a risk." (P12, F, 58)

"I think this is more informative this way. Straight away you get the answers to some questions." (P20, F, 82)

"I liked it because it is clear and because it stands out from the rest of it. You have the key points in bold and I think people are more geared up now for looking for the bullet points and you can go, 'yeah, yeah, need to know about that, don't need to know about that'. And it's just easier to pick out the information rather than getting a mass out of it." (P3, F, 63)

Finding information quickly was particularly important when people were concerned about the risks associated with taking a medicine:

"I think you can read and you think 'I can't really take this' straight away." (P12, F, 58)

4.4.2 Suggested improvements to the headline section

Not all participants suggested improvements to the headline section; they felt that the headline met their needs regarding the information it contained in its current format. When suggestions were recommended, they fell into 3 categories: content, format and the leaflet as a whole.

a) Improvements to the content of the headline section

Key recommendations were for the headline section to contain more information about side-effects, drug interactions and dosage:

"I think saying a little bit more about the dosage and 'stop taking it if'..." (P3, F, 63)

"You haven't got anything there about side-effects. I think you should…you should have it in your box thing…I think you should say like anything this medicine can cause side effects, please see section whatever." (P4, F, 62)

One participant suggested that the information presented be simpler and less technical:

I would have as much information under a simple heading, such as 'do not' and advising you. I would have it like this, because some can get a bit technical…medical." (P10, F, 63)

b) Improvements to the format of the headline section

Suggestions to improve the format of the headline included to enhance the noticeability of the headline by using either a text box or a coloured box:

"I would put a more clear boundary around it so it is separated from the rest, because there is nothing to make it stand out. Even making this little box, the headline, a brighter colour and the one that screams 'important' is red. Otherwise you turn it over and there is nothing there that particularly separates it. If there was a border around it and it was a separate colour then I would be inclined to read that before I go anywhere else. Obviously, if there are things in there which apply then I will go elsewhere in the leaflet. I shouldn't need to read the whole thing." (P16, M,57)

The use of larger, or bolder, text was also raised as a suggestion, and this also related to the use of text to emphasise key points. For example, it was suggested that more emphasis be placed on the statement 'Now read this entire leaflet' using bigger letters.

c) Improvements to the leaflet as a whole.

One suggestion was to adapt the design of the leaflet in some way so it emphasised the headline section. A small number suggested the leaflet take a booklet format, with different pages (with a difference emphasis on each page). Another suggestion was that the leaflet should be folded so that the headline is the first thing the patient sees when they remove the leaflet from the box:

"I think it is a good idea, if these are folded in such a way that it is on the front when you pull it out. You may well get people to at least read that little bit." (P6, M, 65)

"The benefit of that (the headline) is that you would see the whole thing in one….actually, you could just fold up the leaflet so that the first thing that comes up is the important things you need to know because, then, if it is clear with a visible border around it, it's probably more likely that people will take that in and read it." (P16, M, 57)

4.4.3 Signposting and navigation

On the whole, the headline itself was positively viewed as a tool that could help participants locate and retrieve information about the medicine:

"It gives the headline and which section to go to." (P16, M, 57)

a) Graphical signposts

When prompted to express their views most participants were generally quite positive about the graphical markers, considering them to be a potentially useful tool in aiding with finding information. However, several participants stated that they had not noticed the graphical markers at all and despite the participants' enthusiasm for this tool, the graphical marker was commonly skipped over or ignored or misunderstood:

"Oh like A, B and C, Oh yeah I didn't notice them. I didn't see them and I should've and I didn't. I didn't see them. I didn't take any notice. I think a lot of people are like me though. Aha, like A goes with A. Yeah. No, I didn't see them. I didn't take any notice of them or I would have found them answers quicker." (P1, F, 52)

"Oh right, yeah, I've only just noticed these I'm afraid…so yeah, I think I've answered that [question about using the graphical markers]. They seem like a good idea, but I obviously missed them." (P8, M, 56)

Suggestions to address this included the use of colour and a bolder design for the markers:

"I think if that B was in bold, done in a similar manner, but bold rather than shaded. I think it would stand out more." (P5, M, 65)

While the graphical markers did not appear to hinder the reader in any way, a number of participants misunderstood their purpose, were confused about their purpose or didn't notice them at all:

"No, it's not very clear. You know, your A, Bs… I didn't know what they were. I can't see how it adds up. It's A,B & C. I would put a number on it." (P10, F, 63)

b) Textual signposts

Not everyone noticed the textual signposts and some participants reported they skipped over them when looking for information elsewhere in the leaflet. One participant missed the existing textual signposts but recommended that the headline would be improved with a textual signpost:

"It could say 'look at section 4 or section 5.'" (P10, F, 63)

However, it was apparent that others did notice and appeared to value the inclusion of the textual signposts. Some participants described how they helped them navigate the leaflet. This was particularly in reference to specific information such as pregnancy or muscle damage:

"You can see it and I found what I was looking for quite easily because you have got captions and I could follow it quite simply." (P12, F, 58)

"Yeah, once or twice I [used the textual signposts]. I did because those 3 questions looked at, in particular, the muscles, the grapefruit, the pregnant, yeah, for those." (P20, F, 82)

One participant noted how the headline and the textual signposts responded to how people use information in the age of the internet. People are more geared up for bullet points and this participant felt the headline like using a webpage:

"I think that's very good, particularly for those who are impatient. Some people will read things from top to bottom. Quite a lot of us won't. I know I don't. I will pick out the key point and think 'yes, I need more of that.' So if there is something which says to me 'if you want to know more about this go here, then it's the equivalent of if you are on a website. You get the little thing that say's click here and it throws you into that section. I think that because people get a lot more information on the internet now we get a bit lazy and expect to click through, but in the days when written information came on pieces of paper and no other way, you were expected to read through to the end." (P3, F, 63)

4.4.4 Reported influence on behaviours

The participants reported 3 ways in which the inclusion of a headline section might impact upon the way in which they, or others, read their leaflets.

a) People might read more of their leaflets

Not all the participants read all of their leaflets. A small group stated that the headline section might encourage them to read at least the 'important things' section. It was considered that the summary of important information might also encourage them to access and find other relevant information further on in the text:

"I think if [the headline] highlighted something I was concerned about then I would read more of the information." (P11, F, 56)

[I would read] possibly more if there is something in there which rings a bell with you." (P6, M, 65)

"I think this is good because it gives you a brief insight into what problems there might be and then you would be inclined to look at the rest of it." (P18, M, 64)

Overall, the headline was frequently viewed as an innovation which might encourage more people to read their leaflets:

"If you're the type of person who doesn't read leaflets at all, then maybe there is a greater chance that they would read that rather than nothing at all. If you could get the absolute most important information in their memory, then that would be a good innovation." (P8, M, 56)

b) People might read less of their leaflets

Some participants noted that they might only read the headline section and may not be encouraged to read elsewhere in the leaflets:

"I think I would be more liable to read that bit and not any of the other, just read the important things bit and not read any of the other." (P2, F, 56)

Some had concerns that others might not read the whole leaflet if the headline section was present in a leaflet:

"I try to think that I read all my leaflets, but I think that some people might just read that bit and think 'I've read it!' and really they should read the whole lot." (P15, M, 67)

However, it is important to note that some participants reported that only reading the headline section was more of the leaflet than they would read normally and that the headline section itself enabled them to see the important information, rather than wade through the text to try and find relevant information, which frequently led them to give up on reading the leaflet. This could potentially lead to a more streamlined accessing of information:

"I think when people are on medicines they read the most important things and the side effects, not everything. That's what I read into. I don't look for everything. But, what it is with me is it takes me a while to register things and I think I would go for the most important things. "(P1, F, 52)

"I'd go straight to that section, rather than turn it over and look it over. I'd go straight to that part straight away." (P8, M, 56)

To summarise, some participants reported that the inclusion of a headline section might mean they read less of their leaflet, they felt that this was still beneficial as the more targeted information meant they would still find and retrieve more important information from their leaflet than if they had a leaflet without a headline, which they found difficult to read.

c) People would not change their behaviour.

A few participants stated that they would not change their behaviour if their leaflet contained a headline section and that they would continue to read the leaflet as they usually did:

"I would read it as it comes." (P20, F, 82)

"I would read it all anyway." (P17, F, 60)

Finally, one participant made a comment about getting used to the headline section. Although he found himself skipping over the headline section during the user-test, he noted its utility in the long-term:

"Once I had worked out what it was for, I found it more useful." (P8, M, 56)

It is possible that the headline section might become more useful a tool if people became familiar with it if it was routinely included in a regulated PIL.

4.5 Discussion

The aim of this research was to determine how people use a headline section by user-testing a PIL incorporating a headline section. The results showed that a headline section was used just over a third of the time (in total, for 55/140 opportunities (39%). Other notable findings included that 18/20 (90%) of participants used the headline section to find information when they initially began the user-test which suggests it was the first place a participant looked in the leaflet when initially trying to find important information. The results also suggest that there was a tendency for patients to use a headline section to locate self-contained pieces of information which might not be naturally positioned elsewhere within the leaflet.

The headline did not appear to be commonly used as a signpost for the reader to look elsewhere in the leaflet. In particular, the graphical markers used to signpost the reader elsewhere were not used at all. This could be a failing in the design of the graphical markers specifically used in this leaflet and participants reported that the use of bigger and bolder graphical markers might draw their attention. It is possible that further research into the use of graphical markers might suggest a method of best practice. Participants were observed to use the textual signposts to assist with navigation of the leaflet, although this was infrequent and the textual signposts were only helpful for a small minority of people. However, neither of the signpost methods used appeared to hinder the reader in any way and for those that did use them they appeared to help the participant navigate the leaflet. It is possible that if either type of signposting was routinely used in PILs, people would come to learn their function.

The qualitative findings suggested that the participants valued the presence of the headline section. On the whole the headline was viewed as a useful tool which helped the reader engage with the information; it was noticed by participants and appealed to those with concerns about the length and complexity of current PILs. (Dixon-Woods, 2001, Grime et al., 2007, Raynor et al., 2007) It was suggested that the headline

responded to people's needs for information that can match the type and format of information provided on a website; short, succinct information that can be accessed easily.

These findings echo those of another study (Dolk et al., 2011) and also the findings from the study reported in chapter 3, which also found that patients valued the headline section and were enthusiastic about its inclusion in PILs. This is a strong and consistent qualitative finding.

User-testing, as a method, combines qualitative and quantitative aspects of enquiry to identify flaws in a piece of information. There is a growing body of research supporting its use in evaluating and improving the performance of written documents (Knapp et al., 2010, Brooke et al., 2012, Raynor, 2013). It has been shown to improve the readability of PILs and ensure that they are fit-for-purpose. It is commonly used and is the gold standard for testing the performance of PILs in Europe. However, the method has limitations. The user-testing method uses small numbers and so, with regards to the quantitative findings, cannot give statistical certainty (Knapp et al., 2009b). However, these small numbers are well-suited in identifying any key issues with the leaflet and it is often apparent if there is an issue with the leaflet after only a few user-test participants (Raynor, 2013).

The method has also been criticised for using a summative approach with its focus on reaching performance targets set by regulators, rather that the formative approach for which it is designed, i.e. the 'test, amend text and layout, test' cycle (Raynor et al., 2011). However, this study was not bound by pre-defined performance targets. This study planned an iterative approach to evaluate performance. As the leaflet consistently performed well for the headline section questions, no amendments were required to the leaflet between the rounds of testing.

With regards to the wider literature, it has been suggested that a headline section has the potential to be beneficial and engage patients in reading about their medicines (Medicines and Healthcare Products Regulatory Agency, 2005a). However, relatively little is known about the use in practice of a headline section in medicines information. Hartley (2004) suggested that the inclusion of a 'boxed aside' which is used to emphasise text within a larger body of text in educational materials might encourage the reader to skip around the highlighted section and ignore the important text. The headline section used during this research was presented at the top of the leaflet and not within a body of text. The user-testing showed that the headline section was used

on about a third of occasions to locate relevant information. There was no evidence that the participants skipped over the headline section; instead the user-testing findings suggest that the headline section was the first part of the leaflet that the reader viewed.

Similar research exploring the use of the headline section used a 2x2 factorial design to compare the impact of a leaflet with a headline section with a leaflet without a headline section on a reader's performance and perception (Dolk et al., 2011). The headline section used by Dolk et al (2011) was similar to the headline used in this study and was one chosen by the MHRA to illustrate headline sections (Medicines and Healthcare Products Regulatory Agency, 2005a). Dolk et al (2011) did not find any difference between PIL designs in participants' ability to find and comprehend the information provided. Both the headline section and non-headline section groups performed equally well. It was noted that there was no evidence that the headline section had a negative impact on the reader, but nor did it have a positive impact. Dolk et al (2011) used a traditional user-testing format, in which participants were given time to read and familiarise themselves with the entire leaflet before the user-test commenced. It might be considered that as the participants had read the entire document prior to the test they assumed that the headline was a summary and when asked to respond to the questions neglected to use it in favour of the leaflet as a whole.

The research reported in this chapter was a follow on study from Dolk et al (2011) which explored the use of the headline section in a more naturalistic setting, using a modified user-testing approach. The setting was still experimental but the user-test was adapted in order to replicate what might happen when a patient initially receives a PIL. It was hypothesised that the headline might be useful to help a reader find key information when they are unfamiliar with the leaflet and are first looking at it. Therefore, the aim of this study was to evaluate whether the headline section was used in a modified user-test scenario where the participant did not have the opportunity to read the leaflet prior to commencement of the test.

The user-test in this research did not use the same methods as Dolk et al (2011) as there was no leaflet without a headline section control group. The findings show that in a 'modified' user-test scenario, where a participant did not have the opportunity to familiarise themselves with the leaflet, the headline was used about a third of the time to source important information. It was noted that the headline was used to locate information to answer the first question (18/20 opportunities (90%)), which suggests that the headline is seen and used immediately by a participant who is unfamiliar with a leaflet.

4.5.1 **Strengths and limitations of the methods**

This use of this method complements the pragmatic approach used in this study. An important objective of this body of work was to ensure that the findings from the research can be applicable to the real world and provide guidance (recommendations) on the incorporation of a headline section in patient information leaflets. User-testing is a diagnostic process that can facilitate that and is currently the process used to regulate PILs before they are licenced. Since 2005 it has been mandatory for PILs in the EU to be user-tested to ensure that leaflets are legible and easy-to-use (European Commission, 2004).

The evidence-base for the use of this method to test patient information has developed significantly over the past few years and applying this process to a leaflet has been shown to develop information which responds to a patient's needs and which can improve the reader's ability to find and understand key pieces of information (Raynor et al., 2011, Knapp et al., 2010).

User-testing is a more suitable method to test the performance of a piece of writing compared to content-based testing methods (See section 4.2.1).

However there are some limitations with the use of this method and with the application within this thesis. User-testing is a method that was intended to be diagnostic and developmental, rather than one used for evaluation, so it can be difficult to use the approach to make firm conclusions about the effectiveness of the headline section.

User-testing has also been criticised for the use of a small sample size. The choice of rounds of 10 for each user-test is a convention that is not necessarily evidence-based. However, it is accepted that this diagnostic approach can be useful in identifying problems with information using only small numbers. Sless (2004) uses an analogy of a creaking step in order to demonstrate how a small sample can be helpful in identifying and addressing issues with a piece of information:

> *"Suppose you have a staircase that had a few creaking steps: every time someone went up the staircase you could hear it creak annoyingly a number of times. How many people would you need in a sample to climb up and down the staircase to find the location of the creaks, and should you have a representative sample of staircase users to find out which steps creak? Would the sample size be important? Clearly, there are types of consideration – so much a part of social science research – are not relevant in this context. By analogy, the same is true*

of document testing. Moreover, as with the staircase, to find out if the problem in a document has been fixed does not need a large representative sample of users"(Sless. D, 2004, P.31).

User-testing does not rely on undertaking statistical sample size calculations to generate a powered sample and this may enhance the possibility of making a type-II error, which is the failure to reject a false null hypothesis. Also, the user-testing study did not have a control group. It is possible that a controlled trial with a larger sample might come to different conclusions about the inclusion of a headline section in a PIL. Dolk et el (2011) used a controlled design in a user-testing study of leaflets with and without a headline section and found no difference in a participant's ability to find and understand information (Dolk et al., 2011). It is possible that the inclusion of headline section has no discernible impact on the reader's ability to find and understand information in a leaflet. However, there is no evidence that it hinders the reader either, and the findings from the qualitative study suggest it is a popular and welcome inclusion in a PIL.

Participants were recruited with a mix of genders, ages, educational ability and use of literature in everyday life. This adds to the representativeness of the research; however it is important to note that the type of people who engage in research of this type may differ with regards to their health literacy from the population as a whole.

It is also important to note that the user-test is an artificial situation and this might impact upon how participants use and find the information. Certainly it is possible that the use of the questionnaire impacted upon how participants used the headline by diverting the reader elsewhere in the leaflet to answer the next question. This may impact upon the findings, leading to an under-reporting of the use of the headline section as the user-test diverted the participant's attention away from the headline in a way that might not happen in a naturalistic setting.

To conclude, there are some limitations to the findings from the user-testing study, however it is important to note that the use of user-testing complements the pragmatic approach used and reflects the methods used currently to test PILs prior to licencing in the EU.

Impact of the research and recommendations for further research.

Participants tended to use the headline to locate discrete pieces of information; therefore a suggestion is that the headline section should include and prioritise such pieces of information. For example, in the leaflet used for this experiment, information about diet did not necessarily have a natural and noticeable place in a typical PIL structure and tended to be found more frequently in the headline than information that had a larger section dedicated to it, such as complex information about adverse events. Lengthy and complex information, which could be found elsewhere in the leaflet, did not appear to be found during the experiment in the headline, but instead in the appropriate section in the leaflet.

The headline did not appear to be commonly used as a method for the reader to be signposted to elsewhere in the leaflet. The textual signposts were used more frequently than the graphical signposts, although both were used infrequently. The findings of this study suggest that caution should be given when considering the use of graphical markers. Leaflet designers should ensure they are noticeable but some participants reported they were confusing, so consideration should be given to whether they aid the reader to find and understand information before they are routinely included.

One suggestion was to have the headline section folded so it is the first thing seen when a patient removes the leaflet from the box. This is a novel idea and the use of this, and whether it encourages participants to read the headline section, would be something that could be explored in more detail using a modified user-testing process in future research.

4.6 Conclusion

Inclusion of a headline section aims to assist a reader to locate important information about key issues associated with their medicines in a PIL. Previous research into a headline section did not show that it performed any better than a leaflet with a headline section in helping readers find and understand key information about their medicines. This study has shown that a headline section in a PIL is used to locate key information about a third of a time. The research suggests that there does not appear to be any negative impact from including a headline section in a PIL and that it is a technique that is highly valued by the consumers of medicines information. The use of a headline section in a PIL should be considered as a way of communicating key safety issues about medicines in patient information.

Chapter 5:

PILs Content Survey

Chapter 5 Content survey of benefit information (Study 4)

The inclusion of information about the benefits of treatments in patient information leaflets: A content survey of 100 leaflets

5.1 Introduction

Chapter three presented the findings of a focus group study in which medicine users were presented with different formats of benefit information in PILs to explore satisfaction and preference for these formats, as well as the potential impact on knowledge about medicines and medicine-taking behaviour. With regards to the provision of information about benefits in medicines information, the findings were equivocal. It was apparent that benefit information, particularly numerical benefit information, had the potential to provoke an emotional response in some people. Participants valued textual benefit information and there was a strong desire for information about the benefits of treatment to be included to balance the concerns that many people have about the side-effects of their treatments.

This chapter describes a survey and content analysis designed to examine the type and frequency of benefit information that is currently provided in regulated PILs. The aim of this study is to explore the prevalence and range of benefit information presented in PILs currently available for a sample of 100 medicines commonly used, or newly available in the UK.

There is no standard definition of what 'benefit' information might be. Carrigan et al (2008) refer to it as:

> *'Any information that described the potential benefit to health from taking the drug, over and above a simple description of how the drug worked.'* (Carrigan et al., 2008, P.307)

Benefit information could refer to a number of different elements including quantitative and qualitative information about a medicine's efficacy and overall capacity to treat disease. Recently there has been an increased interest in describing what benefit information might entail, with both the MHRA and the EMA undertaking consultations with patients and other stakeholders to describe desirable attributes of benefit information (Medicines and Healthcare Products Regulatory Agency, 2005a, Medicines and Healthcare Products Regulatory Agency, 2005b, European Medicines Agency, 2009).

Propositions to include benefit information in package leaflets have also been given a higher profile recently in current EU pharmacovigilance proposals (European Commission, 2010). Other international organisations, such as the US Food and Drug Administration (FDA), have also recognised the importance of moving towards better risk/ benefit communication by striking a balance and conveying information on benefits as well as harms (Fischhoff et al., 2011).

Leaflets in circulation in Europe conform to the format described by the Quality Review of Documents template, which provides guidance on how to present package leaflets prior to application for marketing authorisations (Co-ordination Group for Mutual Recognition and Decentralized Procedures - Human, 2011). The European Medicines Agency's Working Group on Quality Review of Documents (QRD) develops, reviews and updates these templates**.** Recent changes to the QRD template for PILs have included the recommendation that information about the benefits of the treatment should be included in section 1: What (the medicine) is and what it is used for? (Co-ordination Group for Mutual Recognition and Decentralized Procedures - Human, 2011)

Currently there is limited research which explores the extent to which PILs include information about the benefits of treatments. The inclusion of side-effect information in PILs has been more extensively studied and a survey conducted in 2006 (Carrigan et al., 2008) assessed the leaflets provided with the 50 most frequently prescribed drugs in England to determine the extent to which the likelihood of adverse events was described. This study suggested that patient needs were not being met and that few patient information leaflets contained side-effect information presented using the recommended frequency European Commission terms. A similar study examining the extent to which benefits of medicines are described has not been undertaken.

It has been shown that patients value side-effect information but frequently find that its inclusion in PILs conveys an overall negative message which can resonate quite strongly and impact upon perceptions of medicines in an adverse way (Raynor et al., 2007, Fried et al., 2011). Recently regulatory bodies such as the MHRA have paid more attention to exploring how the provision of information about the benefits of medicines might impact upon perceptions of balance of harm and benefit in a leaflet, and how this might in turn impact upon patient perceptions of medicines (Medicines and Healthcare Products Regulatory Agency, 2005b).

Patients want balanced information, which includes information about the benefits of medicines, so they can weigh up the risk of harm and the likelihood of benefit before making an informed decision about taking a medicine (Grime et al., 2007). Currently benefit information is not required to be included in a PIL, however under EU regulations it can be included as long as it is not promotional (European Commission, 2004). This has been identified as an area that warrants further research by European and other global medicines regulators. The MHRA has made several recommendations for the inclusion of benefit information (Medicines and Healthcare products Regulatory Agency, 2005b).

Currently, it is not known whether these recommendations are being put into place and there is no information about whether benefit information is commonly included in PILs currently licensed for use, or how this benefit information is presented. The aim of the study reported in this chapter is to determine the extent to which information about the benefits of treatments is included in 100 PILs about medicines currently available in the UK and to categorise the different types of benefit information provided.

5.2 Research aims and objectives

Aim

The aim of this survey is to determine the prevalence and type of benefit information that is included in a regulated PIL in the UK.

Objectives

- Identify terminology used to communicate 'benefit information' in a PIL.
- Survey PILs available in the UK to assess the extent to which benefit information is included in a PIL.
- Categorise the range of information about benefits currently included in regulated PILs available in the UK.

5.3 Methods

This is a survey and content analysis of the 'benefit information' content of patient information leaflets. Content analysis can be described as *"the systematic, objective, quantitative analysis of message characteristics"* (Neuendorf, 2002). Content analysis can be a quick and efficient way of exploring written information in order to determine

the presence of specific words, concept or themes, (Berelson, 1952) in this case the prevalence and type of ‘benefit information’ in patient information leaflets.

This survey and content analysis will use a process where ‘concepts’ of ‘benefit information’ in a PIL will be defined according to common characteristics identified from sources of guidance on writing benefit information (Medicines and Healthcare Products Regulatory Agency, 2005b, European Medicines Agency, 2009). These concepts will then be identified in the PIL, grouped according to their common characteristics and the frequency of their use assessed.

The study uses an *a priori* design, where the concepts and sample are pre-determined in order to identify and collect relevant information in a systematic way. The pre-defined sample will then be searched for the presence of the concepts of benefit information and where appropriate, these will be both summarised into common themes and their frequency recorded.

5.3.1 Sample

Sampling was based on a form of random quota sampling of 100 regulated PILs for medicines. The sample size was agreed by consensus in the research team (RD, PK, DKR, JM). 100 PILs was considered a large enough sample to map the breadth and depth of the various types of benefit information that leaflets might include and to identify and measure the frequency of common concepts of ‘benefit information’.

The aim of using a quota sample was to gather data from two representative groups of leaflet types. The 100 medicines were divided into 2 groups of 50:

[1] The top 50 dispensed medicines

[2] 50 newly licensed medicines (from the so-called 'Black Triangle' list)

The rationale for this sampling method was to obtain a range of medicines in common use in the UK. Another justification was that it facilitated the exploration of differences between the inclusion of benefit information in a PIL for medicines that have been available for a long time and are used frequently, compared to more recently licensed medicines. It was hypothesised that PILs for newer medicines were more likely to include benefit information than older medicines, as patient information for newer medicines has been developed at a time when there is increasing interest from European and UK regulators to include benefit information in regulated PILs.

The sampling strategy aimed to obtain leaflets from a wide range of branded and generic products from different manufacturers in order to achieve maximum variation of leaflet type. This was to ensure that the benefit information was not obtained from a narrow, uniform source. The sampling strategy used is as follows:

[1] The top 50 dispensed medicines were identified from prescription cost analysis data collated by the Information Centre for Health and Social Care for 2011 (Information Centre for Health and Social Care, 2011) (appendix 1). This information details of the number of items of prescriptions dispensed in the community in England i.e. by community pharmacists, appliance contractors, dispensing doctors, and items personally administered by doctors. The drugs dispensed were listed by British National Formulary (BNF) therapeutic class.

The top 50 medicines from this list were chosen, as these were reflective of the most common medicines that patients receive in England, and therefore the most common leaflets that people receive.

Where the list of top 50 dispensed leaflets referred to a non-specific medicine for which a leaflet might not be available, for example "Other Emollient Preps", the next item on the list was chosen. The list of the medicines was then randomised using a random list generator (www.random.org). The top half of the list (n=25) was allocated a leaflet from a branded medicine and the bottom half (n=25) a leaflet from a generic medicine. The rationale was to explore whether there were any differences in the type and frequency of ‘benefit information’ provided in generic and branded leaflets. The random sample approach ensured an indiscriminate spread of different manufacturers of leaflets.

[2] Newly licensed medicines were identified from the MHRA “Drugs under intensive surveillance” list (also known as the Black Triangle list and referred to as ‘Black Triangle’ for the purpose of this study) (Medicines and Healthcare Products Regulatory Agency, 2012b). These drugs are subject to intensive monitoring because relatively limited information about their safety is available, although the Black Triangle symbol does not mean that the medicine is unsafe.

The reason for choosing this group of medicines is that they are easily identifiable as products new to the market and therefore provide a comparison to the older, commonly prescribed medicines. This allows for comparison of the frequency and type of benefit information over time. The rationale for including this group was to see whether the manufacturers of PILs were responding to regulatory moves towards for the inclusion of benefit information.

The Black Triangle list includes a number of different types of product. In order to prevent replication from the top 50 dispensed list only products identified as a new substance/ product were included. The following were excluded from the sample as they were identified as products for which the patient might not regularly receive a PIL, e.g. vaccines, or for which existing patient information is in circulation:

- new vaccine
- new combination of drugs
- addition of paediatric use
- different formulation for existing route
- another route of drug administration
- biosimilar product
- change or addition of a therapeutic indication (excluding paediatric).

As the Black Triangle list contained new products, all the leaflets were branded as no generic alternatives were available. The **total sample** therefore contained 75% branded leaflets (50% from the Black Triangle list and 25% from the top 50 dispensed group) and 25% generic leaflets (from the top 50 dispensed list). The full sample can be seen in appendix 23.

5.3.2 Obtaining the leaflets

A copy of each of the 100 PILs was obtained from the Electronic Medicines Compendium (eMC), a website which contains patient information leaflets licensed for use in the UK. The eMC contains more than 9,000 leaflets which have been approved by either the UK or European government agencies which license medicines (http://www.medicines.org.uk/emc). Leaflets were accessed between the period 7.01.13 and 20.02.2013.

The following steps were followed:

[1] The eMC was searched for the medicines on both the branded and generic list.

[2] For generic medicines, the British National Formulary (BNF) was used to identify a single listed manufacturer (Joint Formulary Committee, 2012). Where no single manufacturer was listed a random choice was made from a list provided by the eMC using a random number generator.

[3] Non-generic leaflets were chosen at random as a manufacturer is not explicitly listed in the BNF. A random list generator was applied to the list of manufacturers and the number 1 leaflet chosen.

[4] When a particular manufacturer had a PIL included, that manufacturer was not used again (unless it was the only manufacturer of a leaflet).

[5] If no generic leaflet was available for a medicine randomised to the generic group then the medicine was swapped for an alternative medicine on the branded list.

5.3.3 Benefit evaluation criteria

The information in each leaflet was evaluated for its provision of different types of 'benefit' information. Currently there is no existing categorisation of benefit information for medicines, therefore the benefit information criteria used for this analysis were derived from two sources; a report published by the European Medicines Agency (EMA) which explored patient, consumer and healthcare professional expectations of information on the risk and benefits of medicines (European Medicines Agency, 2009) and guidance developed by the Medicines and Healthcare products Regulatory Agency (MHRA) on patient information about medicines (Medicines and Healthcare products Regulatory Agency, 2005a).

These two organisations enforce the regulation of medicines and medicines information in Europe and the UK and are responsible for maintaining and evaluating standards for medicines information. The reports were chosen because they both provide several potential criteria for what form benefit information might take, but also because they use a patient-centred approach to a definition of benefit information. The aims of this thesis are to investigate patient preference for benefit information and to explore how it impacts upon knowledge, satisfaction and behaviour using a patient-centred approach. The EMA report, in particular, addresses patient's expectations about what benefit information is and what they would be interested in seeing in medicines information. When combined with the MHRA suggestions as to what benefit information might include, there is a comprehensive source of various qualitative and quantitative criteria which describe what benefit information might be and what type of benefit information patients desire. A patient-centred approach to patient information is important to ensure that patient information meets the needs of those it aims to help (Raynor et al., 2007).

In order to create a workable set of criteria to use as a framework for the analysis of the patient information leaflets, a basic content analysis and synthesis of the benefit

information collated by the two reports was undertaken. The documents were searched for definitions of benefit information and these were synthesised and categorised into 10 categories, which included both qualitative and quantitative categories (Figure 16).

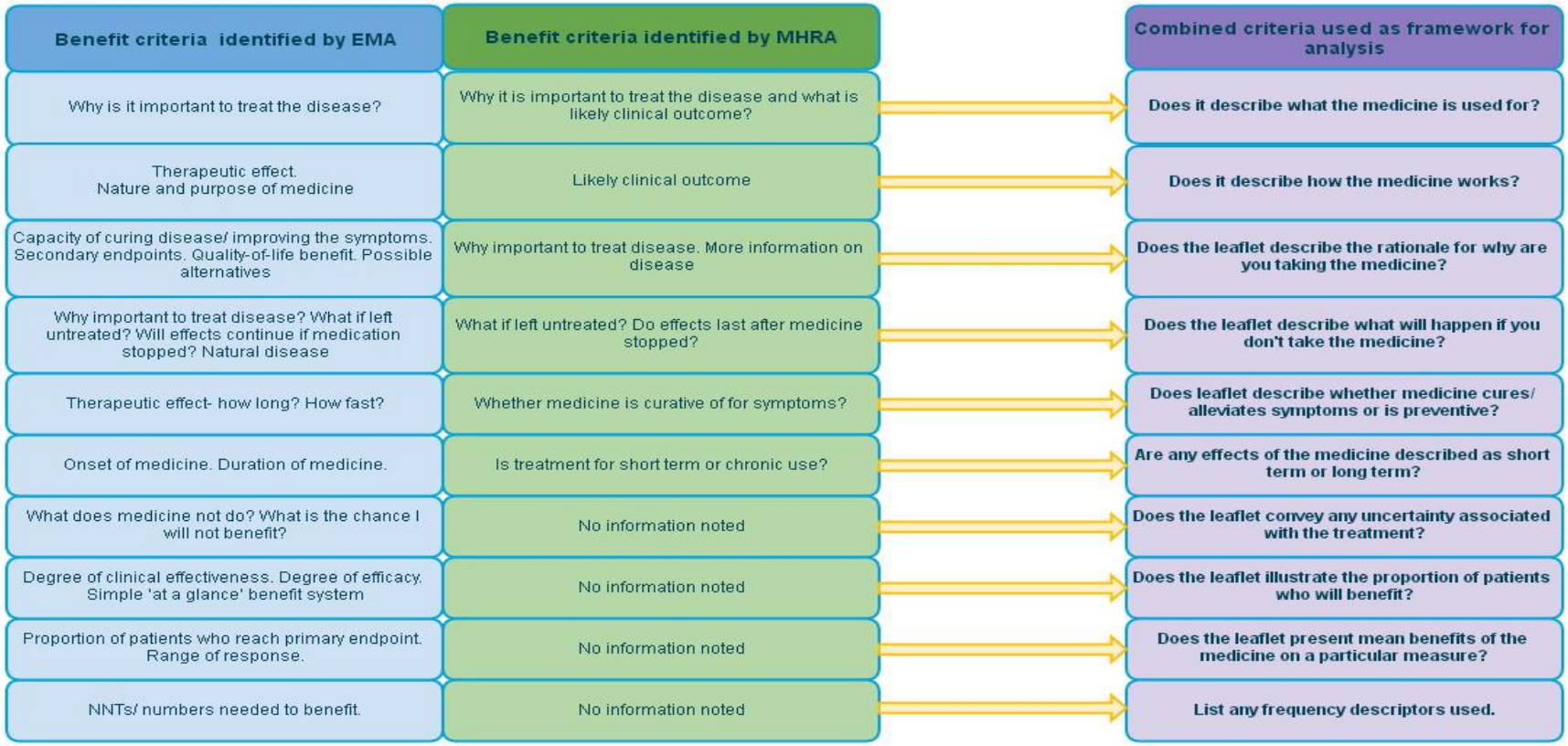


Figure 16: Diagram showing how EMA and MHRA benefit criteria was combined to develop the 10 criteria used for the analysis of the benefit information.

5.3.4 Data extraction and quality assurance

The selected leaflets were searched for potential benefit information which would meet the criteria. This information was extracted and entered into a database which recorded the frequency and type of benefit information contained in the 100 PILs.

Leaflets in the UK are set out according to the QRD human product information template (European Medicines Agency, 2012). This document defines the layout of a leaflet. Information about the benefits of the leaflet would typically be included in section 1 of the leaflet: “What is X and what is it used for?” Hence the contents of section 1 were copied and pasted into an Microsoft Excel spread sheet for further analysis. Additional scrutiny was also paid to Section 3 of the leaflet, which was searched for information regarding the duration of treatment. However, to ensure that no information was missed each leaflet in its entirety was read by RD. The leaflets were also searched for any additional sections which might contain benefit information.

RD undertook the data extraction of relevant information and one of the supervisors, TR, undertook a randomly selected 10% check to assess for accuracy (Split into 2 x 5% checks). The first 5% check revealed a small number of missing data (in particular relating to identifying terms associated with conveying uncertainty). As a result, RD re-checked the remaining data for any missing data. The final 5% check was consistent with both reviewers identifying the same data for each criterion.

5.3.5 Statistical analysis

Data were categorical and the following tests were applied

- Chi-square test
- Fishers exact test - used when the assumptions of the chi-squared test were violated (when cells had an expected count of less than 5)

The Statistical Package for the Social Sciences (SPSS) version 19 was used to perform the analysis (IBM Corp, Released 2010).

5.4 Results

One hundred leaflets were obtained, of these leaflets, 50 were obtained from the prescription cost analysis data collated by the Information Centre for Health and Social Care (Information Centre for Health and Social Care, 2011), 25 of which were branded and 25 generic medicines. The other 50 were obtained from the MHRA black triangle

surveillance list. All 50 of these were branded medicines (appendix 20). Leaflets were included from 59 different manufacturers in all.

Table 11: Benefit criteria met (including statistical difference between leaflets for top 50 dispensed medicines and Black Triangle medicines).

Criteria	Total criteria met n=100	Top50 dispensed n (%)		50 Black Triangle n (%)	Chi-square statistic, probability (p) value. (df=1 for all comparisons)
		Generic n=25	Branded n=25		
1: Does it describe what the medicine is used for?	**100**	25 (100%)	25 (100%)	50 (100%)	-
2: Does it describe how the medicine works?	**85**	21 (84%)	21 (84%)	43 (86%)	0.078 (p=0.779)
3: Does the leaflet describe the rationale for taking the medicine?	**45**	5 (20%)	8 (32%)	32 (64%)	14.586 (p<0.001)
4: Does the leaflet describe what will happen if you don't take the medicine?	**22**	7 (28%)	5 (20%)	10 (20%)	0.233 (p=0.629)
5: Does the leaflet describe whether the medicine will cure or alleviate symptoms or is preventative?	**19**	5 (20%)	4 (16%)	10 (20%)	0.065 (p=0.799)
6: Is the duration of the treatment described as either short term or long term?	**53**	8 (32%)	12 (48%)	33 (66%)	3.305 (p=0.069)
7: Does the leaflet convey any uncertainty associated with the treatment?	**37**	10 (40%)	10 (40%)	17 (34%)	0.386 (p=0.534)
8: Does the leaflet illustrate the likely proportion of patients who will benefit and the extent of the benefit on the symptoms of the condition?	**0**	0	0	0	-
9: Does the leaflet present any mean benefits of the medicine on a particular measure?	**0**	0	0	0	-

5.4.1 Categories one and two: Does the leaflet describe what the medicine is used for and does it describe how the medicine works?

All of the leaflets (n=100) described what the medicine was used for and 85% described how the medicine worked. For example:

> *"Warfarin is used to prevent and treat clots forming in the legs, lungs, brain and heart."* (Warfarin, Branded- Marevan, Top 50 dispensed).
>
> *"Eliquis contains the active substance apixaban and belongs to a group of medicines called anticoagulants. This medicine helps to prevent blood clots from forming by blocking Factor Xa, which is an important component of blood clotting" (*Apixaban, Black Triangle, Branded – Eliquis).

For these criteria there were no statistical differences between the proportion of black triangle leaflets or top 50 dispensed medicines leaflets which described how the medicine worked (n=42 compared to n=43, p= 0.779). Neither was there any difference in the proportions of generic and branded leaflets that met these criteria (n=21 compared to n=21).

5.4.2 Category three: Does the leaflet describe the rationale for why you are taking the medicine?

45 leaflets provided additional information about the rationale for treatment. Of these 45 leaflets, 13 were from the top 50 dispensed leaflets and 32 were from the Black Triangle medicines. Significantly more newly licensed medicines provided additional information about the rationale for treatment when compared to medicines which are commonly dispensed (n=32 compared to n=13, p<0.001). Slightly more branded leaflets contained additional information than generic leaflets (n=8 compared to n=5), although these numbers were small and statistical significance was not measured.

The leaflets contained varied amounts of information; some included only a small amount of detail, for example, a short sentence. Whereas others contained additional paragraphs of information about the disease the medicine was used to treat and/or about how the medicine might impact on quality of life. A post hoc analysis identified 4 different categories of additional information, which were developed iteratively. The frequency of type of additional information was counted. A total of **n=63** additional items of information were counted in the 45 leaflets (Total word count = 2357, mean number of words = 52, Range = 7 - 292, SD = 48).

This most common category was the provision of additional information about the **disease or condition,** for which 26 items of information were counted. An example of this type of information is provided below:

> *"In multiple sclerosis, inflammation destroys the protective sheath around the nerves leading to muscle weakness, muscle stiffness and difficulty walking.*" (Fampridine, Black Triangle. Branded - Fampyra)

The second most common type of additional rationale information was about the **effects of the medicine on the disease or condition,** for which 17 items of this type of information were provided:

> *"It is used after you have had surgery to remove the tumour and together with chemotherapy to kill remaining cancer cells to reduce the risk of cancer coming back".* Mifamurtide, Black Triangle. Branded (Mepact)

10 items were about the **impact on the quality of life**, an example of which is provided below:

> "*RoActemra helps to reduce symptoms such as pain and swelling in your joints and can also improve your performance of daily tasks…RoActemra has been shown to slow the damage to the cartilage and bone of the joints caused by the disease and to improve your ability to do normal daily activities".* (Tocilizumab, Black Triangle. Branded - RoActemra)

Finally, **10** additional items of information about other interventions, such as diet/exercise or treatments to maximise effectiveness were identified:

> *"Bydureon is used in combination with the following diabetes medicines: metformin, sulphonylureas and thiazolidinediones. Your doctor is now prescribing Bydureon as an additional medicine to help control your blood sugar. Continue to follow your food and exercise plan."* (Exenatide, Black Triangle. Branded - Bydureon)

5.4.3 Category 4: Does the leaflet describe what will happen if you don't take the medicine?

22 leaflets described what could happen to the patient if they did not take the medicine. There were no significant differences between the top 50 dispensed medicines and the black triangle medicines (n=12 compared to n=10, p= 0.629). With regards to the top 50 dispensed medicines, 7 of the branded products contained this information compared to

5 of the generic products. 18% of leaflets (n=18) explicitly described the impact of not taking the medicine, for example:

> *"Do not stop taking this medicine as your heart problem may get worse. Talk to your doctor if you want to stop"* (Digoxin, top 50 dispensed, branded – Lanoxin).

One leaflet did not explicitly state what would happen if the medicine was not taken and instead implied what the consequences might be if the condition was left untreated. This information was provided as additional information about the disease:

> *"Early on, osteoporosis usually has no symptoms. If left untreated, however, it can result in broken bones."* (Alendronic Acid, top 50 dispensed, generic).

Three leaflets included some information about what might happen if the patient didn't take the medicine, but were vague and did not refer to any specific impact on conditions or specified symptoms. For example:

> *"If you stop taking lactulose the desired effects of the medicine may not be achieved"* (Lactulose, top 50 dispensed, generic).

Of these 22 leaflets 17 provided information about the impact of not taking the medicine on the condition, 3 reported the impact on symptoms, 1 provided information on withdrawal and 1 described the impact on drug resistance.

5.4.4 Category 5: Does the leaflet describe whether the medicine will cure or alleviate the symptoms or is preventative?

19 leaflets met the criteria for describing the purpose of the medicine (i.e. curative or alleviating symptoms or preventative). Of these leaflets 9 were top 50 dispensed medicines and 10 were Black Triangle medicines. The majority of these leaflets were for treatments which alleviated symptoms (n=13) and the remainder were for preventative treatments (n=6).

A small majority of the statements (n=11) were explicit about whether the treatment was a preventative medicine or one to be used to alleviate symptoms. For example:

> *"Pulvinal Salbutamol inhalation powder is used to help relieve the symptoms of mild, moderate and severe asthma, other chest illnesses and to avoid asthma symptoms brought on by exercise or other 'triggers'. Pulvinal must be used for*

the relief of your asthma symptoms only. You may have other medicines which you take regularly to prevent the symptoms of your asthma." (Salbutamol, top 50 dispensed, branded - Pulvinal)

8 leaflets were more implicit about the nature of the treatment, for example:

"By blocking the activity of IL-1 beta, canakinumab leads to an improvement in these symptoms." (Canakinumab, black triangle, branded - Ilaris)

There was no significant difference between the numbers in the top 50 dispensed group and the black triangle group, or between the generic and branded groups.

5.4.5 Category 6: Is the duration of treatment described as short term or long term?

53% of the leaflets described the duration of treatment. This was more common in the black triangle group (n=33) compared with the most dispensed group (n=20) (p= 0.069) 23 of the 53 leaflets described a timescale for treatment. Sometimes this was described as long-term or short-term treatment:

"*Treatment with Cardicor is usually long-term. Cardicor is used to treat stable chronic heart failure."* (Perindopril, top 50 dispensed, branded - Cardicor)

Other leaflets described a period of time using days, weeks or months, for example:

"It will be given to you twice a week (at least three days apart) for the first 12 weeks, then once a week for 24 more weeks". (Mifamurtide, black triangle, branded - Mepact)

13 leaflets did not describe any particular timescale, but made reference to the duration of treatment as something that should continue as long as the doctor recommends, or as something that should be decided by the doctor. However, although these leaflets did not describe a specific time-scale for treatment, some provided a good explanation for this uncertainty, for example:

"There is no time limit laid down as a general rule for treatment with Levact. Duration of treatment depends upon disease and response to treatment." (Bendamustine, black triangle, branded - Levact)

"You will be treated with Avastin once every 2 or 3 weeks. The number of infusions that you receive will depend on how you are responding to treatment;

you should continue to receive this medicine until avastin fails to stop your tumour growing. Your doctor will discuss this with you." (Bevacizumab, black triangle, branded - Avastin).

13 leaflets described some information about the length of treatment, but the exact nature of the duration of treatment was unclear. So, sometimes the timing of the initial treatment programme was described but there was no further information on whether this was a long, medium or short-term programme.

"Zopiclone is not meant to be used every day for long periods of time." (Zopiclone, top 50 dispensed – generic).

Four leaflets were unclear in their description of the duration of the treatment and described the frequency of dosing but not the duration.

"As COPD is a chronic disease you should take SPIRIVA 18 microgram every day" (Tiotropium, top 50 dispensed, branded - Spiriva)

47 leaflets did not describe the duration of the treatment, nor recommend that patients seek advice from their GP or healthcare professional about the duration of treatment. This was more common in the top 50 dispensed category, where 30 leaflets provided no information on the duration of treatment compared to 17 in the black triangle group. Slightly more branded leaflets (n=12), compared to generic leaflets (n=8) described the duration of the treatment.

5.4.6 Category 7: Does the leaflet convey any uncertainty associated with the treatment?

The content survey identified leaflets which conveyed uncertainty and developed categories for the different types of words used on a post hoc basis. It was noted that a total of 37 leaflets (37%) presented information that conveyed uncertainty in some way. There were no significant differences between the top 50 dispensed medicines and the black triangle medicines (n=20 compared to n=17). These were categorised into different groups as follows:

[1] No uncertainty is conveyed.

The majority of the leaflets did not convey uncertainty (n=63). These leaflets tended to include information about the leaflet which was absolute, describing what the treatment treats. There were no terms used to express any uncertainty. For example:

*"Elaprase is used as enzyme replacement therapy to treat children and adults with Hunter syndrome (Mucopolysaccharidosis II) when the level of the enzyme iduronate-2-sulfatase in the body is lower than normal. If you suffer from Hunter syndrome, a carbohydrate called glycosaminoglycan which is normally broken down by your body is not broken down and slowly accumulates in various organs in your body. This causes cells to function abnormally, thereby causing problems for various organs in your body which can lead to tissue destruction and organ failure. Elaprase contains an active substance called idursulfase which works by acting as a replacement for the enzyme that is at a low level, thereby breaking down this carbohydrate in affected cells." (*Idursulfase, black triangle, branded – Elaprase).

The remaining leaflets (n=37) used a mixture of terms which conveyed uncertainty and were categorised into the following groups:

[2] Uncertainty about the impact of the treatment on the condition (associated with the effectiveness of the treatment)

There appeared to be 2 different methods of conveying uncertainty (these were more implied as opposed to explicit statements about the uncertainty associated with the treatments). Several leaflets conveyed uncertainty through the use of words to qualify the treatment's effectiveness (such as 'helps') ; others used modal auxiliary verbs, which are verbs which help to indicate modality or likelihood (such as 'may') (Palmer, 1986).

2a: Implies uncertainty using the term '*helps*'. For example states 'the treatment ***helps*** to treat'. 'Help/s' was the most commonly used 'qualifier'. Other 'qualifying' terms included 'contributes'.

- Frequency of use in leaflets n=24
  - Helps prevent n=8
  - Help correct n=1
  - Help lower n=4
  - Helps to open n=3
  - Helps protect n=1
  - Helps reduce n=2
  - Helps rebuild n=1
  - Helps relieve n=1

- Helps slow down n=1
- Helps you breathe n=1
- Contributes to lowering n=1

2b: Implies uncertainty using an auxiliary verb. For example states the treatment ***may help*** to treat. The use of the term 'may' appears to add even further uncertainty to the possibility that the treatment might work. Similar terms used include 'can' and 'should'.

- Frequency of use n=14
  - May prevent n=1
  - May help control n=1
  - May treat n=2
  - May relieve n=1
  - May reduce n=2
  - Should have an improvement n=1
  - Should help n=1
  - Can reduce n=2
  - Can help n=1
  - Can help relieve n=1
  - Can raise n=1)

[3] Uncertainty associated with the likelihood of condition

Several leaflets referred to the risk or chance of a condition occurring, these leaflets referred to treatments 'reducing the risk or chance' of that condition. There appeared to be 2 levels of uncertainty:

3a: Implies uncertainty using the terms 'risk' or 'chance'. The treatment ***reduces risk/ chance*** of condition (n=10; reduce risk n=8, reduce chance n=2)

3b: Implies uncertainty using the terms 'risk' or 'chance' and uses an auxiliary verb. The treatment **may *reduce the risk/chance*** of a condition. (n=5; Can reduce risk n=3, may reduce risk n=1, will increase your chances n=1)

5.4.7 Category 8 and 9: Numerical presentations of benefit

None of the leaflets surveyed included any numerical format of benefit information, defined as information which illustrates the proportion of patients who will benefit and/or

the extent of the benefit on the symptoms of the condition, or information that presents any mean benefits of the medicine on a particular measure.

5.5 Discussion

There is evidence that the public desire good quality information about the benefits of their medicines. However this survey and content analysis of 100 currently available PILs shows that benefit information is inconsistently communicated. Current leaflets were found to communicate what the medicine is used for, but other types of benefit information were ambiguous or absent from many leaflets for medicines currently available in the UK. While leaflets are not currently obligated to provide benefit information, there are moves towards encouraging the manufacturers of medicines information to consider adding information about the benefits of treatments in leaflets (Medicines and Healthcare products Regulatory Agency, 2005a, Co-ordination Group for Mutual Recognition and Decentralized Procedures - Human, 2011).

This study showed that currently less than half of leaflets (45%) contained additional information about the rationale for treatment. The most common form of this additional information about the rationale for treatment communicated information about the disease or condition. The inclusion of rationale information was more common in newly licenced medicines (n=32 compared to n=13 top 50 dispensed). It has been shown that the addition of extra information about the effectiveness and benefits of the medicine may have a positive impact of people's judgements and intent to take a medicine (Bersellini and Berry, 2007a, Bersellini and Berry, 2007b, Vander Stichele et al., 2002). Interviews undertaken with the users of simvastatin showed that, when discussing the type of benefit information that would be valued in PILs, additional information about the rationale for treatment was desirable (chapter 6). It has also been shown that patients want information which is set in the context of their illness, but currently few leaflets contain such information (Raynor et al., 2007).

Recent changes to the QRD template, which describes the official content and wording of regulated PILs, now means that it specifies that information about the benefits of the treatment could be included in section 1: 'What X is and what it is used for' (European Medicines Agency, 2012). Guidance on the QRD states that information on the benefits of the treatment could be included in this section, as long as it is compatible with the "Summary of Product Characteristics", useful for the patient, and not promotional. The

guidance says that such information should be presented in a clear and concise way and could include any of the following:

- additional information on the signs and symptoms of the target disease, in particular for non-prescription medicines, but also for medicines to be taken "on-demand" (e.g. treatment of migraine)
- Summary of benefits in descriptive terms (e.g. "this medicine reduces pain associated with arthritis", "this medicine has been shown to reduce blood sugar, which helps to prevent complications from your diabetes"). The benefit may be described in terms of prevention of disease complications (e.g. anti-diabetic), if established.
- Information on the amount of time the medicine usually takes to work may be presented if relevant for the patient (e.g. pain-killer, antidepressant, etc). (Co-ordination Group for Mutual Recognition and Decentralized Procedures - Human, 2011)

For patient-centred communication of medicines information, which is congruous with a patient empowerment approach to producing patient information, it is important that benefit information should communicate patient centred-outcomes, such as how the medicine impacts upon the patient's quality of life. An EMA report which focused on the provision of information on benefit-risk of medicines suggested that *"a quality of life benefit can translate into an enormous added value from the patient's perspective"* (European Medicines Agency, 2009).

The writers of medicines information could consider this an opportunity to include more detail about the rationale for treatment and consider presenting succinct and non-promotional additional information about the disease, how the medicine works and other interventions which will optimise treatment outcomes. In particular, attention could be paid to communication of secondary endpoints which report quality of life benefits for patients.

Just over a fifth of leaflets communicated what might happen if the patient did not take the medicine. Most of these leaflets were explicit about the consequences of not taking the medicine, but a small minority either implied the consequences or were vague. If information about what might happen to the patient if they do not take the medicine is to be included in PILs, then this information needs to be communicated explicitly so as to avoid confusion and better inform the reader about potential consequences.

Many leaflets did not explicitly communicate whether the medicine was intended to cure the condition, alleviate symptoms or be preventative. This is important information which patients may need to be aware of in order to take their medicines to optimum effect, in order to take their medicines safely and effectively. Leaflets would benefit from more explicit information on this in order to better inform the patient about what to expect from their treatment and how it might impact on their condition. Only a small proportion of leaflets provided detailed information about the duration of treatment of the medicine (communicating specified periods of days, weeks, months or for life to the length of treatment). Many leaflets communicated duration of treatment using implicit terms which were unclear or non-specific, and in slightly less than half of the leaflets there was no information about how long the treatment should be used. For some treatments the duration of treatment will be based on the individual patient's circumstances, such as their condition or response to treatment, however, this can be better communicated. An example of this was for bendamustine, which provided a good example of the terminology that could be used to convey that duration of treatment is uncertain or dependent upon individual response.

> *"There is no time limit laid down as a general rule for treatment with Levact. Duration of treatment depends upon disease and response to treatment." (Bendamustine, branded – Levact, black triangle.)*

More leaflets could benefit from using clearer terminology, specifically providing a timescale which describes the duration of treatment or describing whether treatment duration is uncertain.

It was apparent that the majority of leaflets either did not convey the uncertainty associated with treatments, or conveyed uncertainty in a way that was largely inadequate or unclear. For example, the use of the term 'helps', which appears to be used to convey uncertainty about the treatment, can be confusing and seems to imply that the treatment works, but only in a contributing sense. It could be misconstrued as conveying that the treatment is effective, but only in conjunction with other treatments when this is not necessarily the case. The term is ambiguous and not clear enough to convey uncertainty in any meaningful way. The use of axillary verbs such as 'can' or 'may' were also used in some leaflets. This technique conveys more uncertainty than using 'helps' alone, however it is still ambiguous because it is unclear as to how much the treatment may help or may reduce the risk of a condition. There is also some redundancy with the use of axillary verbs when combined with terms such as 'risk' or

‘chance’ which already suggest uncertainty. This might lead to misunderstanding about the potential effectiveness of the medicine.

Communicating uncertainty is a challenge, certainly in healthcare where many conditions and treatments may have ambiguous or individual consequences (Politi et al., 2007). Research has shown that uncertainty about healthcare treatments is not always adequately communicated during medical consultations (Braddock et al., 1999, Elwyn et al., 2004, Towle et al., 2006). Chapter 3 described how patients frequently struggle to comprehend the concept of uncertainty about their treatments. Patients are often unaware of any uncertainty associated with their medicines or that the quantitative benefits of medicines are over-estimated (often by a large proportion) (Hamrosi et al., 2012). The inclusion of well-written harm and benefit information in written medicines information could be a move towards supporting patients in understanding more about the benefits and limitations of their treatments. This may in turn help patients to make autonomous decisions about taking treatments and be part of a number of processes, including shared-decision making, within the GP consultation.

One of the challenges of communicating uncertainty is that many treatments have uncertain or unknown outcomes. The British Medical Journal undertook an evaluation of 3000 treatments that had been reported in randomised controlled trials and were used in healthcare settings. They identified that at least 50% were of unknown effectiveness and that, in the author’s view, a further 7% involved a trade-off between benefits and harms (British Medical Journal, 2013).

Communicating uncertainty is an important challenge to meet if patients are to be aware of and understand the impact of their treatments and also to ensure they engage in informed or shared decision-making. Politi et al (2007) describe 5 main types of uncertainty associated with medical interventions. These are:

1) risk or uncertainty about future outcomes;
2) ambiguity or uncertainty about the strength or validity of evidence about risks;
3) uncertainty about the personal significance of particular risks (e.g. their severity, timing);
4) uncertainty arising from the complexity of risk information (e.g. the multiplicity of risks and benefits or the instability of risks and benefits over time); and
5) uncertainty resulting from ignorance (Politi et al., 2007).

The writers of medicines information should pay attention to the different types of uncertainty when describing treatment outcomes and further research into the

linguistics of communicating uncertainty in PILs would be welcome to highlight terminology which adequately communicates uncertainty.

None of the leaflets conveyed the benefits associated with taking a treatment using numerical terms. The findings from chapter 2 show that techniques such as summary statistics or graphs have been shown to be useful in providing information about the quantifiable benefits of taking a treatment. It is surprising that none of the leaflets conveyed benefit information in numerical terms, particularly in light of an increasing interest in the provision of information about the likelihood of benefit and risk of harm from global medicines regulators (Medicines and Healthcare Products Regulatory Agency, 2005b, European Medicines Agency, 2009, Food and Drug Administration, 2009).

Currently numerical information is provided with side effect information and there is evidence that providing numerical benefit information can counterbalance the impact of what is perceived to be negative risk information. Also, for patients to make informed decisions about their treatments it could be argued that they should be provided with information which is comparable with the presentation of information about the risk of harm. The provision of well-written benefit information in this context would be a welcome accompaniment to the numerical frequency of side-effects already presented in PILs (Raynor et al., 2007, Medicines and Healthcare Products Regulatory Agency, 2005a, Fischhoff et al., 2011).

It has been shown, in previous work within this thesis (See chapters 2, 3 & 6), that there are many challenges to providing numerical/statistical benefit information to the users of PILs. This information can be difficult to understand, can be misconstrued as negative rather than 'benefit' information and can provoke an emotional response in the reader (see chapters 2 & 6). However, it is apparent that the provision of this information can also facilitate a more detailed consideration of the potential benefits of a treatment and provide information about the proportion of patients who benefit. People value this information being made available (Hamrosi et al., 2012, Carling et al., 2009). It is also important to note that many lay-people struggle to understand numerical data. Gigerenzer refers to the problem of 'innumeracy' in the general population. This is the concept that many struggle to understand statistical information and this affects an individual's ability to reason about uncertainty and risk (Gigerenzer, 2002). This might create a reluctance to include additional numerical information in leaflets about the benefits of the treatments. There can also be concerns from the manufacturers about

being seen to be too promotional, which may result in the lack of benefit information in a PIL.

There was a slight tendency for 'black triangle' leaflets to include more benefit information than the top 50 dispensed leaflets on most, but not all, criteria. For two criteria the differences were statistically significant. These were duration of treatment (category 3) and whether the leaflet described the rationale of the treatment (category 6). It is possible that this increased performance relates to the more complex nature of some of the newly licenced treatments. The black triangle list contained a range of different drug types to the list of top 50 dispensed and the differences in the inclusion of benefit information might reflect this difference. There were more monoclonal antibodies in the black triangle list (n=7) compared to the top 50 dispensed list (n=0) and a larger number of drugs for use in malignant disease and immunosuppression. 14 drugs in the black triangle list were new anticancer drugs which have been associated with an increased risk of toxic death and serious adverse events (Niraula et al., 2014, Niraula et al., 2012). It is possible that the differences in inclusion of benefit information reflect the changing nature of the type of drugs that are currently being licensed.

This might also reflect a trend for newer leaflets to produce better quality information in line with some of the recent recommendations about improvements to the communication of medicines information (Co-ordination Group for Mutual Recognition and Decentralized Procedures - Human, 2011). This increased inclusion of benefit information might also reflect a better availability and quality of effectiveness data as a result of undertaking of bigger and better designed trials over recent years.

It is important to note that there was variation amongst the type and frequency of information included in the different leaflets. It is apparent that some providers of medicines information include more information about the benefits of a treatment than others. The use of terminology between the leaflets also varies. This has a potential impact on the reader receiving information about their medicines that varies from product to product and is inconsistent. The impact of this upon a patient’s knowledge and understanding about their medicines is not known.

Good quality written information that is patient-centred has been shown to have a positive impact upon knowledge, satisfaction and confidence with information (Raynor et al., 2007). In order to optimise understanding of medicines and optimise their use, patients need to be aware of how their medicines work and how likely they are to benefit. The provision of good quality benefit information in written medicines

information is one way in which this can be achieved. This study has shown that currently many leaflets on the market in the UK do not contain clear or adequate information about the potential benefits of medicines. Leaflets do not consistently provide simple benefit information such as the rationale for treatment, the impact on patient-centred outcomes, the duration of treatment or whether the treatment is intended to be preventative, curative or symptomatic. Uncertainty about treatment outcomes is largely inadequately communicated, with leaflets using terminology that does not describe the proportion of patients who are likely to benefit from the treatment.

It is also important to note that across Europe leaflets are designed in English and translated into their respective languages (Nisbeth Jensen and Zethsen, 2012). The impact of translation on the meaning of current techniques used to convey uncertainty is not known.

5.5.1 Strength and limitations

The use of the sampling strategy facilitated the collection of 100 leaflets which provided a large sample from which to obtain the benefit information. The inclusion of leaflets that were commonly used and leaflets that were newer facilitated a historic comparison of the frequency and type of benefit information.

The sampling strategy also allowed variation in the type of leaflets that were included in the analysis. A range of leaflets from different manufacturers were obtained and these included a variety of branded and generic products. The inclusion of the newly licenced medicines meant that the sample was weighted towards branded products. As a result, this limited the evaluation of any statistical significance between generic and branded products, due to the small numbers in the comparison. A larger sample comparing generic and branded leaflets would add weight to this analysis. The use of a 10% check ensured there was an acceptable degree of inter-rater reliability in the sample.

The criteria were developed from two sources, the EMA report of benefits and the MHRA's 'Always Read the Leaflet', which described what benefit information might include (European Medicines Agency, 2009, Medicines and Healthcare Products Regulatory Agency, 2005a). It is possible that the consideration of additional sources of benefit information might have led to the development of different criteria to define benefit information. However, there would probably be no impact on the frequency of numerical benefit information observed in patient information leaflets.

The criteria used to evaluate the type and frequency of benefit information was not necessarily evidence-based. There has been some research examining the impact of providing additional rationale information and numerical information in written medicines information on the impact of patient satisfaction and understanding (Bersellini and Berry, 2007b, Carling et al., 2009, Tait et al., 2010b). However, there is limited evidence evaluating the impact on patient satisfaction and understanding of providing information on whether a treatment should be used in the long or short term, or whether the medicine is curative or preventative. Consequently while it has been identified that patient information leaflets lack certain elements of benefit information, the impact of providing this information on patient satisfaction and understanding is not known.

5.6 Conclusion

This survey of a 100 patient information leaflets for licensed medicines showed variety and inconsistency regarding the communication of information about the benefits of medicines. This inconsistency may be problematic for patients who currently are not provided with a standardised format which describes the effects of their medicines. This issue could be greater for patients prescribed more than one medicine as they may receive PILs which use different terms to convey the same meaning.

There is a duty to attempt to inform patients regardless of whether the information being communicated is complex (Fischhoff, 2012). It has been suggested that the package leaflet is an excellent place to communicate information about the benefits of medicines as it is something that is regulated and should be provided with all medicines (Goldacre, 2012). The manufacturers and regulators of medicines information need to be aware that at present PILs for medicines that are currently available in the UK are lacking in their delivery of benefit information.

Chapter 6

Interview Study

Chapter 6 Interview study (Study 5)

What is the impact of providing benefit information about a medicine in a PIL on the attitudes and beliefs that actual users of medicines hold about their treatments?

6.1 Introduction

This chapter describes a study based on qualitative semi-structured interviews undertaken with patients taking simvastatin. The study was designed to elaborate on the findings from the focus group study (chapter 3) and explore the impact of providing benefit information in a more naturalistic setting. A key finding from the previous study was that the provision of numerical benefit information in a PIL provoked varied and often complex responses.

Occasionally the information was viewed as a valuable addition to a PIL, which helped inform the participants about the potential benefits of their treatments and encourage informed decision-making. More commonly, the numerical benefit information was perceived as unsettling and confusing. A great deal of anxiety was reported; there was a considerable emotional response with a significant number of participants expressing a strong dislike for, and concern about, the inclusion of such information. It was also apparent that, despite this dislike, the provision of this type of information also motivated a minority of patients to consider the benefits of their treatments in more detail and as a result these participants stated they might change their medicine or information-seeking behaviour. Currently it is not known whether this response will be reported by those who receive benefit information about their own medicines.

The focus groups in the previous study recruited people representative of typical medicine–users and explored opinions on benefit information based on real-life clinical data, but were hypothetical, to the participant's current situation. This may impact upon the representativeness of the findings. It is unclear whether patients who are taking the medicine concerned would report similar influences on their medicine or information-seeking behaviour, or report similar levels of affect. More research into the impact of providing information about the real-life benefits of medicines to real-life users of medicines will be valuable to understand the impact on patients' perspectives about their treatments. This next stage responds to that need for a more naturalistic setting, by recruiting a sample of patients who receive a prescription for simvastatin and

explores the impact that real-life numerical information has on attitudes, opinions and beliefs about medicines.

6.2 Aims and objectives

Aims

The aim is to evaluate the impact of providing benefit information about medicines in written medicines information on the attitudes, opinions and beliefs that the real-life users of medicine hold about their treatments.

Objectives

- Identify the range opinions held by people taking simvastatin on the inclusion of benefit information about simvastatin in a PIL.
- Identify preferences for different formats of benefit information about simvastatin in a PIL.
- Map the range of factors that affect preference for benefit information in a PIL
- Identify the impact that benefit information has on people's knowledge and satisfaction with their medicines and medicines information.
- Describe the potential impact on medicine-taking behaviour, decision-making and relationships with healthcare professionals.
- Identify the concerns expressed by users of simvastatin about the inclusion of information about the benefits of simvastatin in a PIL.
- Explore any differences in opinions about the inclusion of benefit information between people receiving the information for hypothetical medicines and those receiving the information for the medicines that they are using.

6.3 Methods

For this qualitative, semi-structured interview study a purposive sample of participants was recruited from a single GP practice, via a practice database search. They were invited by letter to participate in audio-recorded interviews (appendix 24). The sample included both males and females and a range of participants from different age bands, levels of education and indications for statin use.

6.3.1 Methodology

A qualitative descriptive approach was used, as described in Chapter 3 (focus group studies).This approach is well-suited to the aims of this research, which are to identify and map the range of opinions about and the potential impact of the provision of benefit information on real-life users of medicines. Further description of the methods for the data analysis can be found in section 6.6 below.

6.3.2 Data collection methods

This study uses semi-structured individual interviews to collect data. This approach was chosen for a number of reasons. Firstly, unlike the focus group study, the aims of this study were more targeted, using personal, real-life scenarios to explore experiences of receiving benefit information for prescribed treatments. This creates the potential for the participants to share more sensitive information than might be imparted during a focus group which is exploring hypothetical scenarios. Therefore it is more appropriate to conduct in a private, one-to-one environment where the participant can share their views and thoughts on a more personal level with the researcher alone, rather than in a group setting. This should promote a deeper exploration of the emotional responses that the benefit information provokes, enabling the participant to share more freely the underlying emotions and thoughts on the provision of benefit information.

In addition, this study provides multiple PILs containing different formats of benefit information to the participants. Individual interviews will enable the researcher to spend more time with each participant to discuss the benefit statements in detail and explore how the statements provoke a deeper understanding of a person's medicines. During the focus groups a large number participants struggled to understand the benefit information and the structure of the focus groups did not allow full explanations to take place.

The semi-structured interviews used a topic guide designed to generate data about specific areas of interest which include the following:

[1] 'Typical' medicine taking behaviour and beliefs about medicines of the participant: participants' previous experience of being prescribed a statin, the information they required and desire, and their typical medicine-taking behaviour. This will provide historic context about the participant's medicine beliefs and behaviour.

[2] Opinions on and experiences of 'typical' PILs – again this will provide some historical context in order to interpret any changes to opinions on patient information that might be elicited by the provision of the exemplar PILs.
[3] Opinions on, and preferences for, the different formats of benefit information in the exemplar PILs: participants were asked their opinions on the 3 benefit statements including their understanding, preferences and thoughts on the different statements.
[4] The potential impact that the provision of benefit information in a PIL might have on medicine-taking behaviour, beliefs about medicines and relationships with HCPs, future information needs, desires and decision-making.

6.3.3 Research ethics consideration

Research Ethics approval was obtained from NRES Committee Yorkshire & the Humber - Humber Bridge (13/YH/0180).

6.4 Recruitment

A purposive sampling strategy was employed and the target sample was patients prescribed simvastatin for prior myocardial infarction (MI) or established coronary heart disease (CHD) (such as angina, unstable angina, previous Coronary Artery Bypass Graft (CABG) or angioplasty) and recruited from one GP practice in a city in northern England. This group of participants are representative of the sample of participants recruited to the Heart Protection Study, which was used to generate the data for the benefit statements. (See section 6.5)

The study used a purposive sample for two main reasons. Firstly this approach facilitates the recruitment of a sub-group of participants whose disease severity is the same as the sample of participants in the clinical trial which was used to derive the numerical data used in the benefit statements. Simvastatin can provide different levels of benefit depending upon whether the patient has existing cardiovascular disease or not, and is used for primary or secondary prevention of cardiovascular outcomes such as MI or stroke. This interview study presented data on the benefits of simvastatin for patients with existing cardiovascular disease derived from the Heart Protection Study (HPS) (Heart Protection Study Collaborative Group, 2002). Consequently, it is important that the patients recruited to this study have the same disease severity as those from the HPS study, to ensure that the data provided is as accurate and relevant to the participant as possible.

Secondly, this approach was used in order to obtain a range of views from a sub-set of participants with a mix of different characteristics but who were also broadly representative of the population of interest. The participant sample had a mix of age groups, genders, educational backgrounds and items of medicines prescribed. A purposive sample is useful in this approach as it can facilitate the deliberate recruitment of participants with a range of characteristics in order to capture variation from the sample. However, this strategy can be criticised as the selection of the participants can be biased by the subjectivity of the researcher and may lead to lack of representation of the sample when compared to the wider population (Spencer et al., 2003). The sample recruited to this study met a range of characteristics that were representative of the general GP population (table 12). No fixed quota was set for each category and no participants were required to be excluded, or additional numbers recruited, as the respondents who replied naturally created a diverse spread across the categories.

Table 12: Demographics of patients taking simvastatin in the General Practice and participants in the study.

Sex	Age range	Patient Count	
		Total in the General Practice (%) n=176	Interviewed in study n=21
Female	40-59	7 (4%)	2 (10%)
Female	60-79	30 (17%)	5 (24%)
Female	80+	29 (16%)	1 (5%)
Male	40-59	15 (9%)	0
Male	60-79	64 (36%)	8 (38%)
Male	80+	31 (18%)	5 (24%)

The Quality and Outcomes Framework (QOF) registers were searched using a number of terms in order to identify participants meeting the inclusion criteria. A note of the number of patients on each register was taken in order to evaluate whether the purposive sample used in the research was representative of the general practice population.

The searches were as follows:

- CHD (Includes MI) n=485
- Peripheral arterial disease n=131
- Stroke n=231

Combined searches:

- MI/CHD and Simvastatin n= 176
- (cerebrovascular disease n=19)
- (diabetes n=45)
- (Peripheral vascular disease (PVD) n=46)

The generated list was then checked by a GP for suitability and the following patients were excluded:

- Care home residents
- Patients receiving palliative care
- Those with cognitive impairments limiting their ability to participate in the research
- Non-English speaking patients.

The remaining patients were sent a research pack inviting them to participate. The research pack contained the following:

- A letter inviting the participant to take part in the research
- A patient information sheet (appendix 24)
- An 'expression of interest' form and a stamped addressed envelope. (Participants were also advised they could contact the researcher by e-mail or telephone)

6.4.1 **Setting**

Interviews were undertaken at the participant's home, apart from one interview undertaken in a room at a local GP practice at the participant's request. Interviews lasted approximately an hour. Participants were provided with written information prior to the interview and informed consent was obtained prior the interview. During the interviews the participants were provided with 3 exemplar PILs containing different benefit statements, plus additional related benefit statements (see section 6.5.6) and were asked to discuss their views.

The interviews were audio-recorded and transcribed by an external company.

6.5 Developing the benefit statements

In total 3 leaflets were developed and provided for discussion during the interviews, and 2 additional statements were also provided alongside the leaflets. The leaflets were all for the medicine simvastatin and contained the following benefit statements:

[1] Textual benefit statement

[2] Numerical benefit statement provided as a NNT

[3] Numerical benefit statements provided as natural frequency with additional statements:

- Natural frequency (Positive frame)
- Natural frequency (Treatment first)

The leaflets were designed to look like PILs typically available in the UK. Simvastatin was given the hypothetical name “Rebastatin” and each leaflet was marked with a highlighted section that stated ‘This leaflet is for research purposes only’ in order to ensure the leaflet was not mistaken for a real-life leaflet and used to provide medicine information out of the context of the research study. During the interviews the participants were informed that Rebastatin was a hypothetical name for simvastatin and the benefit statements were for simvastatin.

The section below describes the various stages to the development of the benefit statements used in the exemplar PILs.

6.5.1 Deciding upon the medicine

The benefit statements were developed by RD in consultation with the members of the supervisory team and 3 pharmacists, including a cardiology specialist (DP, DG, RK). There were several stages to the development of the statements.

The medicine that was chosen for use was simvastatin. Simvastatin is a commonly prescribed medicine used to treat adults with clinical evidence of cardiovascular disease (CVD) and in adults considered to be at risk of CVD (National Institute for Health and Clinical Excellence, 2006). Simvastatin was chosen for the following reasons:

1] It is commonly prescribed and this provides a large sampling frame from which to recruit.

2] It has what may be perceived as a small individual benefit on a condition which can have serious outcomes. Some medicines have better benefits, but others have smaller benefits. Our previous work showed that medicines perceived as having quite small benefits can create upset amongst participants (Hamrosi et al., 2012). Hence the use of a medicine with a perceived small benefit was avoided, although in a previous chapter in this thesis similar responses were reported with benefits presented for simvastatin.

3] A leaflet for simvastatin had been presented in a previous part of this doctoral study, and continuity allows comparisons to be made more easily.

4] Simvastatin is used to treat an asymptomatic condition. As a result there can be an in-depth exploration of the experiences and decisions to take a medicine for which patients may not immediately feel the benefit.

6.5.2 Responding to the findings of the previous focus group study

In the first stage of development of the benefit statements to be used, we excluded two options, as a result of the findings of the focus groups described in Chapter 3. Firstly, the percentage statement was discarded. During the focus groups this was the least popular of the statements and it was reported not to facilitate understanding in a similar way to the other formats. Secondly, as the participants stated they found the combined framing to be challenging to read it was decided that only one type of framing would be used. Initially, in discussions, the supervisory team agreed that the positive statement should be used, as that was identified as the preferred statement during the focus groups.

6.5.3 Identifying the source of data

Simvastatin can have different levels of benefit depending on whether it is used for primary or secondary prevention of cardiovascular disease (Minder et al., 2011, Naci et al., 2013, Taylor et al., 2013). Patients who have already experienced a cardiovascular event, such as a heart attack or stroke, might derive larger benefits than those who have a risk factor for cardiovascular disease, but not a previous cardiovascular event (Taylor et al., 2013). Therefore a decision was made to target the benefit statements to people taking simvastatin who had a particular level of cardiovascular risk. It was important to target the benefit statements so they were as relevant to the participant as possible. It was expected that, as the statements were specific to a patient's condition

and level of cardiovascular risk, this may facilitate a more in-depth discussion about the meaning and relevance the participants might attribute to the benefit information.

In order to do this it was important to identify data that were specific to cardiovascular risk groups. A number of resources were identified as potential sources of data, including NICE guidelines - national evidence-based guidelines in the UK, developed to facilitate clinical decision-making about treatments. The NICE guidelines on statins for the prevention of cardiovascular events are based on a meta-analysis of data related to studies of a variety of statins. Hence this could not be used, as the data needed to be specific to simvastatin. Of the 14 studies used for the NICE guidelines, 4 were relevant to simvastatin (Pedersen, 2004, Teo et al., 2000, Bestehorn et al., 1997, Maas Investigators, 1994). These papers were considered in detail and the Heart Protection Study (HPS) was chosen from which to derive the data for the benefit statements (Heart Protection Study Collaborative Group, 2002)

The HPS is the world's largest trial of simvastatin and was run by the Medical Research Council and the British Heart Foundation. It was chosen for a number of reasons; statin benefits can be variable depending upon condition and previous risk factors. The HPS study provides specific data for a secondary prevention population which describes the benefits in a specific population and is specific to the outcomes of taking simvastatin, rather than the outcomes of taking any statin. Therefore the HPS study can provide the most relevant data from which to derive the benefit statement.

6.5.4 Identifying the specific data to be presented

The next stage of designing the benefit statements was to define the focus of data to be presented. The HPS study measured multiple primary and secondary clinical endpoints including all-cause mortality, coronary events, strokes and revascularisation and it was important to consider which measures of the benefits of simvastatin should be presented in the benefit statements.

Patients generally want to know about what the medicine does and what it is for (Dickinson and Raynor, 2003). When considering benefit information, it has been reported that patients want to know how the medicine treats the disease for which it is designed; the impact on patient-centred outcomes (particularly the impact on their ability to carry out day-to-day activities); the degree of efficacy of the drug and the

proportion of patients who meet primary endpoints (European Medicines Agency, 2009).

After discussion with the supervisory team and other pharmacists and health care professionals (1 GP (AZ), 1 nurse consultant (CG), 3 pharmacists (DP, DG, RK)) it was agreed that for simvastatin the primary endpoint likely to be most of interest from the HPS data would be likelihood of heart attack or stroke. Consideration was given to the inclusion of secondary endpoint data such as reduction in cholesterol level and a decision was made to explore in the interview whether this type of benefit information would be valued.

During review of the HPS data the following was noted in the paper:

> *"Allocation to 40mg simvastatin daily reduced the rates of MI, of stroke and of revascularisation by about one-quarter. After making allowance for non-compliance, actual use of this regimen would probably reduce these rates by about one-third." (HPS 2002, P.7)*

Consideration was given to whether patients would want to know the optimum benefit if they adhered to their treatment. It was considered that data presenting the benefits in **fully adherent patients** might be preferable for patients, as it would give them the optimum benefit associated with taking the medicine. However, the use of this method would be based on an estimation, rather than actual data, which would not be appropriate to real-life patients taking simvastatin. Instead this was something that was incorporated into the topic guide (appendix 25).

6.5.5 Defining the specific participant inclusion criteria

The following group of patients was identified as meeting the inclusion criteria for the HPS study data which were used to create the benefit statements. Therefore the same type of patients were recruited to the study, i.e. patients who have experienced prior MI or angina (including unstable angina, CABG, angioplasty) and one of the following coexisting morbidities.

+ cerebrovascular disease
+ peripheral vascular disease
+ diabetes mellitus

6.5.6 Development of the benefit statements

The benefit statements underwent several rounds of refinement until consensus on the wording was achieved.

In the following boxed examples the nature of the content is labelling for the purpose of reading the thesis. In practice the statements were coloured and labelled with reference to their colours. If there was more than one version of a coloured statement, this was indicated as '1: orange' etc.

The starting point was the following statements:

PURPLE:

Rebastatin can lower levels of cholesterol and tri-glycerides in your blood and can reduce the chance of you having a heart attack or stroke.

GREEN:

If 17 people take Rebastatin over the next 5 years, 1 of them will be prevented from having a heart attack or stroke.

ORANGE:

In 100 people, 72 who take no treatment will not have a heart attack or stroke. If they take Rebastatin for 5 years, then 78 out the 100 people will not have a heart attack or stroke.

Negative or positive statements

It was agreed that the negative statement was easier to read than the positive statement. A decision was made to use the negative statement in order to avoid the double negative associated with the positive. This was ultimately a pragmatic decision but was guided by the findings from the focus groups (which were more ambiguous for the Rebastatin than the Janatriptan group), and the wider literature. The positive frame

was also included as a separate statement for the participants to consider in the topic guide, when their attitudes towards framing were explored.

'People like you'

During one round of amendments the phrase 'people like you' was removed from the statements. This phrase was viewed negatively during the focus groups. However, its removal was problematic, as it meant that the resulting statement 'In 100 people who do not take this medicine…', was inaccurate. The statements do not refer to 100 people, but to 100 people in a high risk group. Consequently the phrase 'people like you' was re-instated. The topic guide was amended to further explore preferences for this.

Text order

A change to the order of the text in the 'orange' statement was considered**.** The initial order followed aetiology, identified here by the term 'treatment second':

Orange Negative (treatment second):

In 100 people like you who do not take this medicine, 28 will have a heart attack or stroke. But if they all take Rebastatin over the next 5 years, 22 will have a heart attack or stroke.

However, a revised order was considered, in order to present the primary outcome from the trials first, followed by the surrogate outcomes ('treatment first')

Orange Negative (treatment first):

If 100 people like you take Rebastatin over the next 5 years, 22 of them will have a heart attack or stroke. But if the 100 people do not take Rebastatin over the next 5 years, 28 will have a heart attack or stroke.

This was because it was surmised that the outcomes of heart attack and stroke prevention are likely the most important to patients, and what they would prefer to read first. Relevant to this were the findings from the focus groups which revealed that patients experienced an emotional response when reading similar benefit statements.

Patients wanted positive information about the benefits of their medicines. The ‘treatment first’ statement presents data in a way could be interpreted to represent an increase in incidence of heart attacks or strokes associated with not taking the medicine. The original statement (treatment second) presented a reduction in incidence of heart attack or stroke associated with taking the medicine.

The potential for increased emotional response from the participants was considered and a decision was made to present the ‘treatment second’ statement in the context of the leaflet, but to also present the treatment first statement separately as part of the topic guide, to explore preferences for these two ways of ordering the text.

Purple:

Rebastatin can reduce the chance of you having a heart attack or stroke. It does this by lowering levels of cholesterol and tri-glycerides in your blood.

Green:

If 17 people take Rebastatin over the next 5 years, 1 of them will be prevented from having a heart attack or stroke.

Orange Negative:

In 100 people like you who do not take this medicine, 28 will have a heart attack or stroke. But if they all take Rebastatin over the next 5 years, 22 will have a heart attack or stroke.

Orange Positive:

In 100 people like you who do not take this medicine, 72 will not have a heart attack or stroke. But if they all take Rebastatin, 78 will not have a heart attack or stroke.

Orange Negative (treatment first):

If 100 people like you take Rebastatin over the next 5 years, 22 of them will have a heart attack or stroke. But if the 100 people do not take Rebastatin over the next 5 years, 28 will have a heart attack or stroke.

Figure 17: The 5 versions of benefit information that were shown to the participants. The top 3 statements were included in the body of the leaflet. The bottom two statements were provided separately and shown as alternatives to the orange negative statement. These were labelled numerically for the participants.

6.6 Data analysis

Data were organised and analysed using framework analysis. This approach is consistent with the use of qualitative description as the underpinning theoretical framework. The aims of qualitative description are not to provide a 'thick' description, to develop theory or create an interpretative meaning of an event or phenomena, but instead to produce a rich, straight description of the phenomena of interest. In this study that is the impact of providing benefit information about simvastatin to patients receiving a prescription for this medicine (Neergaard et al., 2009).

The qualitative description approach tends to favour the use of forms of content analysis with modifiable coding systems as method of data analysis. Framework analysis is a form of content analysis which describes the development of an indexing system that can be clearly applied to large amounts of qualitative data and which uses a well-described and robust method for organising and analysing data.

This method is consistent with previous work undertaken in this area of research (see chapter 3).

The following stages of Framework analysis were undertaken:

[1] Familiarisation

After the interviews field notes were made and initial categories for coding considered (appendix 24). The audio-tapes were listened to and the transcripts re-read and checked for accuracy. Emerging themes were considered and discussed with the supervisory team.

[2] Identifying a thematic framework

The initial framework was developed iteratively. Two transcripts were read in detail and reflected upon. Notes were taken and field notes studied. The audio recordings were listened to again.

One transcript was then used to chart emerging codes. Each quote was considered and an initial 'in vivo' code highlighted. Preliminary thoughts about what this initial code might relate to were noted and these were developed into initial themes. These initial themes were then organised into sub-themes and categories through a process of charting (see appendix 25).

A member of the supervisory team (JM) also undertook this process; however a miscommunication resulted in the application of a previous framework (from study 2) to

the data, as opposed to the generation of a new framework. The ‘alternative’ framework contained several categories which were similar, an example being ‘Relationships with healthcare professionals’ and ‘Talking about natural frequencies’. The author identified the categories which were similar and checked these against each other to identify whether there was consensus with regards to organising the themes. There was a good match between the themes, and consensus achieved when similar themes were applied to the interview data. RD and JM then discussed the process and the key themes and categories they felt were important to include. RD developed the final framework which was then checked by JM.

As JM had familiarised herself with the data through the application of the ‘alternative’ framework she could review the framework that RD had developed and make recommendations for any additions or changes to themes or categories in order to improve the data.

In order to further validate the framework an additional member of the team (PK) was provided with 2 transcripts, one of which was charted, and the stage 4 framework. Comments on the categories framework were obtained from PK.

After comments were received, the author made some minor changes to the framework, including the following:

- Under 'impact of benefit info' knowledge and understanding were combined under one code. PK noted they were different concepts but it was acceptable to combine them into a single code as long as this was explored in the analysis. (PK)
- Under 'initial response to benefit info' PK suggested consideration of the participant's reaction (i.e. emotional or considered / thoughtful) and the differences between gist and impressionistic / thoughtful responses. (PK)
- Under 'talking about uncertainty' PK suggested clarity was needed about coding words or concepts when considering the terms 'chance' and 'risk'. RD created 2 sub-themes which were coded separately in order to explore this in more detail. (PK)
- JM suggested a code that incorporated "trustworthiness of the information". This was included in the code ‘concerns about benefit information’. (JM)

The framework was again scrutinised by the members of the research team. The framework was circulated 3 times in total until there was consensus that the framework identified as many potential themes and categories that could be seen in the data provided.

[3] Indexing

The thematic framework was then applied to each interview. The interview was read and relevant data coded according to the framework. Initially NVivo, a computer programme designed to organise and assist with the analysis of qualitative data, was used to code the data. An example of a coded interview was provided to JM to check for agreement

[4] Charting

The indexed data was then sorted into charts. Each chart presented a main theme; every patient was represented by a row and each column designated a sub-theme. This allowed for all pertinent quotes from patients on a particular sub-theme to be charted in a visually accessible way in order that the researcher could view a summary of the data, yet view the different themes emerging by case and/or category. This facilitated cross-case and cross-category comparisons and enabled the researcher to view sequences and patterns and make deeper level interpretations of the data, rather than just provide a descriptive narrative. JM had opportunity to view the charts and the original interviews; no changes to the charts were made as a result.

[5] Mapping and interpretation

The final stage saw a process of mapping and interpretation which was undertaken by both RD and JM during 2 full-day meetings. RD and JM undertook a 'post-it note' exercise where each category and sub-category in the charts were summarised and arranged in emerging themes. Each researcher took a category and organised the emerging themes into sub-themes. These would then be presented to the other researcher who had the opportunity to discuss each theme and re-arrange the post-it-notes, until a coherent set of sub-themes had been developed for each category.

For some categories, this was a more descriptive process (appendix 26). Occasionally the process of mapping and interpretation meant that themes from different categories were collated and combined to create a coherent, overarching narrative.

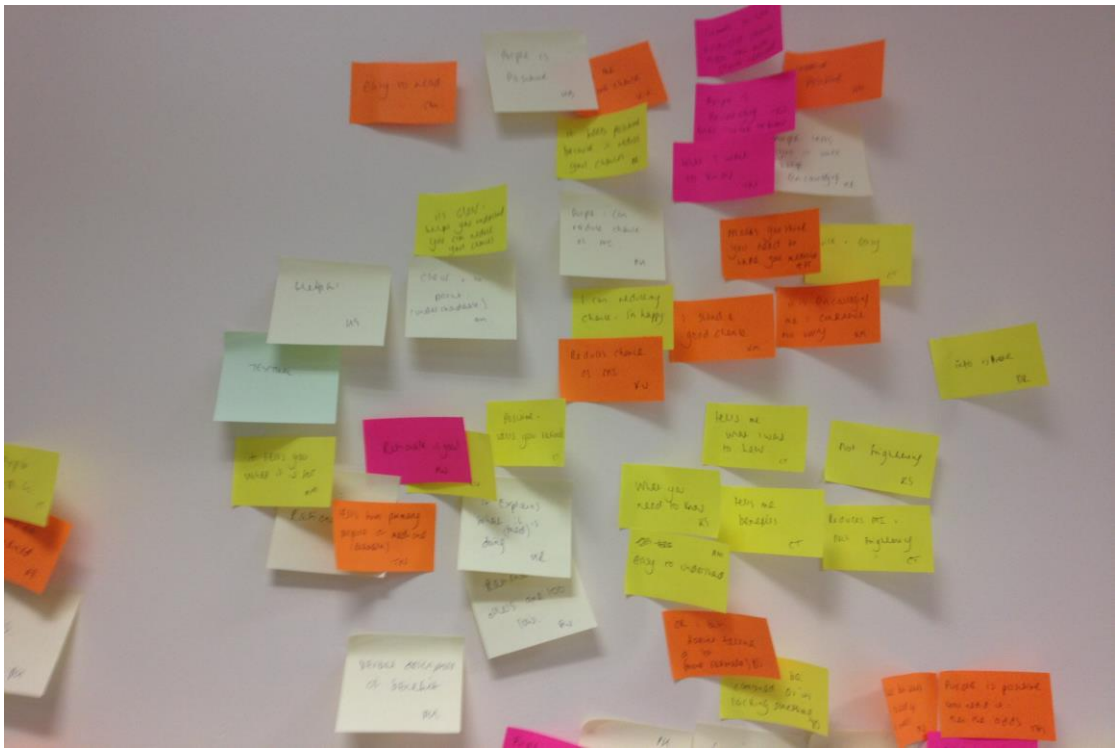


Figure 18: An example of the post-it-note exercise which shows the colour coding used to explore any groupings of opinion by age group.

In order to facilitate this, different coloured post-it-notes were used to represent different age categories, this created a visual representation of whether particular age groups were grouped within particular emerging themes. (Although the findings suggested that different views were spread relatively equally and did not appear to be influenced by age).

When the post-it-note exercise was complete, RD and JM made field notes and mind maps to present the emergent themes and identified the most-important themes from the framework (appendix 27).

6.7 Results

Letters were sent to 120 participants. 21 participants responded positively (17.5% positive response rate) and 4 more replied but declined to be involved. 20 participants were interviewed in their own homes and 1 participant was interviewed at their GP practice. Participant characteristics are reported in table 2. The participant's characteristics were reflective of the typical population receiving a prescription for simvastatin.

8 participants were female. The age range was 55-92 (median age=75). 13 were educated to school level, 3 were educated to age 18 and 5 completed higher education. Participants received a prescription for a range of medicines (range 4-10, median=7).

A range of views and responses were obtained on the inclusion of the different formats of benefit information in a PIL.

6.7.1 Typical perceptions of leaflets and medicines and associated behaviour

This section describes the range of typical behaviours that the participants described regarding leaflet-use and information-seeking and also their reported health beliefs. This context is important in order to be able to interpret and recognise any reported changes in these perceptions and behaviours which might be stimulated by the provision of the benefit information.

- **Information-seeking behaviour**

It was apparent that a majority of participants were passive receivers of information, rather than active seekers. The majority relied on information provided by their GP and/or from the leaflet supplied. A small number spoke of accessing other sources to obtain additional information when they were first diagnosed. One participant used the internet to read about health and medicine information. Two participants, both younger women, obtained information from charities such as the British Heart Foundation, as they did not find the information provided by their doctor, or in the leaflet, to be sufficient.

Therefore, on the whole, interviewees did not appear to access additional sources of information. A small group of participants received their diagnosis and received an initial prescription for simvastatin whilst in hospital. These participants tended to state that they had not received a lot of information about their medicine or its benefits and, although this was not viewed as ideal, it was also not viewed as a significant cause for concern.

Many of the participants had received a prescription for simvastatin for a long time, occasionally decades, and could not recall the quality or type of information they initially received with their prescription.

> *"I was trying to think when I first started taking Simvastatin ……. we are talking 16 years ago. I can't honestly remember how much information I was given about simvastatin at the time …….. I probably took the verbal advice from the doctor at*

the time and didn't, I have never looked very closely at the content of the leaflets that come with medicines." (P09, M, 72)

- **The leaflet as supportive information**

The leaflet was viewed as supportive information, secondary to receiving information from their GP. Not all the participants read their PILs. A number stated they did not read them all:

"Well, they always have these little leaflets in them, but quite frankly, I tend to just ignore them." (P02, M, 92)

Several reasons were offered; PILs were viewed as being too inconsistent; too scary; too complex; containing too much information; too long; too small a font; they 'put people off' and were viewed as provided for legal reasons and not to benefit the patient:

"*Interviewer: What do you think about the leaflets?*

P16: Not a lot really. I don't have a right lot to do with them. You just take things at face value don't you…I know that they've got to cover their selves for certain things. So I think a lot of this information is unnecessary... its insurance isn't it?" (P16, M, 68)

When a participant did read their PILs they said they tended to skim read and pick out the important bits. However, most participants said that PILs in general were helpful and a few used them as a reference point for raising issues with their GP.

- **Positive medicine beliefs**

The participants tended to have very positive beliefs about their medicines. Simvastatin was frequently attributed with positive outcomes. A few participants spoke of how they had seen a marked reduction in their cholesterol levels after taking simvastatin, which was proof to them that the medicine was effective:

"You've only got to go for your blood tests afterwards and it's dropped [cholesterol level] and it makes you feel better in yourself." (P03, F, 66)

Many participants were apathetic about their medicines. They assumed that the medicines were working because the doctor had prescribed them and they trusted the doctor's actions.

"I'm happy taking them, you know, me tablets 'cos I know they're doing me good and I know I can't do without them." (P10, F, 69)

A smaller number expressed negative beliefs about medicines which were linked to previous experience of adverse effects of a particular medicine.

On the whole the participants expressed positive beliefs about their medicines and were passive receivers of information who did not always, or regularly, read their leaflets.

There appeared to be a desire to receive information which reinforced positive beliefs about medicines.

6.7.2 What formats of benefit information are preferable?

Part of the purpose of the research was to map the range of opinions on different options of formats that can be used to communicate the benefits of medicines in order to understand in more detail what patients prefer.

Each format provoked a different range of responses from the participants, and there were also subtle differences in opinion regarding the presentation and framing of the benefit statements. Understanding these responses is important to develop a deeper understanding about which formats best inform patients about the potential benefits of their treatments. In this section the range of responses on each format is reported according to format, presentation and framing.

- **Textual**

The textual format was preferred by most participants and all the participants would be happy to receive a PIL which included such information. The textual statement was viewed as positive, easy to read and helpful. It was perceived as reassuring and met the participants' needs for information that reinforced their decision to take the medicine.

> *"The most positive one to read is obviously [textual statement] because it's just telling you that it's gonna reduce your chance and you think "that's good. I stand a good chance of not having a heart attack or stroke". The other two are a bit more problematic in the sense that they are showing you that there's quite a big percentage still, even though they're taking it, are going to suffer from some sort of problem." (P01, M, 75)*

Reading a statement which explained that the medicine reduced the chance of having a heart attack or stroke was perceived as simple information that the patient needed to know.

> *"It's simple and to the point and there's no frightening statements in it like heart attacks or stroke, well, I mean more than the one [mention]. But when it does mention it it's a positive. It can reduce your chances, which is what we all want." (P04, M, 69)*

However, occasionally the textual benefit statement was perceived as lacking and sometimes considered to be too cautious. The lack of numerical data appeared to mean that a small number of participants' felt they could not develop a deeper understanding about the proportion of participants who would benefit from the treatment, especially when they compared the textual statement to one of the numerical statements:

"I like to see that upfront [textual statement] but I'd perhaps be looking for perhaps something more…quantified benefits to back that up. I have… having, you know, talked about it, I think one of the quantified statements would be helpful." (P09, M, 72)

- **Number Needed to Treat**

The number needed to treat (NNT) format appeared to cause a great deal of confusion. It was frequently misunderstood by the majority of participants, with the misinterpretation that 1 extra person would be saved but the other 16 would have a heart attack. The statement led many to think that they would also have a heart attack:

"It's a bit like saying a lottery, we've got seventeen people, one might be lucky and sixteen won't be lucky, that's what comes out of this…it's almost like saying you've got a one in seventeen chance, haven't you? The ball will roll and it could be that you could be the lucky one or not…your chances are one in seventeen, it almost says it's luck doesn't it…it sounds like sixteen people are not gonna survive but one will." (P19, M, 76)

This was very common and a large number of participants could not understand the statement even after further explanation from the researcher.

The NNT was also viewed as 'poor odds', a low figure that was not worth bothering about:

"You've got a 17 to one chance better than, you know, so people might say "Oh, why bother about that." (P02, M, 92)

The provision of the NNT seemed to create an emotional response in many participants. It undermined their confidence in their medicines, created anxiety and removed hope:

"The one in seventeen, I don't think would give me a lot of confidence." (P11, M, 77)

"I did like it at first, but now, when I've looked at the others and thought about them, the one extra person is a bit frightening…it'll only help one person." (P14, F, 66)

There were, however, a few positive responses about the NNT. The statement was perceived as easy to read by these participants, and they did appear to struggle less when reading the NNT:

"It's just clearer…you don't have to think about it." (P20, F, 55)

This was in comparison to the natural frequency, which often took some time to sink in (although it facilitated a deeper understanding of the benefit data – see under 'Natural frequency' below).

Participants also valued the smaller proportions presented in the NNT. The denominator of 17 was viewed as easier to comprehend than the denominator of 100 used by the natural frequency:

> *"I'd rather the purple one [textual], but I'd rather that one [NNT] than the orange one. As I say, it's going out more towards, you know... People sort of, as I say, can understand it more with just sort of 17 people, whereas when you start talking about hundreds or tens of thousands it sort of blows it all out the window."(P12, F, 64)*

- **Natural frequency**

The natural frequency was liked, although there were significant concerns that participants expressed about this format. It was helpful for those who could invest the time into understanding the statement and it did seem to take several participants effort to read and re-read the statement and let the figures sink in. Several participants struggled to understand the natural frequency, and many did not understand it at all:

> *"This one just takes a little bit of working out but I can understand it now, but if you take the odds are, as opposed to 72 it's 78 isn't it? It's a bit hard…maths wasn't my right good subject." (P05, M, 75)*

The natural frequency format tended to be viewed as positive in comparison to the NNT, as the numbers were viewed as better. However, when considered on its own it did not convey large benefits to the patient and this was frequently viewed as disappointing:

> *"It's not terribly impressive is it? A reduction from 28 to 22? But I suppose as a percentage it's about, mm, it's not a bad percentage, about 25 percent about 25…yeah, 28 down to 22…well, will that worry people being told those figures? I think a lot of people might be worried. They might think "oh, I'm the unlucky 1 in 5", we'll call 22 one in 5." (P17, M, 81)*

The level of benefit perceived from the natural frequency was frequently viewed as not as beneficial as they would have expected or liked, which created a negative perception of the statement. However, it is the benefits of the medicine which are disappointing, rather than the format. It was difficult for participants to separate their disappointment with the data from their disappointment with the format of the statement.

> *"Not a very big decrease is it in people? 28 from 22. It's like saying 28% of you will have a heart attack if you take this tablet 22 of you will, so only 6% won't…I honestly don't think it's a large enough percentage of people, six. I think it should tell you a lot more will [benefit]…I think it's a bit on the low side, you know, it should be more people would benefit from it." (P11, M, 77)*

The natural frequency statement was occasionally viewed as sounding threatening; this undermined confidence in medicines:

"I think that's a bit frightening because you'll be looking out and thinking I might going to be one of those 28 or 22 all the time I think." (P14, F, 66)

There were also concerns that the repetitive emphasis on the disease in the statement was unsettling:

"Interviewer: Which is your favourite?

P04: Definitely not that one [Natural frequency]. I think it's too much emphasis on the heart attack and stroke. I think it is glaring out at somebody who might be a little bit anxious about the tablets anyway. I think you could be told about the benefits without all the 'heart attacks' and 'strokes'." (P04, M, 69)

The natural frequency appeared to require more investment in reading time and was more difficult to understand than the other formats; however it did appear to help a small number of participants develop a deeper understanding about the proportion of people who would benefit from taking the medicine, even if this understanding was ultimately disappointing.

- **Framing of the natural frequency format**

The majority of participants preferred the positive framing. This was viewed as the more positive option as there was focus on **not having** a heart attack or stroke, as opposed to **having** a heart attack or stroke. This provided more hope and encouragement and was perceived as less frightening. Participants described how it gave a good reason for taking the drug:

"It's [positive] not as threatening, you know, 100 people like you do not take 28 will have a heart attack or a stroke, whereas this one 100 people will not…it's the same odds but one says not and one says will." (P05, M, 75)

A small number of participants didn't understand the difference in framing of the statements and were ambivalent to either frame. Only one participant preferred the negative framing. This participant struggled with ease of reading of the double negative that was used on the positive frame and found the negative framing easier to read:

"I think if you tell people a negative "it will not", that doesn't necessarily register. I think if you tell them "You will have", I think that registers linguistically… You see people trying to figure out double negatives in their head and it doesn't work. I prefer the [negative framing]." (P08, F, 56)

However, the overwhelming majority preferred the positive framing because it was seen as more encouraging because of its positive emphasis:

"It's a play on numbers in that you are saying 28 will have a heart attack and this you are saying 72 will not have a heart attack, and in a way that will possibly encourage to take it, whereas the other might not…I think it would ease my mind to know that a lot of people have not had a stroke rather than to know that 28

have. Think looking at its more positive if you think that people have been helped by it." (P15, F, 72)

- **"People like you" in the natural frequency format**

A small number of people were ambivalent to the use of the phrase "people like you" and expressed no preference about its wording. However it was also found to evoke an unexpected and strong response from a larger number of participants. The statement was viewed as too personal or overfamiliar. Many felt very uncomfortable with the phrase which was perceived as negative and occasionally accusatory:

"It's a little bit impersonal but it's to the point. It's a bit blunt…People like you, people who suffer with your symptoms…That sounds something that I would prefer…out of 100 people who suffer with your symptoms, 78 are likely to have a heart attack if you do not take simvastatin... It's <u>people like you</u> that cause all this trouble in the world! [laughs.]" (P11, M, 77)

Alternative suggestions to this phrase included reference to the disease or symptoms.

- **'Treatment first' in the natural frequency format**

When presented with options of having the benefits of treatment data presented first, or second, in the natural frequency statement (**treatment first** compared to **treatment second;** see section 1.5.6), the participants responded in a number of ways. Some ambivalence was expressed, especially as the difference between the two formats was not understood or seen as too subtle to be concerned about for many participants.

One person preferred the statement which presented the treatment second; she reported that the "treatment first" statements made her think she would have a heart attack:

"I think I prefer [treatment second] to be honest…it's like saying if you take this medicine you're still going to have a heart attack. It gets a bit complicated and like I say a lot of people never have a heart attack…I mean, they have only put me on [simvastatin] as a precaution…that's a necessity if you see what I mean is like saying you are going to have a heart attack [treatment first] but the other one is more subtle [treatment second]." (P14, F, 66)

It was more common to prefer the 'treatment first' option because the participants wanted to know first and foremost what happens to those who take the medicine first:

"The way this one is written [treatment first] I feel is more simple…it starts off by '22 will have a heart attack but if they do not take it then 28 will', so they are telling you the good bit first and then the bad bit. If it's me and I'm going to take it I'd like to know what's gonna happen to me first, then hear the other bit and if that changes my mind that will be fine." (P15, F, 72)

6.7.3 Barriers to the inclusion of benefit information in PILs

This category describes the barriers identified by participants regarding the provision of benefit information in PILs. These include a number of barriers which limit initial patient access to the benefit information, as well as a number of concerns which might influence the impact of the benefit information in a PIL in a real-life situation.

It is important to be aware of these limitations and challenges in order to understand what the potential impact of the benefit information might be and to determine how the issues raised by the participants regarding the inclusion of benefit information in a PIL might be overcome.

The biggest barrier was that a large number of participants do not read the leaflets. During the course of the interviews the participants, who would not typically read their leaflets, engaged with and valued the benefit information but still stated that they would be unlikely to read the leaflet in a natural situation.

> *"I don't really think [I would read the leaflet] to be honest because at the moment I'm taking it because I've been told I need it, so that's about it."(P16, M, 68)*

For those who stated they didn't or wouldn't read the leaflet (and therefore the benefit information), the reason why was due to a lack of perceived relevance to their individual situation. The numerical information, in particular, was viewed as irrelevant because participants wanted to know the odds of what would happen to them and not to the wider population, and the numerical benefit statements could not inform the reader of such very personalised statistics.

It was also potentially irrelevant, as many participants pointed out, that by the time you get the leaflet you have already made a decision to get the medicine; therefore the information is superfluous because the decision to take the medicine has already been made. Therefore the timing of the benefit information is an issue:

> *"I mean, you wouldn't see this leaflet though, unless you were taking the medicine would you?" (P05, M, 75)*

Interestingly, denial about the natural consequences of their disease was expressed amongst the participants who appeared to adopt an 'ignorance is bliss' approach to receiving information about their treatments. Many participants do not appear to want to hear the statistical truth about their medicine, as this was viewed as unpalatable.

> *"I don't want to know that, I want them to tell me Simvastatin is doing you good and it will help prevent heart attacks, I don't want to know that X number are still gonna have a heart attack." (P01, M, 75)*

A major barrier to accessing the benefit information was that many participants did not understand the benefit information. Low levels of numeracy were perceived amongst the sample (although not measured). A moderate number of participants struggled to understand the information at all, whilst others made no attempt to try and understand it. Others found the information very difficult to process and understand and this was off-putting as it became a cognitive burden.

> *"As I say, for the everyday person, I don't think they would sort of…you know…just keep it plain and simple and everyday people like myself would understand it more than going into all the technology of, you know, 100 this and "we've done a survey of this, that the other."" (P12, F, 64)*

However, not all the participants struggled to understand the benefit information. A significant proportion did have the level of numeracy skills required to understand the numerical benefit information.

- **Concerns about benefit information**

A small number of participants voiced no concerns about the inclusion of (numerical) benefit information in PILs and thought it a valuable addition to the leaflet and would have either a positive impact or a negligible impact on patients. However, the majority of participants expressed a range of concerns about the inclusion of benefit information in a PIL. These concerns were specifically concerning the inclusion of numerical, rather than textual benefit information.

The users of simvastatin reported that numerical benefit data had the potential to provoke anxiety, worry and doubt and it was apparent that several of the participants found the information upsetting. The cause of this upset was the poor odds associated with the treatment:

> *"It doesn't seem as if it helps a lot of people that, not in that length of time. There are only six people it doesn't help. Does that sound like sense?" (P21, F, 84)*

The statistical information provided was perceived as very poor and negative. Sometimes this undermined the confidence participants had in their medicines and there were concerns that this might put people off taking their medicines because of fear rather than a reasoned decision to not take the medicines:

The information was not viewed as encouraging and this was in direct conflict with the desires of these participants who expressed positive beliefs about their medicines and want information which reinforces and encourages their decision to take the medicine. The numerical benefit information provided in the leaflets did not support patients with this and instead created anxiety and unease:

"It doesn't give me much…it doesn't really give me a great deal of confidence that I'm going to be the one who's going to be prevented from having the heart attack or stroke." (P09, M, 72)

Other concerns included worries that the benefit information contributed to 'too much' information that was provided with the leaflets. Suspicion of the statistics and their trustworthiness were also articulated:

"You don't want bombarding with these [facts and figures]." (P05, M, 75)

"I'm suspicious of these numbers because you are talking about quite a wide population." (P07, M, 85)

While the most common concern was that the benefit information was very negative, conversely it was expressed that the benefit information could be perceived as too promotional or something which could coerce a patient into taking the medicine. It would influence their view that without the medicine the patient might feel like they will die. The numerical benefit data was occasionally viewed as overly persuasive:

"It's more or less…not forcing people, but obviously if you think you are going to have a heart attack if you don't take this medicine, then you'll take it." (P21, F, 84)

"It's just a little bit threatening. It just says if you don't take <u>our</u> statins then you are going to have a heart attack or stroke." (P05, M, 75)

6.7.4 The benefits of benefits

This category describes the potential positive influences of the provision of numerical benefit information in PILs that were reported by participants. It was recognised that the participants tended to focus more on the perceived negative impact of the benefit information which, in both the previous focus groups and the current interview studies, stimulated strong emotional responses. The acknowledgements of the benefits of the benefit information tended to be more subtle. These are nevertheless of significant importance to those participants who desire encouraging, yet truthful, information about their medicines.

The benefit information was seen to have positive attributes. It was viewed as helpful information that was useful to know. They felt that that numerical information provided better rationale about treatments, more information about how the medicine was going to benefit them and how it would do this:

"I think you do need some facts and figures, it's interesting to know that if I take them, people who take statins are less likely and the percentage is worth knowing." (P05, M, 75)

A small number of participants thought it might help them to compare the effects of different medicines. A few thought it might provide them with a stimulus to talk to their

GP about their medicines. A small number of participants felt the information gave them confidence about their medicines and was encouraging and optimistic:

> *"It gives you a wee bit more confidence in the stuff that you are taking. If you know it gives you a better chance by X amount of people being…cholesterol being improved by it." (P11, M, 77)*

For one participant in particular it put the concerns she had about her disease and treatment into context, which surprised her, but was very positive:

> *"Of the five siblings my father died at 44 and his brother died at 40, the first heart attack so I've always thought the percentage was a lot higher from my own personal experience, I thought when I was diagnosed that was it, I wasn't going to make it and nobody ever said what the percentages were. I know that you can't get it exact because you don't know about genes and lifestyle and things. But that's more reassuring to me because, alright, 22 will have a heart attack or stroke but 78 won't if you are good and take the medicine." (P08, F, 56)*

The main benefit stated of providing benefit information was that it met the participant's expectations of healthcare professionals' duty to inform about the benefits of treatments. Participants felt that if this information is known by the producers of medicines information then it should be available for the patients to read. They expressed a sense of 'needing to know':

> *"Not everybody will want quantified information or quantified benefits, but I think equally there'll be a proportion who will look at the leaflet and will be looking for quantified information so they can actually say in quantified terms what the benefits are likely to be, so I would say yes." (P09, M, 72)*

6.7.5 The impact of providing benefit information on users of simvastatin

The provision of benefit information in PILs has been shown in this and the previous focus group study to stimulate an emotional response from the users of medicines and medicines information. However, what is not known from the focus group findings is the potential impact on patient knowledge and understanding about their medicines, nor the impact this might have upon decision-making and medicine–taking.

- **A negative positive: The impact on knowledge and understanding**

The impact of the benefit information on knowledge and understanding about medicines was varied and there was a range of responses. For many, the provision of benefit information in a PIL had no apparent impact on their knowledge or understanding about their medicines. There were several reasons for this. The information, particularly the numerical information, was viewed as too complicated and the participant frequently

didn't understand it. Often this was because the participant appeared not to have the numeracy skills required to make sense of the information.

There were examples where the participant developed a deeper insight into the benefits of their medicine when reading the benefit statements for the purpose of the research study:

Int: "Do you think it's helped you understand in more detail...

P16:Yeah, I do, yeah, honestly it has yeah. It's brought it home to me a bit, yeah… I'll take them with more joy [laughs]." (P16, M, 68)

However, it was apparent from what the participant had stated about their typical medicine taking and leaflet use that, without the stimulus of the research study, they would most likely not read the leaflet, even though they valued the benefit information and reported that it provided a deeper understanding of the benefits of the medicine.

When the information did have an impact this was sometimes a mix of a positive and negative effect. For a few participants it did appear to help them develop a deeper understanding about the benefits of their treatments and encouraged them to weigh up the advantages and disadvantages of treatments in more detail, but it also created more emotional responses and was often perceived as negative by the reader.

Despite the negative emotional responses that the numerical data frequently provoked, many participants were also satisfied that the numerical benefit information was included too. Participants wanted knowledge about the medicines to be made available.

"I know it does make some people anxious, but, as I say, I wouldn't be, but it still think it's a good idea to put 'em in." (P06, M, 88)

- **Decision-making and medicine-taking: Doing what the doctor tells you**

While many participants voiced a concern that information on the benefits of treatments, in particular the numerical information, might put people off taking their medicines, it did not appear that benefit information would be a significant influence on decision-making and medicine-taking for the participants personally.

The biggest reported influence for the majority of the participants regarding their medicine-taking was the recommendations of their GP. The participants stated that if their GP had advised they take a treatment, then they would take the treatment:

"If the doctor told me to stick me head in a gas oven, I would do. I tend to believe in 'em. I've had good results and I mostly go along with 'em…" (P06, M, 88)

For a number of participants the decision whether to take simvastatin or not had been made previously, sometimes decades before. The benefit information presented here was not viewed as something that could impact on decision-making, but instead was something that the participants desired in order to reinforce their decision to take the medicine. In particular, the textual information met this desire and participants frequently described it as encouraging:

> *"I'm not as impressed with that [numerical format], that's not as reassuring and it's not…it doesn't mean a lot to me personally…… it's just numbers and it's not as personal. Reading something like this [textual statement] it's speaking to me personally and it's giving me a bit of reassurance." (P20, F, 55)*

A few participants stated that they found the benefit information encouraging as they could see there were clear benefits to taking the medicine. Others found this information very discouraging and expressed concerns that the benefit information might make them think that the medicine was not worth bothering about.

However, ultimately all of the participants did not appear to be deterred from taking the treatment. Participants reported that the hope they might have regarding their treatment and the confidence in the medicine might be slightly undermined by the numerical benefit information, but did not report that this would change how they took their medicines:

> *"Interviewer: Do you think you would have done anything differently with your medicine?*
>
> *P02: I don't think so, quite honestly I don't think so because I'm one of these who has to trust the person who is doing the prescribing and what he says it will do for me. So, I think it all comes down to a matter of trust." (P02, M, 92)*

One patient had some serious initial concerns about the numerical benefit information (which were more marked than for any other participant). After reading and processing the benefit information he engaged in a process of re-assessment of his situation, where he used his experience of his medicine and his perception of the impact of changes to his lifestyle over recent years to appraise how he thought he would benefit from the treatment - in addition to the benefits presented. So, in order to cope with the negative perception of the benefit information he used his experience with the treatment and his good health to put a positive 'spin' on the information and to create a representation of his illness which led him to consider that the treatment would benefit him more than the proportion we had presented to him:

> *"As I say, I've had no twinges, I'm touching wood, I've had no twinges whatsoever, so in my mind unless I get older and something else goes wrong I'm not gonna have a heart attack, that's the way I feel at the moment. So fair*

enough, that's the best I can do for you….yeah, I don't want to know if I'm gonna have a heart attack 'cos I'm taking it, so if it's doing me benefit I don't need to know the rest, if it's telling me I may still have a heart attack, I don't want to know that." (P01, M, 75)

Despite negative feelings about the benefit information it was apparent that many participants appeared to try to employ coping strategies to apply the benefits of the treatment to their own situation. Where participants could not grasp the meaning they engaged in a reassessment of their situation.

Participants used their previous medicine-taking to measure their experiences against. As this was mostly positive, many of the participants were happy to take a 'suck it and see' approach to taking their medicines. They would try the medicines and see what would happen, or in the case of simvastatin, carry on taking the medicine and hope that they would be the one to benefit from the treatment. The benefit information did not appear to have a negative impact upon this approach to their medicine-taking.

Concerns were frequently expressed that the benefit information might impact on the behaviour of others, particularly the elderly or less numerate. The main concerns were that the numerical benefit data might be worrying or put people off taking their medicines. However, there was little evidence that this would impact upon the participant's own decision-making or medicine-taking behaviour.

6.7.6 Coping with uncertainty: How full is the glass?

This section explores the patient's responses to the uncertainty associated with whether they will be the patient who benefits from taking the treatment. It also reports on whether the patients reported how the benefit information conveyed such uncertainty. Uncertainty is a state of having limited knowledge where it is impossible to predict the future outcomes. With regards to uncertainty about medicines, the benefit information should convey that the treatment has a benefit to more people who take than those who do not take the treatment, but should also convey that not all patients who take the medicine will necessarily benefit from the treatment. In the previous focus group study it was apparent that not all people were aware of the apparent uncertainty associated with medicines, or that the uncertainty was underestimated. This section aims to explore how the participants responded to the uncertainty associated with their treatments in more detail.

It was apparent that there was a strong desire for certainty about the effectiveness of simvastatin. The participants wanted more certainty or better odds from their treatments:

P11: "Well I think that the word "can" it's another word, "will" I honestly believe that "will" is a better word.

Interviewer: Well I think what that is trying to say is that there's a bit of uncertainty about the medicine, so it "might not" benefit you.

P11: I thought that's what the Simvastatin was for actually now that you've said, it was to lower the cholesterol… So it should, it should, will lower the cholesterol or else they're rubbish." (P11, M, 77)

Lack of certainty was frequently perceived as threatening or off-putting and it was apparent that pre-existing issues such as anxiety might impact upon whether an individual had a negative or positive response to the uncertainty associated with the treatment.

Participants wanted absolutes, to know whether the treatment would work for them . The numerical information presented was not always meaningful for the participants, who did not always want to know what would happen to other patients, but only what would happen to them:

"I'd rather the purple one [textual], but I'd rather that one [NNT] than the orange one. As I say, its going out towards, you know…people can understand it more with just 17 people, whereas if you are talking about hundreds or tens of thousands it sort of blows it all out the window…You're sort of thinking, "well, as long as I am the one that benefits that is all that matters!"" (P12, F, 64)

The benefit information provided did not meet the patients' desire for absolutes and certainty regarding their treatment. The concept of uncertainty was complex; many participants felt that the lack of benefit information could increase uncertainty but others expressed concerns that the provision of benefit information might provide a sense of false certainty:

"The [NNT] says 'one extra person will be <u>prevented</u> from having a heart attack', it doesn't give a guarantee that they won't have one. This one [natural frequency] tends to, well it does say 'will <u>not</u> have a heart attack or stroke and that to me is a bit [too certain]. I can imagine if somebody took it and they had a heart attack or stroke they'd say "that blessed leaflet said, you know, we wouldn't" sort of thing. They'd blame the tablet then. No, joking apart, don't think you should promise something that you really have no control over." (P15, F, 72)

At times it was noticed that participants could not comprehend the concept of uncertainty about the effects of their medicine at all, or it was something they did not appear to think about it detail. In order to cope with uncertainty the participants' reported a couple of coping mechanisms. One was to ignore the uncertainty.

"You are, regardless of figures, better taking it and that's the end result. That's all I want to know. I don't want to look at figures personally. That would be good enough for me, basically what they [the leaflets] tell you to so." (P01, M, 75)

Another was to adopt a sense of fatalism, to accept 'what will be, will be'. However, 'what will be' appeared to depend on the outlook of the individual participant. Onê group of participants adopted a more optimistic approach and tended to consider that even though there was uncertainty associated with taking simvastatin, any chance was good enough for them to continue taking the treatment:

"I'm quite happy to take it to be honest. I'd rather have that chance of not having my heart clogged up. It still helps." (P14, F, 66)

These participants also tended to believe that if they adhered to the treatment then their chances would increase.

Conversely, others adopted a pessimistic approach and identified more with the poor odds with the treatment, and rather than taking the chance of benefit associated more with the chance that they would be the unlucky one:

"Everybody thinks at times, if they are down or not well are they the unlucky one? He would do it to himself, you think, well it will be our luck because we have had such a lot of things go wrong and we've just said "It will be our luck."" (P04 Wife, F, age unknown)

6.7.7 **"*I want the benefits to scream out at me*": Desirable attributes of benefit information**

The benefit information stimulated a range of responses, many of which were negative and there was a range of preferences for the specific types of formats that we presented. As has been said, it was apparent that the inclusion of benefit information in PILs can stimulate some negative responses and has the potential to be off-putting and create additional concerns for participants. The participants were questioned about whether the leaflet appeared more 'balanced' with the inclusion of the benefit information. However, a 'balanced' leaflet was not necessarily a desirable feature of the leaflet for participants who appeared to prioritise information that reassures and encourages them to take their medicines and who ultimately desire medicines which are more likely to help and which have fewer side effects.

However, as presented above, the benefit information did not quite redress the balance of the leaflet, and for a proportion of people it only served to make the leaflet appear more negative. One issue was that as the side-effect information was perceived as so negative, the provision of benefit information could never balance that. The benefit

information that was provided about simvastatin did not have a sufficient positive impact to appear attractive:

> *"I think the problem with these sorts of things is that there is too much emphasis on the bad side-effects. I know we've got to know, I know there is a duty of care and all the rest of it to tell us, you know, all the bad things that might happen but I want to be drawn into what is good, what's good about it… I want the benefits to scream out at me." (P20, F, 55)*

The numerical benefits of the medicine were disappointing, but the participants still wanted an emphasis on the benefits. It was suggested that placing the benefit information in a prominent position at the top of the leaflet would help to ensure this information was seen:

> *"I suppose it would [provide balance], yes, provided the top, or near the top of the leaflet. I think I would have given up before I reach the end in most cases." (P19, M, 76)*

Participants acknowledged the challenges of using numerical information and were undecided about the optimum method of presentation for benefit information, however they occasionally suggested the use of textual descriptors such as "by a significant amount" regarding the benefits:

> "*If you compare a hundred people taking the medicine with a hundred people not taking the medicine then the people in the former group, if that's not too difficult a phrase for some folk, will have a reduced chance of a heart attack or a stroke by, you know, whatever it is……. So I think something like that would give you, give them the essence of this and then whether you then actually give them the figure or you say "by a significant amount". You've got a choice of either giving them a number then with my formation, formulation, or just saying "by a significant amount". Then of course they'll say "oh you don't know what it is", you know, mm. [Interviewer laughs] Grumble, grumble, grumble. [Laughs]" (P17, M, 81)*

The appeal of use of qualifying words such as 'drop' to emphasise reduction in risk or 'increase' to emphasise improvements provided by the treatment was noted. Participants wanted the information to be positive and to stress the benefits of the medicine.

> *"The way I'm thinking at the moment is rather than being told, I'd like it you know, to be a positive statement, if you take Rebastatin your chances of having a heart attack will reduce and that could be quantified from twenty-eight in a hundred to twenty-two in a hundred, does that make sense? This is, it gives you the basic statement [reads from leaflet], "in a hundred people like you who take this medicine, twenty-two will have a heart attack or stroke, but if they don't take Simvastatin, Rebastatin, twenty-eight will have a heart attack or stroke", I don't like the way the information's presented, I would like it to be more positive, take Rebastatin and you will benefit in the following terms, whether you know, you will, your likelihood of having a heart attack will drop from twenty-eight in a hundred to*

twenty-two in a hundred, I'd rather it was, any information was presented in a positive way." (P09, M, TN)

For a small amount of participants this could be achieved by using a combined textual and numerical statement. The textual statement was perceived as positive and was generally well-liked. Having this textual statement as a precursor to a numerical statement appeared to reduce the disappointment and reinforce the benefits of the medicines that participants desire to hear more about:

"I still like [textual statement], I think I could just add the bit from 28 out of 100 down to 22 out of 100…Whatever combination of purple and orange adds up to. I like the fact it says how it does it, yeah, but if you're going to say it reduces the chances then tell people exactly how many it will reduce it by." (P08, F, 56)

Participants also desired information which reassured them and encouraged them to take their medicines. The numerical data on simvastatin failed to achieve this and was perceived as disappointing. However, it was apparent that the participants interviewed still desire benefit information from their medicines information, factual information which reassures them and responds to their desire to continue to take their medicines as prescribed.

6.8 Discussion

The aim of this study was to evaluate the impact of providing benefit information about medicines in written medicines information on the attitudes and opinions that the real-life users of medicine hold about their treatments.

This study was novel as it examined the impact of providing this benefit information about the medicines that patients are taking in a non-hypothetical scenario. Chapter 3 described the findings from a focus group study where a sample of medicine-takers was asked their general opinions on benefit information. This discussion includes a comparison of the 2 studies and examines any differences between the opinions and preferences reported from the focus group participants and the real-life users of medicines. First, responses that were similar to those expressed in the focus groups will be explored. There will follow a discussion about the differences that the real-life users of medicine reported about the inclusion of benefit information in PILs.

6.8.1 Key finding: Textual information was preferred, but numerical (natural frequency) information can help with judgements

Most participants preferred the textual statement and were happy to have it included in their patient information. There appeared to be a desire for additional information about

the rationale for treatment that described the condition and treatment in more detail. However, despite the preference for the textual format, it was apparent the numerical statements had the potential to help a select sub-group of participants gain a deeper insight into the benefits of their medicines.

Natural frequencies in particular appeared to foster a greater understanding of the meaning of the benefit information. This finding is supported by the findings of the wider literature, including the findings of the scoping review in chapter 2. Natural frequencies have been shown to facilitate the calculation of probabilities and may help assist with reasoning (Gigerenzer, 2002, Galesic et al., 2009b, Girotto and Gonzalez, 2002). However, it is important to note the natural frequency was still a difficult format for many of the participants to engage with. It only appeared helpful for those with a higher level of numeracy who invested time in reading the statement.

These are findings that are reflective of the preferences of the participants in the focus groups. The preference for textual format over numerical format for most people appears therefore to be a common theme. It must be noted that preference is not indicative of performance and it is possible that, despite some reported hostility to the numerical format, its use may likely facilitate a deeper understanding of the benefits of medicines when compared to the textual statement.

6.8.2 Key finding: NNTs are difficult to understand

It was apparent that, during the focus groups, some participants struggled to interpret the NNT. When it was viewed positively this was because it was regarded as short and easy to read. In comparison to the focus groups, the interviews allowed for more time to explore the participants' understanding of the NNT and it was apparent that many did struggle to understand this format. The NNT was confusing and conveyed a sense of chance that was not accurately interpreted by the most of the patients. There was a tendency for many patients for the NNT statement to mean that 1 patient would survive as a result of taking the medicine and be a 'lucky one', but 16 would not. This misinterpretation generated a considerable emotional response and concern for those participants.

The NNT has been described as 'easy to understand' and as providing 'intuitive meaning' about the measurements of therapeutic effect particularly for healthcare professionals, but it has been anticipated that lay-people might benefit from information presented in this format (Christensen and Kristiansen, 2006). Much of the research into NNTs has examined the persuasiveness of the technique rather than people's

understanding (Malenka et al., 1993, Hux and Naylor, 1995). However, when evaluated in empirical studies it has been noted that lay-people do report difficulties in understanding NNTs.

Halvorsen et al (2007) described NNTs to be like a lottery, where few people win the big prize. They considered that the NNT format did not adequately communicate the proportion of patients who benefit from taking a treatment or who would avoid an adverse event. People frequently perceived the NNT as communicating that the 1 in X was the 'lucky one'. It was apparent that this phenomenon of being a 'lucky one' was conveyed by the NNT in a way which was disconcerting and misleading for the participants (Halvorsen et al., 2007). While the challenges of interpreting NNTs were apparent in the focus groups, this struggle was more obvious in the interviews, which may be due to more time being spent to discussing the different formats in detail.

The findings from the interview study suggest that NNTs are not easily understood by lay people who frequently misinterpret the benefits of their treatments as meaning that 1 in 17 will be 'lucky'. NNTs were reported to be easier to read and patients appeared to have a greater verbatim understanding of this format compared to other formats. However, they frequently appeared unable to understand the gist meaning of the NNT which adversely affected their ability to accurately interpret the benefits of their treatments.

6.8.3 Key finding: A positive frame is valued

After being shown both a positive and a negatively framed statement, all but one of the participants preferred the positive frame. These findings are consistent with the findings reported in the focus groups (chapter 4). The positive frame was valued as it appeared more optimistic and encouraging to the participants who wanted to hear how likely they were to **not** have a heart attack, rather than how likely they were to **have** one. Even though the positive frame contained a double negative, which was not necessarily easy to read, only one person preferred the 'simpler' negative frame.

6.8.4 Key finding: Patients were surprised at the perceived low benefits, but engaged in a process of "self-regulation" in order to adjust their expectations of benefit

Another finding consistent with those of the focus groups was that most of the participants over-estimated the benefits of their statin therapy. Patients receiving a statin therapy did not appear to have a 'realistic' perception of how likely the treatment

was to benefit them. When presented with the numerical statements this provoked surprise and most participants expressed disappointment about the potential effects of simvastatin when presented in a numerical format.

It is unclear why patients over-estimate the effects of their statin therapy. It was frequently reported that the information about the benefits of treatment had not been communicated verbally from HCPs, nor had the participants seen this information provided in written formats.

The participants appeared to have generally positive medicines beliefs and were optimistic about the potential effects of their treatment, so it was unsurprising that they expressed some disappointment when they were given this information.

A striking finding of the interviews was the less extreme emotional responses from the participants to the numerical information, in comparison to those in the focus groups. The focus group participants reported anger and mistrust when presented with the numerical benefit information. Whereas these responses were less apparent in the interview groups (although not non-existent). The real-life users of medicines expressed a good deal of anxiety and worry and disappointment, but less of an emotional response, and appeared to give more reasoned and considered responses to the information.

The focus groups appeared heavily influenced in their decision-making by the affect heuristic i.e. an emotional response. The 'real-life' users appeared to consider the data more carefully. It was apparent that during the interviews the participants engaged in a process of emotional regulation. This could be attributed to the method of data collection. Interviews on a one-to-one basis were able to facilitate more in-depth consideration of the numerical data, as there was more time. Focus groups do not necessarily enable discussion of individual limitations with the understanding and meaning of the numerical statements - as those who do not understand the information may have felt embarrassed or intimidated to share their lack of understanding. And also during the focus groups, the participants can influence each other's views, so if one participant has a particularly strong view, this might impact on the views of others (Kitzinger, 1995, Price et al., 2009)

Another explanation for the responses from the real-life users of simvastatin can be provided using the common sense model of self-regulation (CSM). This model explores the processes that people engage in when they are faced with a threat to their health. The model assumes that people are active problem-solvers, and that in order to return

themselves to a normal state after experiencing a threat to their health, people undertake a process called self-regulation where they process the information they have, reappraise their situation and develop strategies to cope with any negative perceptions or emotions (Cameron and Leventhal, 2003).

This model has been more recently developed to elaborate upon aspects of emotional regulation that patients undertake (Cameron and Jago, 2008). When considering the findings of both this study and those of the focus groups in chapter 4, it is apparent that the participants in the two groups undertook different processes of emotional regulation after receiving the benefit information.

The benefit information was perceived as a threat by members of both groups but different reactions were apparent in each group. The focus group participants were frequently more hostile to the information, whereas those who actually used the medicine for which the benefit statements were created tended to be less hostile and respond more cautiously, expressing less extreme emotions. This suggests the possibility that when presented with information about the benefits of a medicine in a non-hypothetical situation, when that information is perceived as a threat the users of the medicine are more likely to engage in a process of emotional regulation in order to manage their specific health-related distress. Those who do not take the medicine do not need to engage in this process as the threat is entirely hypothetical.

The model identifies different coping strategies used to mediate the relationship between the negative emotions and how the individual perceives their health. Three of these coping strategies include emotional suppression, reappraisal and wishful thinking. (Cameron and Jago, 2008, Cameron and Leventhal, 2003). It was apparent that several of the participants engaged different strategies in order to cope and moderate the emotional impact of receiving the benefit information. Some ignored the information and suppressed their responses to the information provided. Others re-appraised their health status in light of the benefit information. It was also apparent that some engaged in a process of wishful thinking, where they over-estimated the impact to their own situation or considered how their adherence to the treatment would improve their outcomes.

This is important as it marks a difference between the hypothetical and real-life users. When faced with uncertain information, the real-life users appear to employ coping-strategies and frequently use their prior experiences of the treatment to help them make sense of the benefits. In a hypothetical scenario it is not essential to do this therefore

the responses of those in the focus groups may appear more emotional or nihilistic due to the absence of the need for self-regulation.

More research is needed specifically measure the impact of the emotional regulation that participants undertake when provided with benefit information about medicines on both their psychological and physical well-being.

6.8.5 Key finding: The reported impact on behaviour appears to be minimal

A concern about the provision of the benefit information that was identified during the focus groups was that participants reported that the information was 'off-putting' and might impact negatively on whether someone might take a medicine. It was apparent that the focus group participants displayed a lot of negative emotion and there was a concern that this might lead to patients making decisions about their treatment based on the affect heuristic rather than a reasoned consideration of the information (Slovic et al., 2004, Finucane et al., 2000). This subsequent interview study suggested that real-life users did not appear to want to stop taking their medicines, or make changes to their medicines despite reports of the benefit information being 'off-putting'.

The main reported reason for this was due to the faith and trust placed in people's GP. The overwhelming majority of the participants stated they would do what their doctor tells them. The benefit information did not appear to undermine the confidence that people had in their doctor's advice in a way that led to a change in medicine-taking behaviour.

It is possible that patients are influenced by a state of inertia, where they lacked motivation to change their decision to take a medicine. Most participants reported long-term prescriptions for simvastatin and had therefore already made a decision to take this treatment. It is possible that the benefit information did not influence any change in decision-making or reported behaviour due to a status quo bias. The status quo bias is the *"tendency to maintain a previous decision either by actively taking the default or by doing nothing"* (Suri et al., 2013, Samuelson and Zeckhauser, 1988).

It is important to note that this study only explored the opinions of the patients at one point in time, when they had initially viewed the information. It is feasible that decisions to change medicine taking behaviour might happen after the patient has had the opportunity to ruminate over the information and process its meaning. It is also feasible

that benefit information might impact differently on those who are considering whether to take a new treatment or not i.e. for patients who have not yet made a decision.

Finally, it is important to note that some participants reported that this information would not impact upon their behaviours as they don't read the leaflets in the first place. This is a significant barrier in engaging people about the benefits of their treatments using written patient information leaflets.

6.8.6 Key finding: Individual and relevant personalised information is desirable

Difficulties in interpreting personal meaning from the benefit statements were a significant barrier to how helpful the participants found the benefit information. The information was not always perceived to be relevant to the individual and while many participants appeared to understand the verbatim meaning of the information, it was difficult for them to interpret the gist of the numerical statements.

Fuzzy Trace theory explains how people tend to rely on their gist understanding when decision-making (Brainerd and Reyna, 1990). A concern is that if the benefit information does not have relevant meaning for an individual, this may represent a lack of gist understanding about the benefits of the medicine which may lead to inaccurate assessments of the level of potential harms and benefit. This study did not measure whether the benefit statements effected both the verbatim and gist the understanding of the participants.

Another issue to consider is how this lack of meaning was represented as a lack of relevance of the benefit information for the individual. The benefit statements were based on population data and it was reported that this is difficult for the participants to comprehend. There was a desire for more meaningful individualised information that communicates personalised likelihood of benefit to people. This desire for personalised information has been noted in previous research about tailoring patient information (Dickinson et al., 2013). In order to meet the needs of patients who desire a more personalised approach to their medicine's information, the providers of patient information need to address the challenge of how to tailor patient information. This will be particularly pertinent, and indeed challenging for benefit information, especially as the individual benefits of medicines are not always known.

6.8.7 Key finding: The benefit information does not appear to make the leaflet more balanced for patients

In Always Read the Leaflet, the MHRA consider the possibility that the inclusion of 'positive' information in a PIL could provide balance in a leaflet which in turn could minimise concerns patients express after reading about the potential side effects of the medicine.

The textual information was generally perceived as a positive inclusion to the leaflet. However, the textual benefit information did not necessarily provide the reader with an accurate portrayal of the benefits of the treatment, which were largely over-estimated until they were presented in a numerical format.

The numerical benefit information was not described as something which helped make the leaflet more balanced and less frightening, conversely it made the leaflet appear more negatively weighted and more frightening. The participants did not report that they desire balance in their leaflets. This contrasts with the findings from the systematic review of Raynor et al (2007). Instead they appear to desire medicines which are more likely to help and which have fewer side effects. This appears to be a deficiency of the medicine itself, rather than the accompanying information.

This is an important finding, because it prepares us for the possibility that patients might find the inclusion of benefit information in PILs to be a negative addition, as opposed to a positive one. It is also important to note that although the participants in this study did not report they would do anything differently, the inclusion of benefit information might lead some to reject medicines on the basis that the balance of harms and benefits is negatively weighted. This in itself is not a negative concern as such, as long as patients are making informed decisions that are in line with their values. However, further research is required to measure the impact of providing this information and ensure that decisions being made are done so in a reasoned manner, as opposed to a knee-jerk reaction to a perceived imbalance that the provision of benefit information might stimulate.

6.8.8 Key finding: A minority of patients value benefit information being made available

While many participants did not like the inclusion of the numerical benefit data, it is important to note that participants still value and desire the inclusion of benefit information in their PILs. While the benefits of statins were not viewed as heartening,

some participants felt that if this information is known then it should be provided. Although not all participants stated they would value this information being made available, a small group thought this information was very important to include in communications about medicines.

The makers of medicines information and healthcare professionals were viewed as having a duty to inform the patient about the benefits of their treatment, regardless of whether this information was something that was viewed as positive.

6.9 Strengths and limitations of the methods

A strength of this study was that the participants were patients receiving a prescription for simvastatin, in order to explore their opinions on the inclusion of benefit information about their own treatments. This facilitated a deeper exploration of the issues that users of medicines can face when informed about the benefits of their medicines. The research into the provision of, particularly statistical, benefit information to people has tended to use hypothetical samples or hypothetical medicines and situations (see section 2.7.7.) This study adds to the small number of research studies that have examined the provision of benefit information for patients taking the medicine concerned.

The participants recruited to this study were broadly representative of the general practice population who take simvastatin. A range of opinions were obtained from a sample who all received that medicine, but were varied in age, gender, education and number of medicines taken. These different characteristics were recruited in proportions similar to the population of the general practice (although there was an under representation of younger males). However, this group who volunteered to take part in research might hold different views to those who declined to participate.

Also it is important to note that the views on the benefit information were provided in the context of the participant receiving information about a treatment that had previously been prescribed, in some cases for many years. This only provides a snapshot of the possible opinions on the provision of benefit information. It is also possible that the views offered during this study were influenced by the participants' prior experiences with taking simvastatin. People receiving a prescription for a different medicine with different benefits might express opinions or preferences on the provision of benefit information different from the ones expressed during this study.

A limitation of this study is that it did not measure directly the impact of providing benefit information, it only explored self-reported behaviours. It is possible that while the participants might have reported that they would 'do what the doctor tells them' and remain adherent to their medicines, it is possible that the provision of benefit information might change medicine-taking behaviour in some way.

More research evaluating the following will be required to further measure the impact of providing benefit information to patients on medicines on the following:

- adherence (both short-term and long-term intentions)
- participant understanding (with a focus on the differences between patient preference and performance of format)
- decisional-conflict and satisfaction with medicines information
- health beliefs
- status quo bias
- verbatim and gist understanding of benefit information

6.9.1 Conclusion

This study builds upon the findings from the focus group study in chapter 3 by examining the impact that benefit information has when provided to patients who are currently using a medicine, in this case simvastatin. There were many similarities in the findings between the two groups of participants. It was apparent that both groups (the hypothetical and real-life users of medicines) over-estimated the benefits of medicines. This resulted in the provision of, in particular, numerical benefit information creating concern and anxiety as it did not appear to match the expectations the participants had about the effectiveness of their treatments.

The participants in both studies overwhelmingly preferred the textual benefit information, although it was sometimes apparent that this information did not necessarily provide them with enough information to make informed decisions. More research could be undertaken to explore ways in which benefit information can be provided using words rather than numbers in a way that gives a more accurate representation of the proportion of people who might benefit from a treatment.

The numerical information was difficult for many participants to understand. NNT formats in particular are very difficult for participants to understand and can be confusing. Although their shorter sentence structure appealed to many participants, it was apparent that they were frequently misunderstood. Natural frequencies appeared

to be better understood and appear to have potential for communicating the proportions that benefit for treatments more accurately. However, this was only when the reader could invest the time to read and attempt to comprehend the more complex sentence structure the natural frequency used. It is important to note that this numerical information is not valued or understood by everybody.

A concern noted during the focus group studies was the extreme emotion provoked by the numerical benefit information. It was concerning that the routine provision of such information might promote decision-making based on the affect heuristic, rather than a rational consideration of the information. This extreme emotional response was less striking during the interviews with the real-life users of medicines. It was apparent that the participants were often shocked or disappointed with the benefit information, but they appeared to employ a number of coping strategies to help them deal with both the threat posed by the benefit information and the uncertainty associated with the effectiveness of the treatment. This is an important difference as it suggests that the users of medicines will be less likely to reject their treatments due to fear, and engage in a more reasoned considerations of the likelihood of benefit and risk of harm of the treatments before altering their behaviour. This was not measured by this body of work, and an exploration of the impact of benefit information on medicine-taking in the long-term would be valuable in providing further knowledge about how informing people about the effectiveness of their treatment impacts on longer-term health outcomes.

This is not to say that the information should not be given; the concepts of patient empowerment and engagement are based on transparent provision of all relevant information. If the outcome of a reasoned assessment of the information is that a medicine is not right for an individual, then that decision must be respected.

The PIL is a mandatory and regulated piece of information that should be provided to every patient who is prescribed (or who buys) a licensed medicine. While several participants were hostile or ambivalent to the inclusion of this benefit information in their leaflets, a number felt that there was a duty to inform patients about the effectiveness of treatments. The PIL seems a logical place for the inclusion of information about the benefits of medicines – after all that is where the numerical information about side effects and their likelihood is to be found. The findings of this study suggest that people value the addition of extra textual information about the rationale of treatments. The provision of numerical information is more problematic as many people do not understand or value this information. However a small group of participants believed that if the providers of medicines information know the numerical benefits of medicines,

then this should be provided in the leaflet. There was an expectation that extra textual information about the rationale of treatment would be enhanced by the provision of numerical information about the effectiveness of the medicine.

Chapter 7: Discussion and conclusion

Chapter 7 Discussion and conclusion

The inclusion of a headline section and information about the benefits of medicines in patient information leaflets

7.1 Introduction

The final chapter will present a discussion of the overall findings of the thesis, including an assessment of the strengths and limitations of the research. This includes an exploration of the implications of the findings related to the inclusion of both a headline section and information about the potential benefits of medicines in current patient information leaflets. The barriers and facilitators to making such changes are also considered.

The context of the work in the wider literature will be discussed. There will also be recommendations for further research and policy. The chapter concludes with final remarks on the potential impact of including a headline section and information about the benefits of medicines, considering both patient and professional perspectives.

7.2 Summary of findings

The research work addressed the following question and had five aims:

7.2.1 Research question

What is the impact of the inclusion of a headline section and information about the benefits of medicines in patient information leaflets on patients' satisfaction and potential understanding and medicine-taking behaviour?

7.2.2 Research aims

- To investigate methods for the presentation of a **headline** section in a regulated PIL.
- To investigate methods for the inclusion of information about **benefits** in a regulated PIL.
- To explore patient preference for a headline section and information about the benefits of medicines.
- To explore how the inclusion of both headline and benefit information in a regulated PIL can impact upon patient knowledge and understanding of medicines.

- To explore the impact of the inclusion of both a headline section and benefit information on potential medicine-taking.

Chapter one set out the background to the research. A history of the legislation of the patient information leaflet was provided, alongside a discussion of the role of the leaflet. This chapter also described the concepts of:

  - a headline section
  - information about the benefits of medicines

Chapter two presented the findings from two scoping literature reviews. One focused on the **headline** section which suggested that there was a limited amount of research in this field. In contrast, the scoping review on **benefit** information presented a varied and diverse body of empirical research. The findings from this review were equivocal, but several potential formats were identified from which to develop statements about the benefits of medicines.

Chapter three reported the findings from a series of focus groups, showing that most participants were open to the inclusion of a **headline** section in a PIL. The inclusion of information about **benefits** was a more divisive issue and participants reported a number of concerns about the inclusion of numerical benefit information. These concerns were serious and resulted in some emotional responses to the benefit information. Preferences for textual information were noted, although some participants developed a greater understanding of their medicines after reading and absorbing the accompanying numerical benefit information. Despite the expressed concerns about the numerical information a general desire for benefit information in medicines information remained.

The thesis then continued with **chapter four**, a user-testing study which evaluated the performance of a **headline** section. This study found that the headline section was used by lay participants approximately one third of the time to locate key information about a medicine. It was noted that the headline tended to be the first place in a leaflet the reader would look. Participants reported positive opinions on the inclusion of a headline section in a PIL.

A survey undertaken in **chapter five** showed substantial variability in the inclusion and presentation of benefit information in 100 PILs currently in use in the UK. A comparison showed that more recently licenced medicines were more likely to contain benefit

information than PILs for more established medicines. None of the leaflets included in the survey presented any numerical benefit data.

Chapter six reported the final empirical study in the thesis, which recruited users of a medicine (simvastatin) to semi-structured interviews, where the participants were shown leaflets which contained both numerical and textual benefit information about simvastatin. This study reported that actual users of simvastatin found the information to be disappointing, difficult to understand and occasionally upsetting, but that patients did not report that they would change their behaviour after reading the information. While benefit information is complex and can provoke emotional responses from people taking medicines, it was felt that this type of information should be made available.

7.3 What this work adds

7.3.1 Benefit section

This work adds to the understanding of the impact of providing benefit information in written medicines information in a number of ways. Firstly it provides the first evaluation of the extent to which benefit information is currently included in PILs and the first categorisation of the forms of benefit information that are currently in use. There was also been an evaluation of the preferences and opinions on the inclusion of benefit information as a whole, including an exploration of different formats for presenting benefit information. The impact of providing benefit information on patients' understanding about medicines and potential health behaviours has also been evaluated. Several key findings are noted:

- **What is benefit information and how prevalent is it in current PILs?**

The survey provides evidence that currently benefit information is variably communicated to patients. There is no clear existing guidance on how benefit information might ideally be presented and the findings from the survey contribute to our understanding of what type of information might be described as benefit information, and how it might be communicated in a PIL.

The survey raises questions about the most effective methods of communicating uncertainty to patients and identifies inadequacies in current methods. The survey also highlighted the absence of numerical benefit information in PILs. None of the PILs in the sample contained numerical benefit information about the potential benefits of the treatment. While this information is challenging to communicate, and in some instances, for older medicines, may not be available, it is disappointing that newer medicines on

the market are not providing patients with this type of information. Patients will be less able to make informed decisions about their treatments if they are unaware of the magnitude of benefit of their treatments.

- **The development of benefit information is challenging**

The development of benefit information that can be included in written medicines information and be understood by the lay person is not an easy task. There are many barriers and complexities to including this information in a PIL including the following:

  - *There is no consensus for the best format for numerical or textual benefit information in a PIL.*

The thesis explored patient preference for format (discussed below). It is important to note that preference is not indicative of performance and a highly preferred method might also mislead the patient into misinterpreting the benefits of medicines. The scoping literature review identified several potential methods for the presentation of benefits. These were used to explore patient preference and opinion, but their performance was not measured. It is currently not known which method of benefit information performs best at aiding understanding and encouraging patients to make informed, empowered decisions about their medicines. Until more is known then this will be a challenge to the inclusion of benefit information in a PIL.

  - *Identifying a reliable source of data on which to base numerical benefit information*

Developing an accurate benefit statement relies upon the availability of accurate data on the effectiveness of a treatment. Not all medicines, for example older medicines, will necessarily have this type of data available. In recent years, clinical trials have improved in both quality and increased in size; therefore it is possible that the quality of data from which to derive benefit statements differs for older drugs than newer drugs (Sorenson et al., 2011). It might not be possible to calculate accurate benefit information for all medicines.

The clinical database, Clinical Evidence, provides evidence-based summaries about the prevention and treatment of clinical conditions, based on thorough searches and appraisal of the research literature. It has evaluated 3,000 treatments and concluded that 50% were of unknown effectiveness. These treatments are not all medicines, and are not necessarily commonly in use. However, it is important to note that there are potentially a significant number of medicines which are of unknown effectiveness and

this creates significant challenges in communicating this lack of evidence and uncertainty of effectiveness to patients (British Medical Journal, 2013).

Medicines which have been tested extensively in clinical trials will have multiple sources of benefit data, presenting a challenge in choosing the most accurate and appropriate source of information for the benefit statements.

It is broadly accepted that systematic reviews of randomised controlled trials are the gold standard to evaluate effectiveness of medicines (Greenhalgh, 1997). The hierarchy of evidence is one potential approach that could be applied to identify the best available research from which to generate the benefit statements.

However, using this approach in this study was not a simple process. A decision was made to use the hierarchy of evidence from which to identify research on simvastatin and the systematic review was considered 'gold-standard'. However, systematic reviews which include simvastatin combined data from multiple RCTs evaluating the effectiveness of various statins (Ward et al., 2007). The use of a systematic review or meta-analysis as the source of benefit data may not therefore be feasible. This is particularly pertinent if the review:

- combines data from multiple sources
- includes research that is not specific to benefit of interest
- or includes benefit data which is diluted by the inclusion of data that is not specific to the particular population of interest i.e. the indications for which the medicine is licensed.

Similarly, clinical guidelines on statins also combined data from all statins and were not appropriate to use in the context of providing data for one statin (National Institute for Health and Clinical Excellence, 2006).

There is the possibility that benefit statements might be developed from benefit information provided in the European Public Assessment Report (EPAR)(European Medicines Agency, 2014). An EPAR summary is an information resource produced by the European Medicines Agency designed to inform the public about the process by which a medicine was granted a licence. This resource contains information about the benefits of treatments and could be an important source for benefit data which would be seen as impartial. More research into the feasibility of this would be important.

It is important to consider how the quality and rigor of the research can influence the trustworthiness and accuracy of the data being presented to patients and whether the PIL needs to communicate the quality of benefit data too.

- *Where patients have different levels of risk this can be difficult to communicate*

Some meta-analyses and guidelines regarding simvastatin combined data generated from the treatment of patients with varying levels of risk. This means that data for high risk and low risk patients were combined into one single outcome/benefit figure. This leads to a measure of the benefit of the treatment that is less specific to an individual patient's level of risk. It would be inappropriate to provide patients with data that is potentially an under- or over-estimate of their actual benefit. It was apparent that there was potential for this when presenting data for simvastatin. The benefits of other medicines may also vary depending upon the patient's severity of disease. It can be difficult to obtain accurate, reliable data on how a medicine might individually benefit a patient depending upon their level of risk, but this is essential in order to present information that is as accurate as possible. Potentially this might require the development of multiple leaflets tailored to a patient's individual level of risk. However, it has been noted that the use of tailored leaflets, while desirable is also associated with concerns about getting the right leaflet to the right patient (Dickinson et al., 2013).

- *It may be challenging to choose the measure of benefit to present*

Most medicines have effects on multiple outcomes. For example Derry et al presented multiple outcomes from taking sumatriptan including:

- Pain free at 2 hours
- Headache relief at 1 hour
- Headache relief at 2 hours
- Use of rescue medication
- Relief of associated symptoms
- Relief of functional ability

It is not feasible to present all outcome measures in a PIL, as this would be complicated for patients, who tend to want succinct information and would pose a problem regarding the amount of space available. The manufacturers of patient information must carefully consider the type of benefit information likely to be most helpful for patients. This can only come from patients themselves i.e. what outcomes matter most to them.

- *Medicines with multiple indications*

Some medicines, for example prednisolone, have multiple indications. It might not be feasible to present benefit information for all indications in one patient information leaflet. A significant barrier to including benefit information in a PIL is that it can be challenging to identify ways in which a patient can be provided with benefit information specific to their condition.

To conclude, it is important to note that it can be difficult to identify accurate and relevant information from which benefit statements can be generated. Benefit information might not always be specific to all patients, and data should be accurate as possible according to each person's level of risk. For some medicines it is possible that benefit data exists that is of sufficient quality or accuracy. Other medicines have multiple indications and this will be a barrier to providing benefit information that is usable and specific to the patient's particular condition.

- **Benefit information about medicines can provoke emotional responses from the reader**

The focus group study adds to our understanding of how people react when provided with benefit information. It is known that certain types of benefit information can have more influence. The literature review (chapter 2) identified formats which should be avoided, e.g. relative risk, which can negatively influence decision-making by leading to over-estimation of benefit.

A study co-authored by the current writer (Hamrosi et al 2012) presented representative samples of medicine-users with information about an anti-platelet medicine. This was presented as an NNT and stated the following:

If 100 people took this medicine for 2 years:

- 3 of them would be saved from having a heart attack
- 1 of them would be saved from having a stroke

The benefits of this treatment were perceived as low and the benefit information stimulated an emotional, and often angry, response from the participants (Hamrosi et al., 2012).

The findings from the focus groups in the current body of work add to our understanding of the varying responses that different forms of benefit information (in particular numerical benefit information) can provoke. The use of two types of medicine (a statin and a triptan) with different levels of benefit has facilitated a comparison of responses according to magnitude of benefit and enabled a deeper exploration of how people

react to benefit information. A limitation of the Hamrosi study was that, as it presented the benefits of only one medicine, it was difficult to know whether people were hostile to the inclusion of benefit information as a whole, or just the benefit information associated with that particular medicine (Hamrosi et al., 2012). It is apparent however that hostility to numerical benefit information remains even when bigger magnitudes of benefit are presented such as here for sumatriptan. Benefit information is frequently perceived as surprising and concerning, regardless of its perceived magnitude.

Subtle differences in the initial responses from those taking and those not taking the medicine were observed. Although both groups expressed surprise about the perceived poor benefits, there appeared to be less hostility and nihilism expressed during the interviews with the actual users of medicines. Although this group were frequently disappointed by the level of potential benefits from the medicine, they appeared to engage in various coping strategies to help them come to terms with the information. For example there was a type of negotiation, where the participant would consider the benefits in light of their previous experience with the medicine or their past health, which is reflective of the type of behaviour described by the Common Sense model of self-regulation of health and illness (Cameron and Leventhal, 2003, Leventhal et al., 1998).

Benefit information can provoke a strong response from people. There is evidence that people tend to over-estimate the benefits of their treatments by thinking that they will work more effectively than they actually do and when shown numerical data about their medicines this can provoke an emotional response (known as the affect heuristic) (Finucane et al., 2000). This response is noted with medicines with varying degrees of benefit; even treatments with relatively greater benefits can stimulate a negative response. There do appear to be differences in how people initially respond to the benefit information. Real-life users of medicines appear to engage in a process of self-appraisal which involves consideration of what the benefits mean in light of their personal experience with taking the medicine and an appraisal of their current health states. It is possible that this process of self-appraisal reduces the impact of the affect heuristic meaning that, despite disappointment, benefit information might not lead to poor judgements based on an emotional, rather than reasoned response. To some extent this mirrors findings in the wider literature where it has been shown that moderately raised anxiety can lead to a more thorough examination of information, but high levels can lead to the application of heuristics which are not conducive to informed decision-making (Bekker et al., 1999, Loewenstein and Lerner, 2003). While the

participants in the interview study were influenced by an emotional response to the benefit information, it did not appear to hinder their decisions significantly.

To conclude, there was evidence that numerical benefit information can provoke an emotional response from the reader. This response exists regardless of the magnitude of benefit being presented but does not appear to hinder decision-making. Prior experience of taking a medicine and having a health condition appears to moderate the extent of this emotional response.

- **Patients desire additional information about the rationale of their medicines**

The survey indicated that current leaflets contain limited amounts of information on the rationale for the medicine. The findings from the qualitative studies indicate that patients desire more information about the rationale for their treatment. Additional information about what the medicines is for and how likely it is to help them would be welcome in a leaflet. A recent survey showed that the provision of information about the risks of medicines, specifically adverse drug reactions, which are currently included in PILs helped patients feel more knowledgeable about the risks of their medicines (Krska and Morecroft, 2013). It is possible that the inclusion of additional information about the rationale for taking a medicine will help patients feel more knowledgeable about the benefits of their medicines. More research is needed into the best methods of presenting such verbal descriptions of benefit information and how this impacts upon patients' knowledge about their medicines.

- **Numerical formats are challenging and not easily understood**

There is a significant body of research showing that large proportions of the population have low numeracy skills and find it difficult to interpret statistical information, such as the benefit information presented here (The Department for Education and Skills, 2003, Gigerenzer et al., 2007). There also is a body of research which shows that healthcare professionals can also struggle to understand and can be misled by statistical information (Gigerenzer, 2002, Gigerenzer et al., 2007). The issue is not something that can be easily resolved. Many people simply cannot understand numerical benefit information, although it has been argued that *"problems in understanding numerical information often do not reside in people's minds, but in the representation of the problem"* (Garcia-Retamero et al., 2010, P.1019).

There is evidence that different formats can lead to better understanding, and that this can include a deeper understanding of what the information means to the individual (Akl et al., 2011a, Carling et al., 2009, Tait et al., 2010a, Tait et al., 2010b).

The findings from this study reflect the consensus that large proportions of people find it difficult to understand numerical formats of benefit information. However, the study showed that, where people can invest the time and cognitive effort into understanding the benefit information, they report developing more knowledge about the benefits of their medicines (even if this knowledge is unwelcome) and frequently a deeper understanding about their medicines.

- **Which formats of benefit information are most preferred?**

A range of perspectives and preferences on the formats was reported. The **textual** format was frequently the most preferred. However, a small number of participants noted that this format did not help them gain perspective about the benefits of their medicines when compared to the numerical formats. The numerical formats were often perceived as upsetting and difficult to understand. However, the **natural frequency** was more often observed to be helpful and was preferred above the NNT and percentage formats. Participants tended to find the percentage format 'off-putting' and difficult to understand. It was apparent that there was significant scope for the patients not just to fail to get the meaning of NNTs, but to actually misunderstand them.

- **Does the inclusion of benefit information impact upon understanding about medicines?**

While the impact of benefit information on patient understanding was not explicitly measured it was apparent that its provision did have at least one significant impact on patient's estimations about the benefits of their medicines, although this was frequently negative. Most participants appeared to over-estimate the benefits of their medicines and after reading the benefit information appeared more aware of the limitations of their treatments.

For patients to make informed choices about their medicines it is essential that they understand their limitations. As well as their considerable potential benefits, medicines also have the capacity to harm. Currently patients do not appear to be in possession of accurate harm/benefit information. This is concerning. While harm information is currently provided in a leaflet (e.g. 'common – affects less than 1in 100 people), this is not the case for benefit information. If a patient experiences any significant side-effect then it is important they are aware of the likelihood of benefit before making a decision

about the trade-offs of continuing to take the medicine. Without an awareness of the benefits, patients might expose themselves to additional harm, for example by tolerating side-effects because they are over-estimating the potential benefits of their treatments (McCartney, 2012b).

It was observed that after reading the benefit data, most participants became more aware of the limitations of their treatment, but it was difficult to evaluate whether this helped increase their knowledge and understanding about their treatments. While a small number of participants were able to invest time and effort into understanding the information, others found this difficult. This is concerning as it might mean that patients only understand the limitations of the treatment and not then go on to make risk-benefit analyses and understand the trade-offs they might have to make. More research is needed to examine how well patients can interpret and apply the meaning of the benefit information to their own situation.

The natural frequency format was more frequently reported as facilitating understanding when compared to the other numerical formats, although there are still significant problems in using this format. The natural frequency format was viewed as complicated and many people complained that it took time to read and comprehend. However, when it was understood it did appear to provide a better insight into the benefits than other formats.

Another challenge with the natural frequency format was that many patients did not appreciate the need for the baseline information about those who did not take the treatment. It was frequently felt that this information was irrelevant to an individual's situation and that the information was therefore not personal enough. People desire individualised information that is relevant to their personal health outcomes (Dickinson et al., 2013). This type of information is challenging to communicate and, almost always, the individual likelihood of benefit is not known. More effort is required to communicate this to patients in order to facilitate a deeper understanding about medicines, support informed decision-making and ensure transparency.

One suggestion made by participants was the possibility of a combined textual and numerical statement, although it is possible that a combined numerical statement, for example percentages and natural frequencies, might help facilitate understanding. This approach has been recommended by both the MHRA and NICE (Medicines and Healthcare Products Regulatory Agency, 2005b, National Institute for Health and Care Excellence, 2009), however, requires more research into effectiveness. Research has

shown that when participants are provided with combined textual and numerical statements about the harms of their medicines this tends to be preferred over single presentations of risk. A study into a combined textual and numerical format suggested that this combined format did not show any improvement understanding (Knapp et al., 2013).

- **The impact of benefit information upon behaviour**

A concern about the inclusion of benefit information in a PIL is that it might impact negatively upon medicine-taking behaviour by creating an emotional response to the information which causes patients to reject their medicines. It is a concern that patients may make a decision not to take a medicine based upon information they might not be able to critically understand (Hamrosi et al., 2012) and this undermines the aim of providing benefit information.

The findings from the focus groups suggested that patients might change their behaviours after reading the benefit information. The potential for this to happen was explored in more detail in study 5 (Chapter 6) during individual interviews with people who were users of simvastatin. Most patients in this study reported that they would not change their medicine-taking behaviour after reading the benefit information and would rely upon the advice of their GP. While the focus group participants appeared more likely to reject their medicines it is feasible that in reality they would undertake a different assessment of their medicine-taking behaviour. However, this was not measured, nor was any long-term impact evaluated.

It is important to note that the majority of patients using simvastatin had taken the medicine for many years, often decades. The provision of benefit information may not influence their medicine-taking behaviour because of status quo bias; a preference for the current state of affairs (Suri et al., 2013, Samuelson and Zeckhauser, 1988).

- **What is the role of patient information: Education or empowerment?**

This study takes the perspective that the aim of providing benefit information is not to educate the patient to be adherent to their medicines but to provide accurate information about the relative harms and benefits of a medicine, to facilitate informed decision-making. This is something that sits within the patient empowerment discourse on medicines information. It is important to note that a patient empowerment view acknowledges that patients might make decisions to not take a medicine. From this perspective, the ultimate goal of providing benefit information is not to increase adherence but to help people make their own decisions (The Lancet, 2012).

The findings of this work suggest that the patient information leaflet is not frequently used as a decision-making tool. The majority of patients preferred to rely on their doctor's advice to assist their decision about taking a medicine. However, currently benefit information is not present in the PIL, so a patient cannot use their leaflet to assist in informed decision-making, even if they want to do so.

It is apparent that not every participant will wish, or have the ability to engage in informed decision-making (Flynn et al., 2006, Chewning et al., 2012). The findings from this study showed that some participants did not value the PIL and, despite their willingness to participate in research about them, did not read their leaflet. This is a significant barrier to engaging with patients about the benefits of their medicines. The findings from the headline section studies suggest that current leaflets do not meet patient expectations for good design and it is possible that responding to this may increase readership. In order to educate or empower the reader it is important to at least engage with them first.

An important finding of this research is that patients appear to over-estimate the benefits of their treatments. This situation needs to be resolved. Patients need good quality information which provides realistic expectations about the benefits of their treatments. It has been noted that a regulated and standardised PIL is a good place for this information to be included (Goldacre, 2012).

Currently in the United Kingdom there is a public debate focussing on the wider prescribing of statins. The National Institute for Health and Care Excellence has recently published draft guidance which recommends a wider use of statins (National Clinical Guideline Centre, 2014), reducing the prognostic threshold for initiating treatment. Opponents to this change suggest that the benefits for low-risk patients often do not outweigh the possible side-effects of the drug (McCartney, 2012a).

Figure 19: An example of news headlines regarding the current debate about the prescribing of statins in the UK.

The debate has focused upon how an increased use of statins at a population level may decrease the deaths from cardiovascular disease, which currently results in about 140,000 deaths each year in the UK (Department of Health, 2013). This debate is currently not focused upon the individual benefits, but instead on the population benefits, which include both health outcomes and costs, when compared to the potential individual harms that a patient might experience as result of having a side effect.

Opponents of the extended prescribing recommendations for statins express the view that the side-effects of statins are not adequately communicated and there is current debate about the accuracy of the side-effect data currently available (Godlee, 2014, Finegold et al., 2014). There is evidence that current methods used to express the likelihood of side-effect happening have several limitations which can lead patients to over and under-estimate risk (Berry et al., 2003a, Berry et al., 2003b, Knapp et al., 2009a, Knapp et al., 2013). However at least this information is made available in a PIL and should be provided to every patient with their medicines. Currently this cannot be said for benefit information. For a patient to make an informed decision about their medicines they need accurate and impartial information about both the risk of harms and the likelihood of benefit.

This debate about statins is timely and very relevant to the findings of this thesis. While there are significant barriers to the inclusion of this information, and it has been shown that the inclusion of benefit information might increase concerns about medicines and decisional conflict about taking treatments, it's availability to patients is essential if they are to engage in decision-making about their medicines. More research is needed to explore ways in which this information can be delivered with minimal emotional impact.

A patient should be able to access unbiased information about the likelihood of benefit and the risk of harm associated with their treatments. The findings of this thesis suggest that patients both desire benefit information and feel there is a duty to be informed about the potential harms and benefits of their treatments by their healthcare professionals. As the only regulated information for patients about medicines, a PIL is the obvious place for such information in order to optimise patient understanding and decision-making, although this is limited by the timing of the provision of a PIL, which generally is provided after a patient has been prescribed a medicine.

To conclude, patients do not appear to be making fully informed decisions about their medicines because they are not aware of the limitations of their medicines' benefits. The inclusion of numerical benefit information in a PIL might be a good way to communicate this information to patients, and while not every patient will use the leaflet to make decisions about their medicines, if a patient is to be empowered then this information should be made available.

- **The wider impact of the provision of information about the benefits of medicines**

The wider impact of informing the public about the likelihood of benefit from medicines on medicine-taking is not known. There is the possibility that patients might choose not to take a medicine which, in the absence of benefit information, they would have otherwise adhered to. In an RCT of 'decision analysis' and an information video for newly diagnosed hypertensive patients these interventions were measured as having a moderate, negative effect on participant's intentions regarding starting treatment (Montgomery et al., 2003).

If presenting patients with additional information about their treatments stimulates changes in medicine-taking behaviours, this might have an impact upon public health. With regards to statins this could potentially result in the rejection of treatments, which in turn might impact negatively upon cardiovascular death rates (Taylor et al., 2013).

There is potentially a significant public health impact to informing patients about the benefits of their medicines. However, there is also an ethical obligation to make sure this information is available to patients. If the likelihood of benefit of various treatments is known by the medical establishment then there is a duty to inform. Engaging honestly about the likelihood of benefit of medicines should be a central part of clinical consultation, with written information providing a supportive role.

As a result, the inclusion of benefit information, particularly numerical benefit information, might also influence the way in which health professionals consult and counsel their patients about medicines. The face of modern healthcare has changed over the last few decades and there has been a move away from a more paternalistic approach to consultation with the adoption of models of shared-decision making (Towle et al., 2006). However, the findings from this thesis suggest perhaps the goal of shared decision-making has not been fully achieved as patients are unaware of the limitations of their treatments and are making decisions about taking medicines based on false assumptions that the medicines are more effective than they are.

If information about both the likelihood of benefit and risk of harm is included in written information accompanying medicines then healthcare practitioners will be required to ensure that they can also communicate it during spoken consultations. There is evidence that patients desire both spoken and written information (Raynor et al., 2007). Healthcare practitioners will need to develop techniques for communicating uncertainty, which is something that is challenging to do so effectively. There is the possibility that the communication of the uncertainty of treatments and health outcomes might be something that could alter and potentially undermine the relationship between healthcare practitioners and patient.

There is evidence that despite the complexities associated with harm-benefit communication, there can be positive outcomes that result from communicating harm-benefits to patients. High levels of patient satisfaction have been reported, however it is important to note that additional training costs have been identified as important to facilitate this approach and the time that can be devoted to increased engagement in communicating harm-benefit is limited in a real life setting where consultation length is limited. (Davis et al., 2003).

The language used during consultation might require consideration and standardisation. While there are agreed terms used to communicate risk, for example the verbal descriptors ‘common’ and ‘rare’, there is currently no agreed similar banding for terms

used to communicate benefit. The complexities of communicating this and how patients might respond to the language of benefit is not known (Knapp et al., 2013). While attempts to standardise the language of harm-benefit communication have been investigated, it is difficult to place this within consultation.

> *"Such attempts to standardise have some immediate appeal, but most commentators believe they fail to recognise the dynamic linguistic reality of variable use of terminology and rapid evolution of meanings. Hence we do not believe this is an appropriate solution to the undoubted problem of the language of risk." (Thomson et al., 2005, P.466)*

7.3.2 Headline section

In contrast to the topic of benefit information, the subject of a headline section proved less controversial. The range of views expressed regarding the inclusion of a headline section was narrower than the range of views expressed regarding benefit information. There was a greater level of unanimity of opinion regarding the inclusion of this adaptation, and the opinions expressed were overwhelmingly positive. The topic was not accompanied with the same level of emotional response and none of the participants expressed anger or significant concern about the inclusion of a headline in a PIL. Overall, the research suggested that the inclusion of headline section was simpler and less divisive than the inclusion of benefit information.

Existing research on the inclusion of a headline section in written medicines information is limited. Currently there is very little evidence on which to base decisions about the inclusion of this adaptation. This body of research adds to the small amount of literature in this field.

The findings are generally supportive of the inclusion of a headline section in a PIL. The focus group study (reported in chapter 3) is the only qualitative research in this field which explores patient perspectives on the inclusion on a headline in a PIL. It also examines patients' reporting on the likelihood of using one. This study found that a headline section is valued by patients and viewed as a welcome addition. The user-testing study tested whether patients would use a headline section. The headline was observed to be the first place the reader would look in a document. Patients tended to use the headline to find short, self-contained pieces of information; it was used approximately a third of the time to locate relevant information during the test.

The headline section was viewed very positively by the large majority of participants. It was viewed as an improvement to the leaflet, something which met the readers' needs

for simple information that was easy to access. The headline section addressed concerns about the complexity of the technical document a PIL is viewed to be. While a few concerns were expressed that the headline might potentially put some people off reading the entire leaflet, it was also considered that the headline might encourage those who did not read the leaflet to read at least the important facts contained in the headline section.

There is limited evidence that a headline section does not impact upon a patient's ability to find and locate relevant information. Dolk et al (2011) allowed a participant to read and familiarise themselves with the leaflet prior to applying the test. The study in the current work used a modified user-test method to evaluate whether a headline section would be used when a patient was first presented with a PIL, as would happen in real life.

There was no evidence that the use of graphical signposts within a PIL aided the reader in any way. The graphical signposts used in this study were rarely noticed by the reader and their use should therefore be carefully considered. Currently the findings from this thesis suggest that the use of textual signposts is preferable to the use of graphical signposts.

Overall, the inclusion of a headline section in a PIL does not appear to hinder the reader and is viewed as a welcome addition. The findings from this body of work are supportive of the inclusion of a headline section in a PIL, similar to the type suggested by the MHRA.

7.4 Strengths and limitations of this thesis

The strengths and limitations of each method have been discussed in the respective chapters; this section discusses the strengths and limitations of the research as a whole.

7.4.1 Strengths and limitations of the methods

The pragmatic approach employed to investigate the research question was useful for this body of work which aimed to focus on the outcomes of the research as opposed to the underlying philosophies of the methods. Consequently the studies conducted prioritised methods that were best placed to answer the research question, rather than focussing on one particular method or a specific epistemology.

This absence of commitment to any one system of philosophy of research means that the researcher is not limited to one particular methodological perspective, such as

quantitative or qualitative, and that a mix of appropriate methods can be used to address the research problem (Creswell, 2013). A strong point of this approach is that it can facilitate a broader and more in-depth exploration of the research question.

The pragmatic approach has received criticism for a lack of focus on epistemological underpinnings and critics express concern this might impact on the reliability and generalisabilty of research findings, especially when compared to approaches which have a stronger theoretical underpinning, for example grounded theory. However, this perceived lack of theoretical grounding can be addressed with a focus on rigour and credibility (Creswell, 1994, Onwuegbuzie and Leech, 2005). The use of a pragmatic approach was well-suited to address the research questions and the use of a mix of methods facilitated the use of different approaches to examining the concepts of a headline and benefit information.

A significant limitation of this thesis is that the use of a qualitative approach to explore the inclusion of **benefit** information in a PIL meant there was no measure of the performance of the benefit information. (The performance of the **headline** section was evaluated using user-testing, discussed in the section below). Opinions on the inclusion of benefit information were explored but there was no objective measurement of whether the participants had understood the information. (Originally user-testing of the benefit statements was planned but unable to be undertaken due to the lack of consensus from the focus groups on the preference for wordings). It was apparent that many participants did not understand the numerical information and it was difficult to assess the varying levels of understanding among them. It was possible to observe whether a participant could read and recite the benefit statements verbatim but it was not possible to examine whether the provision of this information made an impact on what the information actually means in the context of the patient's individual health, or their decision-making.

Because the performance of the different formats was not measured, this study cannot conclude whether one particular method of presenting benefit information is more or less effective. The participants expressed a preference for one particular method over another but preference is not necessarily indicative of performance (Garcia-Retamero et al., 2010). Formats such as the NNT were observed to be difficult for the participants to understand, but understanding was not measured formally. Previous research in this field has shown that relative risk formats of benefit information are valued by participants and viewed as intuitive and easy to understand. However, when understanding of this format is measured, relative risk has been shown be misleading

(Akl et al., 2011a), particularly when provided in the absence of absolute risk information. There is the possibility that the views and opinions expressed in this study are not indicative of the performance of the difference formats in facilitating understanding about the benefits of medicines.

Another limitation of the qualitative approach taken was that while the aims of the study were to explore the potential impact that the provision of benefit information had on health behaviours, this was not measured objectively. During the focus groups many participants reported that they may be influenced by the numerical benefit information, for example some patients reported they might choose not to take a medicine. It is not known whether patients would choose to reject a medicine in real-life and so the longer-term impact on issues such as adherence, satisfaction with treatment, and health outcomes in terms of months and years, of providing benefit information is not known.

Subtle differences were noted between the findings from the focus groups, where the participants were less involved in a hypothetical scenario, and the interview study, where the participants were given information about the medicines they currently use. Those less involved were more likely to express hostility to the numerical benefit information and more likely to state they would be 'put off' from taking the medicine. Patients already using simvastatin appeared less likely to state they would not take the treatment. These findings were based on self-report and this study did not measure the impact of providing benefit information on initial decision-making about whether to take a treatment. As the patients were not followed up it is not known whether the provision of this information has influenced long-term decision-making. There is no evidence on whether the benefit information has any impact on adherence to medicines, or whether it helps a patient make more empowered decisions about whether to take a treatment. This is an area that warrants further research.

To conclude, this research used a pragmatic approach which focuses on the outcomes of the research rather than on the underlying epistemology. Alternative paradigms were considered but their lack of flexibility towards the use of a mixture of methods was not considered conducive to the aim of the research. A mixed methods approach was chosen as multiple methods were better suited to answer the research questions identified, although the methods used in this body of work are more a 'mixture' of methods rather than a mix of methods as the findings from each study were not triangulated (Burke Johnson et al., 2007, Williamson, 2004). The research methods used have several limitations which have been described. However there were also

several strengths which include the employment of well-defined, robust processes of analysis in order to maintain the credibility of the research.

This thesis presents a number of studies with slightly different sampling strategies. The aim of the qualitative research was to obtain a range of opinions from a sample that was representative of the wider population, but diverse enough to generate a mix of views and opinions on the interventions of interest.

The focus group study used a convenience sample, although this sample did include a mix of different age, genders and education levels. A criticism of a convenience sample is that it can be difficult to extrapolate convincingly from the findings and apply them to the wider population.

The user-testing study used a quota sampling technique to obtain a sample of participants with certain age, gender and education characteristics. This was necessary to ensure that a mix of participants was recruited. Without such a fixed quota, which stipulates a proportion of certain characteristics such as educational ability, the sample might not be representative of the population as a whole and this could impact upon the generalisability of the findings. Restricting the number of graduates and ensuring that the sample is reflective of the educational abilities of the wider population facilitates a fairer test of the leaflet and reduces potential over-performance of the leaflet (Raynor, 2013, Raynor, 2008).

The interview study also recruited a quota of participants who were representative of a 'typical' group of patients receiving a prescription for a simvastatin registered with a GP practice in the UK. The study recruited slightly fewer younger men receiving a statin than the general practice population, so the views of this group are under-represented in this research.

All of the participants in this research study were aged over 50. The views of people younger than 50 receiving medicines have not been examined and it is possible they might hold different views to the views obtained here, especially with regards to views on relationships with doctors, as the under-50 population are more likely to have taken part in shared decision-making as opposed to a more paternalistic approach to their healthcare (Godolphin, 2009, Charles et al., 1997). It is possible that younger people's views on the level of involvement in decision-making, and the assistance that providing benefit information has on this, may differ from the opinions of the older population. Equally, the lack of representation of younger participants in the sample might impact

upon the generalisability of the findings from the headline section. It is possible that younger people might use or respond to the headline section in a different way.

7.4.2 Transferability of the findings

There are limitations to the applicability of the findings from this body of work to the wider population of medicine users. We do not know the impact of providing benefit information for other types of medicines to patients. It is possible that patients may react differently to benefit information depending upon a number of different criteria including:

- Magnitude of benefit (Dahl et al., 2007)
- Severity of health condition the treatment is for (Horne et al., 1999)
- Whether the medicine is preventative, curative or symptomatic (Pound et al., 2005)
- The relative availability of alternative medicines or other interventions

However, this study designed benefit statements for two medicines (simvastatin and sumatriptan) for different conditions, in order to obtain a range of responses to explore this.

It is possible that the findings of the focus group study were limited by the recruitment of patients who were asked to make decisions about a hypothetical medicine. It has been shown that participants who are less 'involved' in a scenario may make different decisions to those who are; therefore hypothetical decisions may have different outcomes to real-life decisions (Kühberger et al., 2002, Bryant et al., 2013). In order to make the scenario as realistic as possible the participants were asked to imagine they had been prescribed this medicine and had to make a decision about whether to take it. The benefit information was not hypothetical and was derived from clinical trial data for commonly used medicines. However, it is important to note that the findings of the focus group study might not be reflective of decisions made in real-life.

This is one of the first studies in this field to recruit actual users of medicines and provide specific benefit information that had been tailored to the patient's level of risk. This is a strength, as there has previously been little research into the impact of providing benefit information to real-life users of medicines; most research in this area uses hypothetical scenarios or non-representative samples (chapter 2: Literature review).

One consequent limitation is that the participants had frequently been taking simvastatin for a long period; hence their decisions may be more fixed and immovable

than those of someone prescribed a new medicine. This phenomenon is called status quo bias and describes how frequently people make decisions that disproportionately maintain the status quo (Samuelson and Zeckhauser, 1988). The findings of the interview study might not be applicable to patients who are prescribed a new medicine and having to make a decision about whether to take a treatment or not.

7.5 Recommendations for further research

7.5.1 Headline section

- An evaluation of the most effective format for a headline section. This study used a shaded box. However the use of this format was not compared with any other format. An alternative format, for example boxes or outlines, may perform better.
- The longer-term impact of the inclusion of a headline section in a PIL on patients' satisfaction with the information and their information-seeking behaviours are not known. If such an intervention is to be included in a PIL (as is recommended here) then the longer-term impact needs monitoring to understand whether it increases the number of people accessing key information about their medicines.
- An evaluation of the impact of the headline section on a patient's beliefs about medicines would also be valuable. If the headline promotes the accessibility of key information for patients, does this impact upon decisions about medicines, understanding and long-term health behaviours? A quantitative evaluation of these measures would enhance our understanding of the impact of including a headline section in a PIL.
- Exploring the use of graphical signposts could help identify whether this technique can be improved in order to aid the patient to navigate the leaflet. The ones used in this study were not noticed and it was decided that no further investigation into their use was to be undertaken, as this was not a primary outcome of the study. However, there is the potential to undertake more research to explore whether a different format of graphical signpost performs better.

7.5.2 Benefit information

Implications for further research

The issue of including benefit information in a PIL is complex and many unanswered questions remain. Overall, it is argued that benefit information should be included in a PIL, largely because there is a duty to inform patients about the benefits of their medicines. This is an ethical issue. However to ensure the provision of good quality information to patients more research into benefit information is required:

- A quantitative evaluation of the format which best promotes understanding is required. Currently this is unclear; there are multiple formats which have potential. Patients report preferences for some formats above others, but preference is not indicative of performance and it is not known which format best promotes understanding about medicines when presented in a PIL. The best formats for presenting benefit information would then require user-testing.
- The impact of providing benefit information on behaviour is also not known. More research will be required to examine how the provision of benefit information influences decisions to take medicines and adherence to long-term treatments.
- The participants in the studies reported significant emotional impact from the benefit information. An evaluation of whether this type of information and resulting emotional impact affects decisional-conflict, which is defined as a state of uncertainty about which course of action to take, would add to our understanding of the impact of benefit information in a PIL.
- Further research into the development of textual methods of presenting benefit information will be valuable. Patients' desire detailed information about the rationale for their medicines. The best method to undertake this, and the impact of providing more detailed rationale, will be valuable. For example: what is the impact of providing additional information on whether a treatment is long-term or short-term on patient knowledge and understanding, satisfaction with information and medicines and medicine taking behaviour?
- Also, the consideration of using verbal descriptors will be helpful. Currently verbal descriptors are used to present harm information, with side effects being described as 'rare' or 'common' alongside numerical information. A similar method might be considered for the use of benefit information. More research into the feasibility and effects of this would add to our understanding of the topic.
- There is research into the use of a combined format for side-effect information, which showed that while a combined format was preferred it did not appear to impact upon estimations of side-effects incidence. A similar exploration of the

use of a combined format for benefit information, or for both benefit and harm information, would be beneficial to contribute of our understanding of the impact of combined textual and numerical formats (Knapp et al., 2013).

- A linguistic evaluation of the optimum method for communicating uncertainty about treatments to patients would help develop understanding about the most effective ways to communicate uncertainty.
- An evaluation of the best approaches to communicate the quality of benefit data is essential. Currently little is known about what patients want and what they understand about the quality and rigor of the data used to communicate information about medicines.
- This study did not examine patient opinion on visual formats such as graphs and charts. This was due to the limitations of including such formats in a PIL. However, as we are moving towards web-based provision of medicines information the potential impact of including visual benefit information in web-based medicines information will be valuable. This is especially with regards to the consideration of the use of interactive formats of benefit information.
- Finally, there is a need for an exploration of what healthcare professionals think about the inclusion of benefit information in PILs. Currently their views are not known. The PIL could be a valuable source that healthcare professionals might use to provide education and involve the patient in shared decision-making. A deeper understanding about what healthcare professionals think about the inclusion of benefit information in written medicines information and how they might use it to facilitate shared decision–making is needed.

Implications for policy

- Policy makers should work towards standardising the definition of benefit information and provide regulated evidence-based guidance on the type of benefit information that should be provided in a PIL. It is important that all mean the same thing.
- Serious consideration should be given to the inclusion of a headline section in a PIL. The headline section should be the first thing the reader sees and should be placed before any statutory information required. A well-designed headline section will set out the key messages for safe and effective use and help the reader assimilate the more detailed information with the body of the document.
- While it is apparent that the provision of numerical benefit information is a complex process, the producers of medicines information need to consider how

this type of information can be best incorporated into a PIL. The information provided must not be promotional but should aim to support the patient with their decision-making about medicines.

- The producers of medicines information need to be aware that subtle differences in the wording of a benefit statement can influence how a patient might respond to the information provided. It is important to note that a preference for a positive, as opposed to negative framing and the provision of information which presents the treatment first, as opposed to last, can influence patient satisfaction with information. In order to ensure satisfaction with medicines information, the producers of such information should pay attention to how this information is developed and build aspects of user-involvement into the process. The end product should be subject to appropriate user-testing.
- The regulators of medicines should provide guidance on the best methods for presenting the benefits of treatments ensuring that the needs of patients are at the forefront of any recommendations.

Implications for practice

- Currently many patients over-estimate the benefits of their treatments. The prescribers of medicines need to ensure that the benefits and potential limitations of treatments are clearly explained to patients to ensure they have a more accurate understanding of the benefits of their treatments.
- While this thesis focused upon the inclusion of information in a written format, healthcare professionals should be aware of the different ways in which benefit information can be communicated. Methods of benefit presentation, such as the formats presented here, could be helpful to explore the benefits of treatment in consultation with the patient and facilitate informed decision-making.
- Healthcare professionals also need to be aware of the potential for benefit information provoking negative responses in some patients. There was no evidence that the provision of benefit information would influence patients to reject medicines. However it is possible that this information may stimulate patients to seek additional information about their treatments, specifically in relation to alternative treatments. In this respect, healthcare professionals need to be able to respond to patients' needs and concerns, and cater for the varied responses the provision of benefit information may provoke.

7.5.3 Headline section and benefit information combined

- An initial aim of the research was to explore a combination of the headline section and benefit information. Due to time limitations a full exploration of this is was not possible. Further research which evaluates providing benefit information in a headline section is necessary to understand the impact of this.

7.6 Plans for dissemination

The aims of this body of research were pragmatic and the plan for dissemination has reflected that. The development of a deeper understanding of the impact of a headline section and information about the benefits of medicines in a PIL were evaluated and recommendations are being made to the appropriate regulatory bodies.

This research has already been disseminated to both the MHRA and EMA, who regulate the type of information that is included in a PIL. A presentation was made in July 2013 to the MHRA's expert advisory group. In March 2014 the findings from the PhD were reported at the EMA plenary meeting of the QRD working group. This is potentially the highest level of impact for European medicines information.

The research has also been disseminated through poster and presentation sessions at the following:

7.6.1 Conferences and meetings

- **European Medicines Agency. London, 2014**

Information about benefits in patient information leaflets: Patient perspectives. **R. Dickinson.**

- **Medicines and Healthcare Products Regulatory Agency. London, 2013**

Including a headline section and information about benefits in patient information leaflets: Patient perspectives. **R. Dickinson.**

- **Health Services Research and Pharmacy Practice Conference. Preston, 2013**

Headline, headline read all about it! The impact of a headline section in patient leaflets on satisfaction, knowledge and behaviour. **R. Dickinson**, DK. Raynor, P. Knapp and J. MacDonald. Abstract: http://onlinelibrary.wiley.com/doi/10.1111/ijpp.12028_3/pdf

- **European Patient's Academy on Therapeutic Intervention: A vision for 2020. Rome, 2013**

What do patients think about 'benefit' information in patient leaflets? **R. Dickinson.** Presentation: http://www.patientsacademy.eu/index.php/en/news/168

- **Yorkshire Concordance Conference. Leeds, 2013**

Information about treatment benefits in written medicines information: Patient Perspectives. **R. Dickinson**

- **School of Healthcare Postgraduate Research Conference. Leeds, 2013**

Providing headline and 'benefit' information in patient information leaflets: Does the inclusion of a 'Headline' section & information on benefits in written medicines information impact on patients' satisfaction and understanding? **R.Dickinson**

- **Medicines and Healthcare Products Regulatory Agency. London, 2011**

Providing tailored and 'benefit' information in patient information leaflets: patient perceptions and opinions in the UK and Australia: A focus group study

7.6.2 Posters

- **Royal Pharmaceutical Society. Birmingham, 2013**

Do patients use a headline section in a patient information leaflet to find key information about their medicines? Findings from a user-testing study. **R. Dickinson**, DK. Raynor, P. Knapp and J MacDonald.

7.6.3 Academic journals

Further dissemination will include articles to academic journals.

7.7 Conclusions

This thesis examined the impact of the inclusion of a headline section and information about the benefits of medicines in patient information leaflets on patients' satisfaction and potentially also on their understanding and their medicine-taking behaviour. An

important finding was that the two adaptations provoked very different responses from medicine-users.

The inclusion of a headline section was viewed positively by the large majority of participants in these studies. It was an adaptation that the participants noticed and engaged with. It was viewed as a potential solution to the prospect of reading an existing leaflet; which is frequently viewed as a daunting prospect and a boring, technical document of limited personal relevance. The addition of the headline section responded to a reported desire for good information design and it contained information that was regarded as important by current medicines users.

When tested in a user-test scenario it was noted that information was found in the headline section approximately a third of the time and that its inclusion did not appear to hinder the reader. A potential concern about this adaptation is that it might deter people from reading the entire leaflet, encouraging the reader to only engage with the information in that section. However, it was reported that it had the potential to engage those who did not normally read their leaflets to at least read that one section. The use of a headline section was viewed as a valuable adaptation in a patient information leaflet.

In contrast to this, the inclusion of benefit information in a PIL was far more divisive and provoked strong and complex responses from the users of medicines. The inclusion of benefit information has the potential to better inform patients about the benefits of their treatments. It also has the potential to be viewed negatively and not as information which communicates benefits of treatments, but instead is information which is negative and which only highlights the limitations of a treatment. There was evidence of an over-estimation of the benefits of current preventative treatments and the provision of benefit information in a PIL. While frequently disappointing for medicines users this is something that may reduce this misunderstanding about medicines.

There was very limited evidence that the provision of benefit information would impact negatively upon medicine-taking behaviour. Despite initial reports that the benefit information was upsetting and might put people off, when patients actually taking the medicine were asked about their intentions, it did not appear that the benefit information had a negative influence on medicine taking. Relationships with GPs and previous experience of taking the treatments appeared to exert stronger influences on decisions. Other influences on the response to the benefit information appear to be mediated by

patients' perceived severity of their condition, an individual's perception of themselves as an optimist or a lucky person, and their ability to cope with uncertainty.

There are significant barriers to the inclusion of benefit information in a PIL. Firstly, not all patients read these leaflets and they are frequently viewed as documents designed to protect pharmaceutical companies rather than serve the needs of patients. There is a desire for better design of leaflets to make them more visually appealing, and a headline section might contribute to this.

Designing benefit information is a challenge. It might not be possible to provide accurate, reliable information for all medicines and all indications. Although this should not mean that the producers of medicines information could not rise to the challenge. There is significant interest in the communication of risk and benefit information to patients and over recent years the field of risk communication has seen the development of many innovations which can facilitate understanding. The survey of PILs highlighted a need for clearer terminology when communicating the benefits of treatment, as well as less variability in the type of information that might be communicated. While numerical data might be challenging to report, a more consistent approach to presenting textual benefit data is essential.

Even after consideration of the best formats for the presentation of benefit information it is apparent that people struggle to understand complex numerical presentations of benefits. Formats such as the NNT were frequently misunderstood. Significant effort was required by participants to understand the natural frequency format, although this format appeared to provide better insight into the benefits of the medicines when participants invested effort into reading it. While more research is required into measuring which formats can best promote understanding of the proportion of patients that will benefit, it is valuable to have a deeper insight into the emotional responses that can be provoked by the provision of this information.

The emotional impact of the provision of benefit information in a PIL was notable. Benefit information has the potential to be upsetting and provoke anxiety, anger and fear. If it is to be included in a PIL, this needs to be framed in a way which minimises any negative emotional impact and reduces potential decisional conflict.

Finally, despite the significant barriers and concerns regarding the inclusion of benefit information and the unwillingness of groups of patients to engage with it, it is important to note that the inclusion of benefit information fulfils a duty to inform patients about both the potential benefits of their treatments and the potential limitations. Without this

information a patient cannot make an informed decision about whether to take a treatment. The inclusion of benefit information also has the potential to facilitate a relationship with the providers of medicines information that is based on respect:

> *"I think that seems like a good reason to come clean. To put it in the patient information leaflet, because you know, that's what it is: An information leaflet, it is not advertising. I think that the patient deserves to be treated with enough respect to have this information, and to be able to understand this information. I didn't know either how few people would benefit from this medicine." (M, 60, FG4, JANA)*

The patient information leaflet is a regulated document; it is made available with most, if not all medicines. Despite concerns that the leaflet is not the right place, nor provided at the right time, as some patients prefer verbal information and/ or might not read the leaflet, it is a place where a standardised format can be provided.

The provision of benefit information in a patient information leaflet has the potential to support patients to understand more about the benefits and the limitations of their medicines.

References

AJZEN, I. 1991. The theory of planned behavior. *Organizational behavior and human decision processes,* 50**,** 179-211.
AKL, E., OXMAN, A., HERRIN, J., VIST, G., TERRENATO, I., SPERATI, F., COSTINIUK, C., BLANK, D. & SCHÜNEMANN, H. 2011a. Using alternative statistical formats for presenting risks and risk reductions. *Cochrane Database Syst Rev.,* Mar 16.
AKL, E. A., OXMAN, A. D., HERRIN, J., VIST, G. E., TERRENATO, I., SPERATI, F., COSTINIUK, C., BLANK, D. & SCHUNEMANN, H. 2011b. Framing of health information messages. *Cochrane Database Syst Rev,* 7.
ALMASHAT, S., AYOTTE, B., EDELSTEIN, B., MARGRETT, J., ALMASHAT, S., AYOTTE, B., EDELSTEIN, B. & MARGRETT, J. 2008. Framing effect debiasing in medical decision making. *Patient Education & Counseling,* 71**,** 102-7.
ALTMAN, D. & BLAND, J. 1995. Abscence of evidence is not evidence of abscence. *BMJ***,** 311:485.
AMERY, W. K. 1999. Coming full circle in pharmacovigilance: Communicating safety information to patients through patient package inserts. *Pharmacoepidemiology and Drug Safety,* 8**,** 121-129.
ANONYMOUS 2003. Dare you drink from a garden hose? *Consumer reports 68 (7)***,** 7.
ARKSEY, H. & O'MALLEY, L. 2005. Scoping studies: Towards a methodolgical framework. . *International Journal of Social Research Methodology,* 8**,** 19-32.
BARLOW, J. H. & WRIGHT, C. C. 1998. Knowledge in patients with rheumatoid arthritis: a longer term follow-up of a randomized controlled study of patient education leaflets. *Rheumatology,* 37**,** 373-376.
BEKKER, H., THORNTON, J. G., AIREY, C. M., CONNELLY, J. B., HEWISON, J., ROBINSON, M. B., LILLEYMAN, J., MACINTOSH, M., MAULE, A. J., MICHIE, S. & PEARMAN, A. D. 1999. *Informed decision making: an annotated bibliography and systematic review*, Health Technol Assess. 1999;3(1):1-156.
BELL, R., KRAVITZ, R. & WILKES, M. 1999. Direct-to-Consumer Prescription Drug Advertising and the Public. *Journal of General Internal Medicine,* 14**,** 651-657.
BERELSON, B. 1952. *Content Analysis in Communication Research.,* New York: , Free Press.
BERGUS, G. R., LEVIN, I. P. & ELSTEIN, A. S. 2002. Presenting risks and benefits to patients - The effect of information order on decision making. *Journal of General Internal Medicine,* 17**,** 612-617.
BERRY, D., HOLDEN, W. & BERSELLINI, E. 2004. Interpretation of recommended risk terms:differences between doctors and lay people. *International Journal of Pharmacy Practice,* 12**,** 117-124.
BERRY, D., RAYNOR, D. & KNAPP, P. 2003a. Communicating risk of medication side effects: an empirical evaluation of EU recommended terminology. *Psychology, Health & Medicine,* 8**,** 251-263.
BERRY, D. C. 2006. Informing people about the risks and benefits of medicines: implications for the safe and effective use of medicinal products. *Current Drug Safety,* 1**,** 121-6.
BERRY, D. C., RAYNOR, D. K., KNAPP, P., BERSELLINI, E., BERRY, D. C., KNAPP, P. & BERSELLINI, E. 2003b. Patients' understanding of risk associated with medication use: impact of European Commission guidelines and other risk scales. *Drug Safety,* 26**,** 1-11.
BERSELLINI, E. & BERRY, D. 2007a. The benefits of providing benefit information in a patient information leaflet. *International Journal of Pharmacy Practice,* 15**,** 193-199.
BERSELLINI, E. & BERRY, D. 2007b. The benefits of providing benefit information: Examining the effectiveness of provision of simple benefit statements on people's judgements about a medicine. *Psychology & Health,* 22**,** 61-82.

BESTEHORN, H.-P., RENSING, U., ROSKAMM, H., BETZ, P., BENESCH, L., SCHEMEITAT, K., BLÜMCHEN, G., CLAUS, J., MATHES, P. & KAPPENBERGER, L. 1997. The effect of simvastatin on progression of coronary artery disease The Multicenter Coronary Intervention Study (CIS). *European heart journal,* 18**,** 226-234.

BHANDARI, M. & TORNETTA, P. 2004. *Communicating the risks of surgery to patients*, European Journal of Trauma. 30 (3) (pp 177-181), 2004. Date of Publication: Jun 2004.

BIGMAN, C. A., CAPPELLA, J. N., HORNIK, R. C., BIGMAN, C. A., CAPPELLA, J. N. & HORNIK, R. C. 2010. Effective or ineffective: attribute framing and the human papillomavirus (HPV) vaccine. *Patient Education & Counseling,* 81 Suppl**,** S70-6.

BISHOP, P., KIRWAN, J AND WINDSOR, K. 1996. The ARC Patient Literature Evaluation project. Chesterfield: The Arthitis and Rheumatism Council.

BRADDOCK, I. C., EDWARDS, K. A., HASENBERG, N. M., LAIDLEY, T. L. & LEVINSON, W. 1999. Informed decision making in outpatient practice: Time to get back to basics. *JAMA,* 282**,** 2313-2320.

BRAINERD, C. & REYNA, V. 1990. Gist is the grist: Fuzzy-trace theory and the new intuitionism. *Developmental Review,* 10**,** 3-47.

BRITISH MEDICAL JOURNAL. 2013. *What conclusions has Clinical Evidence drawn about what works, what doesn't based on randomised controlled trial evidence?* [Online]. Clinical Evidence. Available: http://clinicalevidence.bmj.com/x/set/static/cms/efficacy-categorisations.html [Accessed 06.11.2013 2013].

BROOKE, R. E., ISHERWOOD, S., HERBERT, N. C., RAYNOR, D. K. & KNAPP, P. 2012. Hearing Aid Instruction Booklets: Employing Usability Testing to Determine Effectiveness. *Am J Audiol,* 21**,** 206-214.

BROWN, S. M., CULVER, J. O., OSANN, K. E., MACDONALD, D. J., SAND, S., THORNTON, A. A., GRANT, M., BOWEN, D. J., METCALFE, K. A., BURKE, H. B., ROBSON, M. E., FRIEDMAN, S. & WEITZEL, J. N. 2011. Health literacy, numeracy, and interpretation of graphical breast cancer risk estimates. *Patient Education and Counseling,* 83**,** 92-98.

BRUG, J., RUITER, R. A., VAN ASSEMA, P., BRUG, J., RUITER, R. A. C. & VAN ASSEMA, P. 2003. The (ir)relevance of framing nutrition education messages. *Nutrition & Health,* 17**,** 9-20.

BRYANT, J., SKOLARUS, L., SMITH, B., ADELMAN, E. & MEURER, W. 2013. The accuracy of surrogate decision makers: informed consent in hypothetical acute stroke scenarios. *BMC Emergency Medicine,* 13**,** 18.

BURKE JOHNSON, R., ONWUEGBUZIE, A. & TURNER, L. 2007. Toward a Definition of Mixed Methods Research *Journal of Mixed Methods Research,* 1**,** 112-113.

CAELLI, K., RAY, L. & MILL, J. 2003. 'Clear as mud': Toward greater clarity in generic qualitative research. *International Journal of Qualitative Methods,* 2.

CAMERON, L. & LEVENTHAL, H. 2003. *The self-regulation of health and illness behaviour,* London, Routledge.

CAMERON, L. D. & JAGO, L. 2008. Emotion regulation interventions: A common‐sense model approach. *British Journal of Health Psychology,* 13**,** 215-221.

CARLING, C., KRISTOFFERSEN, D. T., HERRIN, J., TREWEEK, S., OXMAN, A. D., SCHUNEMANN, H., AKL, E. A. & MONTORI, V. 2008. *How should the impact of different presentations of treatment effects on patient choice be evaluated? A pilot randomized trial*, PLoS ONE. 3 (11) , 2008. Article Number: e3693. Date of Publication: 24 Nov 2008.

CARLING, C. L., KRISTOFFERSEN, D. T., MONTORI, V. M., HERRIN, J., SCHUNEMANN, H. J., TREWEEK, S., AKL, E. A., OXMAN, A. D., CARLING,

C. L. L., KRISTOFFERSEN, D. T., MONTORI, V. M., HERRIN, J., SCHUNEMANN, H. J., TREWEEK, S., AKL, E. A. & OXMAN, A. D. 2009. The effect of alternative summary statistics for communicating risk reduction on decisions about taking statins: a randomized trial. *PLoS Medicine / Public Library of Science,* 6**,** e1000134.

CARLING, C. L., KRISTOFFERSEN, D. T., OXMAN, A. D., FLOTTORP, S., FRETHEIM, A., SCHUNEMANN, H. J., AKL, E. A., HERRIN, J., MACKENZIE, T. D., MONTORI, V. M., CARLING, C. L. L., KRISTOFFERSEN, D. T., OXMAN, A. D., FLOTTORP, S., FRETHEIM, A., SCHUNEMANN, H. J., AKL, E. A., HERRIN, J., MACKENZIE, T. D. & MONTORI, V. M. 2010. The effect of how outcomes are framed on decisions about whether to take antihypertensive medication: a randomized trial. *PLoS ONE [Electronic Resource],* 5**,** e9469.

CARRIGAN, N., RAYNOR, D. K., KNAPP, P., CARRIGAN, N. & KNAPP, P. 2008. Adequacy of patient information on adverse effects: an assessment of patient information leaflets in the UK. *Drug Safety,* 31**,** 305-12.

CENTRE FOR REVIEWS AND DISSEMINATION 2009. Systematic reviews: CRD's guidance for undertaking systematic reviews in healthcare. York: NHS centre for reviews and dissemination.

CHANDLER, P. & SWELLER, J. 1991. Cognitive load theory and the format of instruction. *Cognition and instruction,* 8**,** 293-332.

CHARLES, C., GAFNI, A. & WHELAN, T. 1997. Shared decision-making in the medical encounter: what does it mean?(or it takes at least two to tango). *Social Science & Medicine,* 44**,** 681-692.

CHEWNING, B., BYLUND, C. L., SHAH, B., ARORA, N. K., GUEGUEN, J. A. & MAKOUL, G. 2012. Patient preferences for shared decisions: a systematic review. *Patient Educ Couns,* 86**,** 9-18.

CHRISTENSEN, P. M. & KRISTIANSEN, I. S. 2006. Number‐Needed‐to‐Treat (NNT)‐Needs Treatment with Care. *Basic & clinical pharmacology & toxicology,* 99**,** 12-16.

CO-ORDINATION GROUP FOR MUTUAL RECOGNITION AND DECENTRALIZED PROCEDURES - HUMAN. 2011. CMDh annotated QRD template for MR/DC procedures (based on version 8 of the QRD template for CP). Available: http://www.hma.eu/uploads/media/QRD_annotated_template_CMDh.pdf [Accessed 04.03.2013].

COOPER, G. 1998. Research into cognitive load theory and instructional design at UNSW. *Retrieved August,* 8**,** 2003.

COUNCIL OF THE EUROPEAN COMMUNITIES 1992. Council Directive 92/27/EEC of 31 March 1992 on the labelling of medicinal products. *In:* COMMISSION, E. (ed.).

CRESWELL, J. 1994. *Reseach Design. Qualitative and Quantitative Approaches,* Thousand Oaks, California, SAGE publications.

CRESWELL, J. 2013. *Qualitative inquiry and research design,* Thousand Oaks, California.

CUITE, C. L., WEINSTEIN, N. D., EMMONS, K. & COLDITZ, G. 2008. A test of numeric formats for communicating risk probabilities. *Medical Decision Making,* 28**,** 377-384.

DAHL, R., GYRD-HANSEN, D., KRISTIANSEN, I. S., NEXOE, J. & NIELSEN, J. B. 2007. Can postponement of an adverse outcome be used to present risk reductions to a lay audience? A population survey. *Bmc Medical Informatics and Decision Making,* 7.

DAVIS, C. R., MCNAIR, A. G. K., BRIGIC, A., CLARKE, M. G., BROOKES, S. T., THOMAS, M. G. & BLAZEBY, J. M. 2010. Optimising methods for

communicating survival data to patients undergoing cancer surgery. *European Journal of Cancer,* 46**,** 3192-3199.
DAVIS, K., DREY, N. & GOULD, D. 2009. What are scoping studies? A review of the nursing literature. *International Journal of Nursing Studies,* 46**,** 1386-1400.
DAVIS, R. E., DOLAN, G., THOMAS, S., ATWELL, C., MEAD, D., NEHAMMER, S., MOSELEY, L., EDWARDS, A. & ELWYN, G. 2003. Exploring doctor and patient views about risk communication and shared decision-making in the consultation. *Health Expect,* 6**,** 198-207.
DEPARTMENT OF HEALTH 2010. Equity and excellence, liberating the NHS: White Paper. *In:* DEPARTMENT OF HEALTH (ed.). London, UK.
DEPARTMENT OF HEALTH 2013. Cardiovascular Disease Outcomes Strategy: Improving outcomes for people with or at risk of cardiovascular disease
DERRY, C., DERRY, S. & MOORE, R. 2012. Sumatriptan (oral route of administration) for acute migraine attacks in adults. *Cochrane Database of Systematic Reviews,* 2.
DICKINSON, D., GALLINA, S., NEWSOME-DAVIS, E. & TEATHER, J. 2010. Medicine package leaflets - does good design matter? *Information Design Journal***,** 18 (3) 225-240.
DICKINSON, D., RAYNOR, D. K. & DUMAN, M. 2001. Patient information leaflets for medicines: using consumer testing to determine the most effective design. *Patient Education & Counseling,* 43**,** 147-59.
DICKINSON, D. & RAYNOR, D. K. T. 2003. Ask the patients—they may want to know more than you think. *BMJ,* 327**,** 861.
DICKINSON, R., HAMROSI, K., KNAPP, P., ASLANI, P., SOWTER, J., KRASS, I. & RAYNOR, D. K. 2013. Suits you? A qualitative study exploring preferences regarding the tailoring of consumer medicines information. *International Journal of Pharmacy Practice,* 21**,** 207-215.
DIXON-WOODS, M. 2001. Writing wrongs? An analysis of published discourses about the use of patient information leaflets. *Social Science & Medicine,* 52**,** 1417-1432.
DOLK, S., LENTZ, L., KNAPP, P., MAAT, H. P. & RAYNOR, T. 2011. Headline section in patient information leaflets: Does it improve reading performance and perception? *Information Design Journal,* 19**,** 46-57.
DONOVAN, R. J. & JALLEH, G. 2000. Positive versus negative framing of a hypothetical infant immunization: the influence of involvement. *Health Education & Behavior,* 27**,** 82-95.
EDWARDS, A. & ELWYN, G. 1999. How should effectiveness of risk communication to aid patients' decisions be judged? A review of the literature. *Medical Decision Making,* 19**,** 428-434.
EDWARDS, A., ELWYN, G., COVEY, J., MATTHEWS, E. & PILL, R. 2001. Presenting risk information - A review of the effects of "framing" and other manipulations on patient outcomes. *Journal of Health Communication,* 6**,** 61-82.
EDWARDS, A., THOMAS, R., WILLIAMS, R., ELLNER, A. L., BROWN, P., ELWYN, G., EDWARDS, A., THOMAS, R., WILLIAMS, R., ELLNER, A. L., BROWN, P. & ELWYN, G. 2006. Presenting risk information to people with diabetes: evaluating effects and preferences for different formats by a web-based randomised controlled trial. *Patient Education & Counseling,* 63**,** 336-49.
EDWARDS, A., UNIGWE, S., ELWYN, G. & HOOD, K. 2003. Effects of communicating individual risks in screening programmes: Cochrane systematic review. *British Medical Journal,* 327**,** 703-707.
ELLIOT, A. J. & MAIER, M. A. 2014. Color psychology: effects of perceiving color on psychological functioning in humans. *Annu Rev Psychol,* 65**,** 95-120.

ELWYN, G., EDWARDS, A., HOOD, K., ROBLING, M., ATWELL, C., RUSSELL, I., WENSING, M., GROL, R. & STUDY STEERING, G. 2004. Achieving involvement: process outcomes from a cluster randomized trial of shared decision making skill development and use of risk communication aids in general practice. *Family Practice,* 21**,** 337-346.
ENGLAND, L. 2000. Chronic biscuit poisoning. *Journal of the Mississippi State Medical Association***,** 41(11):795.
EUROPEAN COMMISION 2009. Guideline on the readability of the labelling and package leaflet of medicinal products for human use. Brussels: European Commision.
EUROPEAN COMMISSION 1998. A guideline on the readability of the label and package leaflet of medicinal products for human use. *EC Pharmaceutical Committee*
EUROPEAN COMMISSION 2004. Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use (Text with EEA relevance) Official Journal L 136 , 30/04/2004 P. 0034 - 0057.
EUROPEAN COMMISSION 2009. Guideline on the readability of the labelling and package leaflet of medicinal products for human use. Brussels: 2009.
EUROPEAN MEDICINES AGENCY 2009. Information on benefit-risk of medicines: patients', consumers' and healthcare professionals' expectations. *In:* EUROPEAN MEDICINES AGENCY (ed.). London.
EUROPEAN MEDICINES AGENCY 2012. Quality Review of Documents (QRD) human product information annotated template: revision of the product information. London.
EUROPEAN MEDICINES AGENCY. 2014. *European public assessment reports: background and context* [Online]. Available: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/general/general_content_000433.jsp [Accessed 07/0502014 2014].
FAGERLIN, A., ZIKMUND-FISHER, B. J. & UBEL, P. A. 2007. "If I'm better than average, then I'm ok?": Comparative information influences beliefs about risk and benefits. *Patient Education and Counseling,* 69**,** 140-144.
FERGUSON, E. & GALLAGHER, L. 2007. *Message framing with respect to decisions about vaccination: The roles of frame valence, frame method and perceived risk*, British Journal of Psychology. 98 (4) (pp 667-680), 2007. Date of Publication: November 2007.
FINEGOLD, J. A., MANISTY, C. H., GOLDACRE, B., BARRON, A. J. & FRANCIS, D. P. 2014. What proportion of symptomatic side effects in patients taking statins are genuinely caused by the drug? Systematic review of randomized placebo-controlled trials to aid individual patient choice. *European Journal of Preventive Cardiology,* 21**,** 464-474.
FINUCANE, M., ALHAKAMI, A., SLOVIC, P. & JOHNSON, S. 2000. The affect heuristic in judgements of risks and benefits *Journal of Behavioral Decision Making,* 13**,** 1-17.
FISCHER, P., JONAS, E., FREY, D. & KASTENMULLER, A. 2008. Selective exposure and decision framing: The impact of gain and loss framing on confirmatory information search after decisions. *Journal of Experimental Social Psychology,* 44**,** 312-320.
FISCHHOFF, B. 2012. Communicating uncertainty: Fulfilling the duty to inform. *Issues in Science and Technology,* 28.
FISCHHOFF, B., BREWER, N. & DOWNS J (EDS) 2011. Communicating Risks and Benefits: An Evidence-Based User's Guide. *In:* FOOD AND DRUG

ADMINISTRATION (FDA) & DEPARTMENT OF HEALTH AND HUMAN SERVICES (ed.). Silver Spring, Maryland.
FLYNN, K. E., SMITH, M. A. & VANNESS, D. 2006. A typology of preferences for participation in healthcare decision making. *Social Science & Medicine,* 63**,** 1158-1169.
FOOD AND DRUG ADMINISTRATION 2009. Providing effective information to consumers about prescription drug risks and benefits: the issues paper. Silver Spring, Maryland: US Department of Health and Human Sciences.
FRANCE, J., KEEN, C. & BOWYER, S. 2008. Communicating risk to emergency department patients with chest pain. *Emergency Medicine Journal,* 25**,** 276-8.
FRICK, M. H., ELO, O., HAAPA, K., HEINONEN, O. P., HEINSALMI, P., HELO, P., HUTTUNEN, J. K., KAITANIEMI, P., KOSKINEN, P., MANNINEN, V. & ET AL. 1987. Helsinki Heart Study: primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia. Safety of treatment, changes in risk factors, and incidence of coronary heart disease. *N Engl J Med,* 317**,** 1237-45.
FRIED, T. R., TINETTI, M. E., TOWLE, V., O'LEARY, J. R. & IANNONE, L. 2011. Effects of benefits and harms on older persons willingness to take medication for primary cardiovascular prevention. *Archives of Internal Medicine,* 171**,** 923-928.
FULLER, R., DUDLEY, N. & BLACKTOP, J. 2001. Risk communication and older people - Understanding of probability and risk information by medical inpatients aged 75 years and older.
GALESIC, M., GARCIA-RETAMERO, R., GIGERENZER, G., GALESIC, M., GARCIA-RETAMERO, R. & GIGERENZER, G. 2009a. Using icon arrays to communicate medical risks: overcoming low numeracy. *Health Psychology,* 28**,** 210-6.
GALESIC, M., GIGERENZER, G. & STRAUBINGER, N. 2009b. *Natural frequencies help older adults and people with low numeracy to evaluate medical screening tests*, Medical Decision Making. 29 (3) (pp 368-371), 2009. Date of Publication: May-June 2009.
GARCIA-RETAMERO, R. & GALESIC, M. 2010. How to reduce the effect of framing on messages about health. *Journal of General Internal Medicine,* 25**,** 1323-1329.
GARCIA-RETAMERO, R., GALESIC, M. & DHAMI, M. 2013. Reducing Denominator Neglect. *In:* GARCIA-RETAMERO, R. & GALESIC, M. (eds.) *Transparent Communication of Health Risks.* Springer New York.
GARCIA-RETAMERO, R., GALESIC, M., GARCIA-RETAMERO, R. & GALESIC, M. 2009. Communicating treatment risk reduction to people with low numeracy skills: a cross-cultural comparison. *American Journal of Public Health,* 99**,** 2196-202.
GARCIA-RETAMERO, R., GALESIC, M., GARCIA-RETAMERO, R. & GALESIC, M. 2010. Who profits from visual aids: overcoming challenges in people's understanding of risks [corrected].[Erratum appears in Soc Sci Med. 2010 Jun;70(12):2097]. *Social Science & Medicine,* 70**,** 1019-25.
GEIS, S. B., FULLER, R. L. & RUSH, J. 1986. Lovers of AIDS victims: Psychosocial stresses and counseling needs. *Death Studies,* 10**,** 43-53.
GEORGE, W., NICHOLAS 1983. Prescription infomration leaflets: a pilot study in general practice. *British Medical Journal 287***,** 1193-1196.
GIGERENZER, G. 2002. *Reckoning with risk: Learning to live with uncertainty,* London, Penguin Books.
GIGERENZER, G. & EDWARDS, A. 2003. Simple tools for understanding risks: from innumeracy to insight. *British Medical Journal,* 327**,** 741-744.
GIGERENZER, G., GAISSMAIER, W., KURZ-MILCKE, E., SCHWARTZ, L. M. & WOLOSHIN, S. 2007. Helping Doctors and Patients Make Sense of Health Statistics. *Psychological Science in the Public Interest,* 8**,** 53-96.

GIROTTO, V. & GONZALEZ, M. 2002. Chances and frequencies in probabilistic reasoning: rejoinder to Hoffrage, Gigerenzer, Krauss, and Martignon. *Cognition,* 84**,** 353-359.
GLASER, B. & STRAUSS, A. 1967. *The Discovery of Grounded Theory,* Chicago, Thousand Oaks.
GODLEE, F. 2014. Adverse effects of statins. *British Medical Journal,* 348.
GODOLPHIN, W. 2009. Shared decision-making. *Healthc Q,* 12**,** e186-e190.
GOLDACRE, B. 2012. Bad Pharma: How drug companies mislead doctors and harm patients. London: Fourth Estate.
GOODYEAR-SMITH, F., ARROLL, B., CHAN, L., JACKSON, R., WELLS, S., KENEALY, T., GOODYEAR-SMITH, F., ARROLL, B., CHAN, L., JACKSON, R., WELLS, S. & KENEALY, T. 2008. Patients prefer pictures to numbers to express cardiovascular benefit from treatment. *Annals of Family Medicine,* 6**,** 213-7.
GOODYEAR-SMITH, F., KENEALY, T., WELLS, S., ARROLL, B. & HORSBURGH, M. 2011. Patients' Preferences for Ways to Communicate Benefits of Cardiovascular Medication. *Annals of Family Medicine,* 9**,** 121-127.
GREENHALGH, T. 1997. How to read a paper : getting your bearings (deciding what the paper is about). *BMJ,* 315**,** 243-246.
GRIME, J., BLENKINSOPP, A., RAYNOR, D. K., POLLOCK, K. & KNAPP, P. 2007. The role and value of written information for patients about individual medicines: a systematic review. *Health Expectations,* 10**,** 286-298.
GYRD-HANSEN, D., KRISTIANSEN, I. S., NEXOE, J. & NIELSEN, J. B. 2003. How Do Individuals Apply Risk Information When Choosing Among Health Care Interventions? *Risk Analysis,* 23**,** 697-704.
HALVORSEN, P. A., SELMER, R. & KRISTIANSEN, I. S. 2007. Different Ways to Describe the Benefits of Risk-Reducing TreatmentsA Randomized Trial. *Annals of Internal Medicine,* 146**,** 848-856.
HAMROSI, K., DICKINSON, R., KNAPP, P., RAYNOR, D., KRASS, I., SOWTER, J. & ASLANI, P. 2012. It's for your benefit: exploring patients' opinions about the inclusion of textual and numerical benefit information in medicine leaflets. *International Journal of Pharmacy Practice*.
HARTLEY, J. 2004. Designing Instructional and Informational Text. *In:* JONASSEN D (ed.) *In Handbook of Research on Educational Communications and Technology: A Project of the Association for Educational Communications and Technology* New York: Taylor & Francis Group.
HARTLEY, J. & TRUMAN, M. 1982. The effects of summaries on the recall of information from prose text. *Human Learning,* 1**,** 63-82.
HAWLEY, S. T., ZIKMUND-FISHER, B., UBEL, P., JANCOVIC, A., LUCAS, T., FAGERLIN, A., HAWLEY, S. T., ZIKMUND-FISHER, B., UBEL, P., JANCOVIC, A., LUCAS, T. & FAGERLIN, A. 2008. The impact of the format of graphical presentation on health-related knowledge and treatment choices. *Patient Education & Counseling,* 73**,** 448-55.
HEART PROTECTION STUDY COLLABORATIVE GROUP 2002. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebocontrolled trial. *The Lancet,* 360**,** 7-22.
HESS, R., VISSCHERS, V. H., SIEGRIST, M. & KELLER, C. 2011. How do people perceive graphical risk communication? The role of subjective numeracy. *Journal of Risk Research,* 14**,** 47-61.
HEVEY, D., PERTL, M., THOMAS, K., MAHER, L., CRAIG, A., CHUINNEAGAIN, S. N. & CHUINNEAGAIN, S. N. 2010. Body consciousness moderates the effect of message framing on intentions to use sunscreen. *Journal of Health Psychology,* 15**,** 553-9.

HIGGINS, J. & GREEN, S. 2001. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. . *The Cochrane Collaboration*.
HOFFNER, C., YE, J., HOFFNER, C. & YE, J. 2009. Young adults' responses to news about sunscreen and skin cancer: the role of framing and social comparison. *Health Communication,* 24**,** 189-98.
HOLSTEIN, J. A. & GUBRIUM, J. F. 1995. *The active interview*, Sage Publications, Inc.
HORNE, R., WEINMAN, J. & HANKINS, M. 1999. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and health,* 14**,** 1-24.
HUX, J. E. & NAYLOR, C. D. 1995. Communicating the benefits of chronic preventive therapy: does the format of efficacy data determine patients' acceptance of treatment? *Medical Decision Making,* 15**,** 152-7.
IBM CORP Released 2010. IBM SPSS Statistics for Windows. Version 19.0 ed. Armonk, MY: IBM Corp.
INFORMATION CENTRE FOR HEALTH AND SOCIAL CARE. 2011. *Prescription Cost Analysis: England 2011 - Totals by chemical entities; BNF Chapters 1 to 19* [Online]. Prescribing and Primary Care Services. Available: https://catalogue.ic.nhs.uk/publications/prescribing/primary/pres-cost-anal-eng-2011/pres-cost-anal-eng-2011-rep.pdf.
JOINT FORMULARY COMMITTEE 2012. British National Formulary. London: BMJ Group and Pharmaceutical Press.
KITZINGER, J. 1995. Qualitative Research: Introducing focus groups. *BMJ,* 311**,** 299-302.
KNAPP, P., BERRY, D. C. & RAYNOR, D. K. 2001. Testing two methods of presenting side effect risk information about common medicines. *International Journal of Pharmacy Practice,* 9**,** 6-6.
KNAPP, P., GARDNER, P., CARRIGAN, N., RAYNOR, D. & WOOLF, E. 2009a. Perceived risk of medicine side effects in users of a patient information website: A study of the use of verbal descriptors, percentages and natural frequencies. *British Journal of Health Psychology,* 14**,** 579-594.
KNAPP, P., GARDNER, P., MCMILLAN, B., RAYNOR, D. K. & WOOLF, E. 2013. Evaluating a combined (frequency and percentage) risk expression to communicate information on medicine side effects to patients. *International Journal of Pharmacy Practice,* 21**,** 226-232.
KNAPP, P., RAYNOR, D. K., SILCOCK, J. & PARKINSON, B. 2009b. Performance-based readability testing of participant information for a Phase 3 IVF trial. *Trials,* 10**,** 1-15.
KNAPP, P., RAYNOR, D. K., WOOLF, E., GARDNER, P. H., CARRIGAN, N. & MCMILLAN, B. 2009c. Communicating the Risk of Side Effects to Patients An Evaluation of UK Regulatory Recommendations. *Drug Safety,* 32**,** 837-849.
KNAPP, P., WANKLYN, P., RAYNOR, D. K., WAXMAN, R., KNAPP, P., WANKLYN, P. & WAXMAN, R. 2010. Developing and testing a patient information booklet for thrombolysis used in acute stroke. *International Journal of Pharmacy Practice,* 18**,** 362-9.
KRISTIANSEN, I. S., GYRD-HANSEN, D., NEXOE, J. & NIELSEN, J. B. 2002. Number needed to treat: easily understood and intuitively meaningful? Theoretical considerations and a randomized trial. *Journal of Clinical Epidemiology,* 55**,** 888-892.
KRSKA, J. & MORECROFT, C. 2013. Patients' Use of Information about Medicine Side Effects in Relation to Experiences of Suspected Adverse Drug Reactions: A Cross-Sectional Survey in Medical In-Patients. *Drug Safety,* 36**,** 673-680.

KÜHBERGER, A., SCHULTE-MECKLENBECK, M. & PERNER, J. 2002. Framing decisions: Hypothetical and real. *Organizational Behavior and Human Decision Processes,* 89**,** 1162-1175.
KUHN, K. M. 1997. Communicating uncertainty: Framing effects on responses to vague probabilities. *Organizational Behavior and Human Decision Processes,* 71**,** 55-83.
LACEY, A. & LUFF, D. 2007. Qualitative Data Analysis. Yorkshire & the Humber: The NIHR RDS for the East Midlands.
LALOR, K. M. & HAILEY, B. 1989. The effects of message framing and feelings of susceptibility to breast cancer on reported frequency of breast self-examination. *International Quarterly of Community Health Education,* 10**,** 183-192.
LASSER, K. E., SEGER, D. L., YU, D. T., KARSON, A. S., FISKIO, J. M., SEGER, A. C., SHAH, N. R., GANDHI, T. K., ROTHSCHILD, J. M. & BATES, D. W. 2006. Adherence to Black Box Warnings for Prescription Medications in Outpatients. *Arch Intern Med,* 166**,** 338-344.
LEADER, A. E., WEINER, J. L., KELLY, B. J., HORNIK, R. C., CAPPELLA, J. N., LEADER, A. E., WEINER, J. L., KELLY, B. J., HORNIK, R. C. & CAPPELLA, J. N. 2009. Effects of information framing on human papillomavirus vaccination. *Journal of Women's Health,* 18**,** 225-33.
LEVAC, D., COLQUHOUN, H. & O'BRIEN, K. K. 2010. Scoping studies: advancing the methodology. *Implementation Science : IS,* 5**,** 69-69.
LEVENTHAL, H., LEVENTHAL, E. A. & CONTRADA, R. J. 1998. Self-regulation, health, and behavior: A perceptual-cognitive approach. *Psychology & Health,* 13**,** 717-733.
LEY, P. 1988. *Communicating with patients. Improving communication, satisfaction and compliance.,* London, Chapman and Hall.
LINGARD, L., ALBERT, M. & LEVINSON, W. 2008. Grounded theory, mixed methods, and action research *BMJ,* 337**,** 459-461.
LOEWENSTEIN, G. & LERNER, J. S. 2003. The role of affect in decision making. *Handbook of affective science,* 619**,** 3.
LONG, A., GODFREY, M., RANDALL, T., BRETTLE & MJ, G. 2002. Developing evidence based social care policy and practice. Part 3: feasibility of undertaking systematic reviews in social care. Leeds: Nuffield Institute for Health.
MAAS INVESTIGATORS 1994. Effect of simvastatin on coronary atheroma: the Multicentre Anti-Atheroma Study (MAAS). *The Lancet,* 344**,** 633-638.
MACFARLANE, J. T., HOLMES, W. F. & MACFARLANE, R. M. 1997. Reducing reconsultations for acute lower respiratory tract illness with an information leaflet: a randomized controlled study of patients in primary care. *Br J Gen Pract,* 47**,** 719-22.
MALENKA, D. J., BARON, J. A., JOHANSEN, S., WAHRENBERGER, J. W. & ROSS, J. M. 1993. The framing effect of relative and absolute risk. *Journal of General Internal Medicine,* 8**,** 543-548.
MATSUYAMA, R., REDDY, S. & SMITH, T. J. 2006. Why do patients choose chemotherapy near the end of life? A review of the perspective of those facing death from cancer. *J Clin Oncol,* 24**,** 3490-6.
MCCARTNEY, M. 2012a. *The Patient Paradox,* Great Britain, Pinter and Martin.
MCCARTNEY, M. 2012b. Statins for all? *BMJ,* 345.
MEADE, C. D. & SMITH, C. F. 1991. Readability formulas: Cautions and criteria. *Patient Education and Counseling,* 17**,** 153-158.
MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY 2005a. Always Read the Leaflet: Getting the best information with every medicine. The Stationary Office.

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY 2005b. Guideline on Communication of Risks and Benefits in Patient Information Leaflets.
MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY 2012a. Best Practice Guidance on Patient Information Leaflets. *In:* MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY (ed.). London.
MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY. 2012b. *The Black Triangle List December 2012 - UK marketed drugs under intensive surveillance* [Online]. Available: http://www.mhra.gov.uk/home/groups/pl-p/documents/websiteresources/con216899.pdf [Accessed December 2012.
MINDER, C., BLAHA, M. J., TAM, L. M. & ET AL. 2011. MAking the case for selective use of statins in the primary prevention setting. *Archives of Internal Medicine,* 171**,** 1593-1594.
MISSELBROOK, D. & ARMSTRONG, D. 2001. Patients' responses to risk information about the benefits of treating hypertension. *British Journal of General Practice,* 51**,** 276-9.
MOHER, D., LIBERATI, A., TETZLAFF, J. & ALTMAN, D. G. 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ,* 339.
MONTGOMERY, A. A., FAHEY, T. & PETERS, T. J. 2003. A factorial randomised controlled trial of decision analysis and an information video plus leaflet for newly diagnosed hypertensive patients. *The British Journal of General Practitioners,* 53**,** 446-453.
NACI, H., BRUGTS, J. J., FLEURENCE, R., TSOI, B., TOOR, H. & ADES, A. 2013. Comparative benefits of statins in the primary and secondary prevention of major coronary events and all-cause mortality: a network meta-analysis of placebo-controlled and active-comparator trials. *European Journal of Preventive Cardiology,* 20**,** 641-657.
NATIONAL CLINICAL GUIDELINE CENTRE 2014. Lipid modification: Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease - Clinical guideline Methods, evidence and recommendations. London: National Institute for Health and Care Excellence.
NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE 2009. Medicines Adherence: Involving patients in decisions about prescribed medicines and supporting adherence. London.
NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE 2006. Statins for the prevention of cardiovascular events. *In:* NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE (ed.). London.
NATTER, H. M. & BERRY, D. C. 2005. Effects of presenting the baseline risk when communicating absolute and relative risk reductions. *Psychology, Health & Medicine,* 10**,** 326-334.
NEERGAARD, M., OLESEN, F., ANDERSEN, R. & SONDERGAARD, J. 2009. Qualitative description - the poor cousin of health research? *BMC Medical Research Methodology,* 9.
NEUENDORF, K. 2002. *The Content Analysis Guidebook,* Thousand Oaks, California, Sage Publications.
NICOLSON, D., KNAPP, P., RAYNOR, D. K., SPOOR, P., NICOLSON, D., KNAPP, P., RAYNOR, D. K. T. & SPOOR, P. 2009. Written information about individual medicines for consumers. *Cochrane Database of Systematic Reviews***,** CD002104.
NIRAULA, S., AMIR, E., VERA-BADILLO, F., SERUGA, B., OCANA, A. & TANNOCK, I. F. 2014. Risk of Incremental Toxicities and Associated Costs of New

Anticancer Drugs: A Meta-Analysis. *Journal of Clinical Oncology,* 32**,** 3634-3642.
NIRAULA, S., SERUGA, B., OCANA, A., SHAO, T., GOLDSTEIN, R., TANNOCK, I. F. & AMIR, E. 2012. The Price We Pay for Progress: A Meta-Analysis of Harms of Newly Approved Anticancer Drugs. *Journal of Clinical Oncology*.
NISBETH JENSEN, M. & ZETHSEN, K. 2012. Translation of patient information leaflets : trained translators and pharmacists-cum-translators – a comparison. *Linguistica antverpiensia : new series - themes in translation studies* No. 11**,** p.31-49.
O'CONNOR, A. M. 1989. *Effects of framing and level of probability on patients' preferences for cancer chemotherapy*, Journal of Clinical Epidemiology. 42 (2) (pp 119-126), 1989. Date of Publication: 1989.
ONWUEGBUZIE, A. J. & LEECH, N. L. 2005. On Becoming a Pragmatic Researcher: The Importance of Combining Quantitative and Qualitative Research Methodologies. *International Journal of Social Research Methodology,* 8**,** 375-387.
PAAS, F., RENKL, A. & SWELLER, J. 2003. Cognitive load theory and instructional design: Recent developments. *Educational psychologist,* 38**,** 1-4.
PALMER, F. R. 1986. *Mood and Modality,* Cambridge, England, Cambridge University.
PARROTT, R., SILK, K., DORGAN, K., CONDIT, C. & HARRIS, T. 2005. Risk Comprehension and Judgments of Statistical Evidentiary Appeals: When a Picture is Not Worth a Thousand Words. *Human Communication Research,* 31**,** 423-452.
PEDERSEN, T. 2004. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Atherosclerosis Supplements,* 5**,** 81-87.
PETERS, E., HART, P. S., TUSLER, M. & FRAENKEL, L. 2014. Numbers matter to informed patient choices: a randomized design across age and numeracy levels. *Med Decis Making,* 34**,** 430-42.
PETERS, E. & LEVIN, I. P. 2008. Dissecting the risky-choice framing effect: Numeracy as an individual-difference factor in weighting risky and riskless options. *Judgment and Decision Making,* 3**,** 435-448.
PICTON, C. & WRIGHT, H. 2013. Medicines Optimisation: Helping patients make the most of medicines. Good practice guidance for healthcare professionals in England. *In:* ROYAL PHARMACEUTICAL SOCIETY (ed.). London.
POLITI, M. C., HAN, P. K. J. & COL, N. F. 2007. Communicating the uncertainty of harms and benefits of medical interventions. *Medical Decision Making,* 27**,** 681-695.
POPAY, J., ROBERTS, H., SOWDEN, A., PETTICREW, M., ARAI, L., RODGERS, M., BRITTEN, N., ROEN, K. & DUFFY, S. 2006. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC Methods Programme.
POUND, P., BRITTEN, N., MORGAN, M., YARDLEY, L., POPE, C., DAKER-WHITE, G. & CAMPBELL, R. 2005. Resisting medicines: a synthesis of qualitative studies of medicine taking. *Social Science & Medicine,* 61**,** 133-155.
PRATCHETT, T. 1987. *Mort,* Great Britain, Corgi Books.
PRICE, H. C., DUDLEY, C., BARROW, B., KENNEDY, I., GRIFFIN, S. J., HOLMAN, R. R., PRICE, H. C., DUDLEY, C., BARROW, B., KENNEDY, I., GRIFFIN, S. J. & HOLMAN, R. R. 2009. Use of focus groups to develop methods to communicate cardiovascular disease risk and potential for risk reduction to people with type 2 diabetes. *Family Practice,* 26**,** 351-8.
PRICE, M., CAMERON, R., BUTOW, P., PRICE, M., CAMERON, R. & BUTOW, P. 2007. Communicating risk information: the influence of graphical display format

on quantitative information perception-Accuracy, comprehension and preferences. *Patient Education & Counseling,* 69**,** 121-8.
RAJKUMAR, S. V., SAMPATHKUMAR, P. & GUSTAFSON, A. B. 1996. Number needed to treat is a simple measure of treatment efficacy for clinicians. *J Gen Intern Med,* 11**,** 357-9.
RAYNOR, D. K. 2008. Testing, Testing: The benefits of user-testing package leaflets. *PIPA newsletter,* 86**,** 4-5.
RAYNOR, D. K. 2013. User testing in developing patient medication information in Europe. *Research in Social and Administrative Pharmacy,* 2013**,** 1-6.
RAYNOR, D. K., BLENKINSOPP, A., KNAPP, P., GRIME, J., NICOLSON, D. J., POLLOCK, K., DORER, G., GILBODY, S., DICKINSON, D., MAULE, A. J. & SPOOR, P. 2007. A systematic review of quantitative and qualitative research on the role and effectiveness of written information available to patients about individual medicines. *Health Technology Assessment (Winchester, England),* 11**,** iii.
RAYNOR, D. K., KNAPP, P., SILCOCK, J., PARKINSON, B. & FEENEY, K. 2011. "User-testing" as a method for testing the fitness-for-purpose of written medicine information. *Patient Education and Counseling,* 83**,** 404-410.
RIEGELMAN, R. & SCHROTH, W. S. 1993. Adjusting the number needed to treat: incorporating adjustments for the utility and timing of benefits and harms. *Med Decis Making,* 13**,** 247-52.
ROTHMAN, A. J., SALOVEY, P., ANTONE, C., KEOUGH, K. & MARTIN, C. D. 1993. The Influence of Message Framing on Intentions to Perform Health Behaviors. *Journal of Experimental Social Psychology,* 29**,** 408-433.
SAMUELSON, W. & ZECKHAUSER, R. 1988. Status quo bias in decision making. *Journal of Risk and Uncertainty,* 1**,** 7-59.
SANDELOWSKI, M. 2000. Whatever happened to qualitative description? *Research in Nursing and Health,* 23**,** 334-340.
SANDELOWSKI, M. 2010. What's in a name? Qualitative description revisited. *Research in Nursing and Health,* 33**,** 77-84.
SARFATI, D., HOWDEN-CHAPMAN, P., WOODWARD, A. & SALMOND, C. 1998. *Does the frame affect the picture? A study into how attitudes to screening for cancer care are affected by the way benefits are expressed*, Journal of Medical Screening. 5 (3) (pp 137-140), 1998. Date of Publication: 1998.
SCHWARTZ, L. M., WOLOSHIN, S. & WELCH, H. G. 2009. Using a drug facts box to communicate drug benefits and harms: two randomized trials. *Annals of Internal Medicine,* 150**,** 516-27.
SCHWARTZ, L. M., WOLOSHIN, S., WELCH, H. G., SCHWARTZ, L. M., WOLOSHIN, S. & WELCH, H. G. 2007. The drug facts box: providing consumers with simple tabular data on drug benefit and harm. *Medical Decision Making,* 27**,** 655-62.
SHAMASKIN, A. M., MIKELS, J. A. & REED, A. E. 2010. Getting the message across: Age differences in the positive and negative framing of health care messages. *Psychology and Aging,* 25**,** 746-751.
SHERIDAN, S. L., PIGNONE, M. P. & LEWIS, C. L. 2003. A randomized comparison of patients' understanding of number needed to treat and other common risk reduction formats. *Journal of General Internal Medicine,* 18**,** 884-892.
SIMES, R. J. & COATES, A. S. 2001. Patient Preferences for Adjuvant Chemotherapy of Early Breast Cancer: How Much Benefit Is Needed? *JNCI Monographs,* 2001**,** 146-152.
SLESS, D. & SHRENSKY, R. 2007. *Writing about medicines for people,* Sydney, Australian Self Medication Industry.
SLESS. D 2004. Designing Public Documents. *Information Design Journal* 12**,** 24-35.

SLOVIC, P., FINUCANE, M. L., PETERS, E. & MACGREGOR, D. G. 2004. Risk as analysis and risk as feelings: Some thoughts about affect, reason, risk, and rationality. *Risk Analysis,* 24**,** 311-322.
SMITH, J. & FIRTH, J. 2011. Qualitative data analysis: the framework approach. *Nurse Res,* 18**,** 52-62.
SORENSON, C., NACI, H., CYLUS, J. & MOSSIALOS, E. 2011. Evidence of comparative efficacy should have a formal role in European drug approvals. *BMJ,* 343.
SPENCER, L., RITCHIE, J. & O'CONNOR, W. 2003. *Qualitative Research Practice: A guide for social science students and researchers. ,* London, Sage Publications.
SPIEGELHALTER, D. 2012. *Understanding Uncertainty: Spinning the risk.* [Online]. Available: http://understandinguncertainty.org/files/animations/RiskDisplay1/RiskDisplay.html [Accessed 20.03.2012.
SPRAGUE, D., LAVALLIE, D. L., WOLF, F. M., JACOBSEN, C., SAYSON, K. & BUCHWALD, D. 2011. Influence of Graphic Format on Comprehension of Risk Information among American Indians. *Medical Decision Making,* 31**,** 437-443.
STUDTS, J. L., ABELL, T. D., ROETZER, L. M., ALBERS, A. N., MCMASTERS, K. M. & CHAO, C. 2005. Preferences for Different Methods of Communicating Information Regarding Adjuvant Chemotherapy for Breast Cancer. *Psycho-Oncology,* 14**,** 647-660.
SURI, G., SHEPPES, G., SCHWARTZ, C. & GROSS, J. J. 2013. Patient Inertia and the Status Quo Bias: When an Inferior Option Is Preferred. *Psychological Science,* 24**,** 1763-1769.
SWELLER, J. & CHANDLER, P. 1991. Evidence for cognitive load theory. *Cognition and instruction,* 8**,** 351-362.
TAIT, A. R., VOEPEL-LEWIS, T., ZIKMUND-FISHER, B. J. & FAGERLIN, A. 2010a. The effect of format on parents' understanding of the risks and benefits of clinical research: A comparison between text, tables, and graphics. *Journal of Health Communication,* 15**,** 487-501.
TAIT, A. R., VOEPEL-LEWIS, T., ZIKMUND-FISHER, B. J. & FAGERLIN, A. 2010b. Presenting Research Risks and Benefits to Parents: Does Format Matter? *Anesthesia and Analgesia,* 111**,** 718-723.
TAIT, A. R., ZIKMUND-FISHER, B. J., FAGERLIN, A. & VOEPEL-LEWIS, T. 2010c. *Effect of various risk/benefit trade-offs on parents' understanding of a pediatric research study*, Pediatrics. 125 (6) (pp e1475-e1482), 2010. Date of Publication: June 2010.
TAYLOR, F., WARD, K., MOORE, T., BURKE, M. & DAVEY, S. 2013. Statins for the primary prevention of cardiovascular disease. *Cochrane Database of Systematic Reviews,* 1.
TEO, K. K., BURTON, J. R., BULLER, C. E., PLANTE, S., CATELLIER, D., TYMCHAK, W., DZAVIK, V., TAYLOR, D., YOKOYAMA, S. & MONTAGUE, T. J. 2000. Long-term effects of cholesterol lowering and angiotensin-converting enzyme inhibition on coronary atherosclerosis: The Simvastatin/Enalapril Coronary Atherosclerosis Trial (SCAT). *Circulation,* 102**,** 1748-54.
THE DEPARTMENT FOR EDUCATION AND SKILLS 2003. The Skills for Life survey: A national needs and impact survey of literacy, numeracy and ICT skills. *In:* THE DEPARTMENT FOR EDUCATION AND SKILLS (ed.). Norwich: Her Majesty's Stationery Office,.
THE LANCET 2012. Patient empowerment?who empowers whom? *The Lancet,* 379**,** 1677.
THOMSON, R., EDWARDS, A. & GREY, J. 2005. Risk communication in the clinical consultation. *Clin Med,* 5**,** 465-9.

THORNE, S. 2008. *Interpretive Description,* Walnut Creek, CA, Left Coast Press.
THORNE, S., HISLOP, T. G., KUO, M. & ARMSTRONG, E. A. 2006. Hope and probability: Patient perspectives of the meaning of numerical information in cancer communication. *Qualitative Health Research,* 16**,** 318-336.
TIMMERMANS, D. R. M., OCKHUYSEN-VERMEY, C. F. & HENNEMAN, L. 2008. Presenting health risk information in different formats: The effect on participants' cognitive and emotional evaluation and decisions. *Patient Education and Counseling,* 73**,** 443-447.
TOWLE, A., GODOLPHIN, W., GRAMS, G. & LAMARRE, A. 2006. Putting informed and shared decision making into practice. *Health Expectations,* 9**,** 321-332.
TVERSKY, A. & KAHNEMAN, D. 1974. Judgment under Uncertainty: Heuristics and Biases. *Science,* 185**,** 1124-31.
TVERSKY, A. & KAHNEMAN, D. 1981. The framing of decisions and the psychology of choice. *Science,* 211**,** 453-8.
VAHABI, M. 2010. *Verbal versus numerical probabilities: Does format presentation of probabilistic information regarding breast cancer screening affect womens comprehension?*, Health Education Journal. 69 (2) (pp 150-163), 2010. Date of Publication: June 2010.
VAN DEN BERG, M. & DONYAI, P. 2010. How was patient empowerment portrayed in information leaflets describing the community pharmacy Medicines Use Review service in the UK? *Patient Educ Couns,* 80**,** 274-6.
VANDER STICHELE, R. H., VANDIERENDONCK, A., DE VOOGHT, G., REYNVOET, B. & LAMMERTYN, J. 2002. Impact of Benefit Messages in Patient Package Inserts on Subjective Drug Perception. *Drug Information Journal,* 36**,** 201-208.
VISSCHERS, V. H., MEERTENS, R. M., PASSCHIER, W. W., DE VRIES, N. N., VISSCHERS, V. H. M., MEERTENS, R. M., PASSCHIER, W. W. F. & DE VRIES, N. N. K. 2009. Probability information in risk communication: a review of the research literature. *Risk Analysis,* 29**,** 267-87.
WALDRON, C. A., VAN DER WEIJDEN, T., LUDT, S., GALLACHER, J. & ELWYN, G. 2011. What are effective strategies to communicate cardiovascular risk information to patients? A systematic review. *Patient Education and Counseling,* 82**,** 169-181.
WARD, S., JONES, M. L., PANDOR, A., HOLMES, M., ARA, R., RYAN, A., YEO, W. & PAYNE, N. 2007. A systematic review and economic evaluation of statins for the prevention of coronary events.
WILLIAMSON, G. R. 2004. Illustrating triangulation in mixed-methods nursing research. *Nurse researcher,* 12**,** 7-18.
WOGALTER, M. S. & VIGILANTE, W. J., JR. 2003. Effects of label format on knowledge acquisition and perceived readability by younger and older adults. *Ergonomics,* 46**,** 327-44.
WOLFE, S. M. 2002. Direct-to-Consumer Advertising — Education or Emotion Promotion? *New England Journal of Medicine,* 346**,** 524-526.
WOLOSHIN, S. & SCHWARTZ, L. M. 2011. Communicating Data About the Benefits and Harms of TreatmentA Randomized Trial. *Annals of Internal Medicine,* 155**,** 87-96.
WOLOSHIN, S., SCHWARTZ, L. M., TREMMEL, J. & WELCH, H. G. 2001. Direct-to-consumer advertisements for prescription drugs: what are Americans being sold? *The Lancet,* 358**,** 1141-1146.
ZAMARIAN, L., BENKE, T., BUCHLER, M., WENTER, J., DELAZER, M., ZAMARIAN, L., BENKE, T., BUCHLER, M., WENTER, J. & DELAZER, M. 2010. Information about medications may cause misunderstanding in older adults with cognitive impairment. *Journal of the Neurological Sciences,* 298**,** 46-51.

ZIKMUND-FISHER, B., SMITH, D., UBEL, P. & FAGERLIN, A. 2007. Vaidation of the Subjective Numeracy Scale: Effects of low numeracy on comprehension of risk communications and utility elicitations. *Medical Decision Making*, (27) 663.

ZIKMUND-FISHER, B. J., FAGERLIN, A. & UBEL, P. A. 2005. What's Time Got to Do with It? Inattention to Duration in Interpretation of Survival Graphs. *Risk Analysis,* 25, 589-595.

ZIMMERMANN, C., BALDO, C. & MOLINO, A. 2000. *Framing of outcome and probability of recurrence: Breast cancer patients' choice of adjuvant chemotherapy (ACT) in hypothetical patient scenarios*, Breast Cancer Research and Treatment. 60 (1) (pp 9-14), 2000. Date of Publication: 2000.

Appendices

Appendix 1: Combination of search terms employed in the search strategy for the literature review

Key Concept	Keywords	MESH Terms
Risk Benefits	Risk*, benefit*, harm*, risk-benefit*, framing (Fram*), risk communication, ?decision making, numeracy, risk perception, risk factor*, risk analys*, pharmaceutical decision making, risk benefit analys*, patient risk*, risk perception*, risk analys*, risk taking, framing effect*	Risk, uncertainty, risk assessment, risk factors
Headline Information	Key information, text design, priority information, instructional design, instructional text, informational text design, outline*, summary box*, summary information, information box*, drugs facts box*, format, category header*, patient safety, label design, 'warning' label*, safety design, safety sign*, hazard communication, warning label*, boxed aside*, graphical device*, *persuasive communication, printed communication media, visual perception, visual attention, visual display, eye scanning headline sections, key information, key points design and layout, macro theme*[1]	
Medicines Information	Patient information leaflet*, pamphlet*, written medicines information, consumer medicines information, package insert*, Information literacy, drug labelling, drug packaging, product labelling, print* material*, booklet, brochure, information resource*, teaching material*, consumer health information, patient education, medicines information, drug information, patient information sheet*, written communication, medication instructions,	Patient education, consumer health information, pamphlets,
1	Suggestions from librarian (Deirdre Andre, Research Support Officer, LUCID Health, Health Sciences).	

Appendix 2: Example of search strategy for both headline section and benefit information as initially employed in Medline

Searches	Results	Search Type	Actions
1		risk.mp. or exp Risk/	1200924
2		benefit*.mp.	336189
3		harm.mp.	16629
4		harmed.mp.	825
5		fram*.mp.	185190
6		(risk* adj2 communicat*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]	1448
7		exp Decision Making/	97922
8		(numeracy or numerate).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]	309
9		(risk* adj2 perception*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]	2757
10		(risk* adj2 analys*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]	8853
11		pharmaceutical decision making.mp.	1
12		(patient* adj2 risk*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]	52286
13		1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12	1712526
14		patient information leaflet.mp.	85
15		exp Patient Education as Topic/	61711
16		exp drug labelling/ or exp drug packaging/	8409
17		exp product packaging/ or exp product labelling/	13885
18		information literacy.mp. or exp Information Literacy/	151
19		exp Health Education/	120739
20		exp Pamphlets/ or booklet*.mp.	4196
21		brochure*.mp.	1172
22		information resource.mp.	434
23		exp Consumer Health Information/	1293
24		medicine* information.mp.	171
25		drug information.mp.	4757
26		(patient information adj sheet*).mp. [mp=protocol supplementary concept, rare disease supplementary	66

	concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]	
27	written communication*.mp.	255
28	medication instruction*.mp.	92
29	medicine* instructions.mp.	4
30	14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29	141115
31	key information.mp.	561
32	(design adj2 text).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]	28
33	priority information.mp.	30
34	instructional design.mp.	180
35	instructional text.mp.	18
36	summary box.mp.	1
37	information box.mp.	3
38	(drug adj box*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]	20
39	category header*.mp.	1
41	(label adj2 design).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]	640
42	warning label.mp.	69
43	safety design.mp.	53
44	safety sign*.mp.	270
45	hazard communication.mp.	101
46	graphical device*.mp.	12
47	exp Persuasive Communication/	2502
48	printed communication media.mp.	0
49	visual perception.mp. or exp Visual Perception/	172444
50	visual attention.mp.	2450
51	key point*.mp.	2817
52	(design adj3 layout).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]	94
53	macro theme.mp.	0
54	31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53	180472
55	30 and 54	753
56	13 and 30	30900

Appendix 3: Revised search strategy for the benefit information scoping search (PyscInfo/ Embase/ Web of Science)

RISK (HARM) BENEFIT

((risk* or harm* or benefi*) adj3 (communicat* or understand* or explain* or explan* or educat* or inform* or present* or percept* or analys*)).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

PATIENT INFORMATION

(patient* adj (educat* or informat* or communicat*)).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

(health adj (informat* or communicat* or educat*)).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

(drug or medicine* or medicat*) adj1 (literature or leaflet* or instruct* or label*)

Decision AID search(patient* adj (educat* or informat* or communicat*)).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

OR

(health adj (informat* or communicat* or educat*)).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

AND

((risk* or harm* or benefi*) adj4 (communicat* or understand* or explain* or explan* or educat* or inform* or present* or percept* or analys*)).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

AND

Decision Aid (as keyword.)

Other keywords

Numeracy

Framing

Search Strategy: Web of Science

Topic= ((risk* or harm* or benefit*) SAME (communicat* or understand* or explain* or educat* or inform* or present*)) AND Topic= ((patient*) SAME (Educat* or informat* or communicat*

Appendix 4: Example of data extraction form used during the scoping literature reviews to record the characteristics of the included studies. An example is provided for both the headline section and the benefit reviews

ARTICLE	WHO	WHAT	WHERE	HOW		SUMMARY of AUTHOR CONCLUSION	RELEVANCE
	Population	Intervention	Setting	Design	Outcomes	Findings	Conclusion
BERSELLINI et al 2006	**Study 1:** n=454. **Age:** 22 (16-65). **Females:** n=293. High levels of education. **Study 2:** n=292. **Age:** 18-75. **Female:** n=150. **Education:** 15.4% no formal qualifications, 19.9% GCSEs, 26% A-levels, 38.7% degree. **Study 3**: n=248. **Age:** 18-80. **Female:** n=142. **Education:** 21.8% GCSE, 23.3% A-level, 38% degree.	**Textual** **Study 1:** Simple benefit (effectiveness) statement in explanation about a medicine. **Study 2:** simple statement about medicine's effectiveness and short rationale about how medicine worked. Participants received either	UK. **Study 1:** Participants recruited from a University campus and questionnaire undertaken on the spot. **Study 2:** Participants recruited from general population in a town centre. Undertook questionnaire on the spot. **Study 3:** Participants	**Study 1:** A two-factor (with/without benefit information X severe/mild disease) cross-sectional between participants design. **Study 2:** A two-factor (with/without effectiveness statement X with/without rationale statement) cross-sectional	[1] Satisfaction with information. [2] Perception of effectiveness of medicine [3] Perception of benefit to health. [4] Perception of risk to health. [5]Intention to take medicine. [6] Perception of overall effect on health of taking medicine.	**Study 1:** information about benefits enhanced the judgements but did not influence the intention to comply. **Study 2:** both the forms of benefit information were effective in improving judgements but had no effect on intention to comply. **Study 3:** found both types of benefit information (plus side effect information) improved the intention to comply, as well as	All three studies show positive effects of the inclusion of simple benefit information in an explanation about a prescribed medicine. Higher ratings of intention to take the medicine in the group where participants are presented with side effects information too. It is likely the provision of this information increased perceptions of the perceived barriers to taking the drug, which increased the need for information

		effectiveness statement, rationale statement or a combination or neither intervention. **Study 3:** two types of benefit information when presented with side effect information.	recruited from town centre. Undertook questionnaire on the spot.	between participants design. **Study 3:** A two-factor (with/without rationale statement) cross-sectional between participants design Randomised groups	[7] Beliefs about side effects.	ratings on the other measures.	about the drugs benefits. Inclusion of benefit information positively influenced people's judgements, including their intention to take the medicine.

ARTICLE	WHO	WHAT	WHY	WHERE	HOW	SUMMARY of AUTHOR CONCLUSION	RELEVANCE
	Population	**Intervention**	**Setting**	**Design**	**Outcomes**	**Findings**	**Conclusion**
Dolk et al 2011	**N=80** potential users of medicines. Those with background in medicines information excluded. • Age 18-34 (49 mean) • 37 females For each round match in terms of gender, education & age	**Headline section** in PIL for carbamazepine. The headline section consisted of light grey shaded box containing key safety messages about the medicine	**UK & Netherlands.** Participants recruited from the general population Interviews untaken in interview rooms with little external stimuli to avoid distractions.	**User test methods** 2x2 factor design (English & Dutch, with headline & without headline) Varying language was a moderating rather than independent variable.	Findability of information, comprehensibility of information perception of the design	**Findability**: headline did not have a negative effect on findability and comprehensibility of information. **Comprehension:** information was found and comprehended in both sections - headline section did not have a positive effect on findability and comprehension of information. **Perception of design**: scores for PIL with headline did not differ statistically from those without. Headline section was perceived to be as difficult, well-designed or useful as without. Semi-structured interviews showed that participants were enthusiastic about headline section, but UT suggested they didn't seem to use it.	A user-test did not reveal differences in how well participants could find and understand the information in the leaflets. When asked for general impressions of headline section most participants evaluated it positively.

Appendix 5: Topic guide for the focus group studies (chapter 3/ study 2)

General leaflet questions (5-10 mins)

K, B[1] **–** Have you ever seen an information leaflet like this inside your packet of medicine? What have you done with this information?
(Prompts: Do you read it? When? Do you refer to it? How often? Do you keep the leaflets? How do you use the information?)
A –In general, what do you think of this leaflet?
Prompts:

- *Easy/ hard to read? How do you find reading the leaflet?*
- *Easy/hard to find the information you need?*
- *Length?*
- *Design/ layout?)*

(Refer to colleague to check for any information that could be expanded upon)

HEADLINE section Questions (30 mins)

We would like to show you an amended leaflet. (10 minutes - tea if required)

I refer you to the grey shaded box on leaflet 2. This is titled 'important things to know about your medicine'.

A, K – Did you notice this section on the leaflet? What do you think of it by comparison with this leaflet that doesn't have a headline section?
A, K – What do you think of this style of presentation? *(**Prompt:** Ask about colour, text size, font, shading)*
A, B – If you could receive a leaflet which included a headline or summary section, what information would be most important to include?
*(**Prompt**: specific age group, condition, safety message)*
B – If you received a leaflet containing this information, rather than an existing one, do you think you would do anything differently?
***(Prompt:** Read more or less of the leaflet? Change or stop your medication? Take it differently? Seek advice from Doctor or other HCP?)*
A-On balance would you prefer a leaflet with or without this information?
(Refer to colleague to check for any information that could be expanded upon)

BENEFIT Information Questions (40 mins)

I now refer you to leaflet 3. This leaflet contains information about the possible benefits from taking the medicine. *these are the multi-coloured flaps that are on the leaflet. There are 4 different formats, they are coloured purple, blue orange and green*
K, A - What did you think of this information?
K, A- Which of these different formats do you prefer? Why?
B- Imagine you were first prescribed this medicine, what difference would this information make to what you did and thought about the medicine?

[1] K= Knowledge, A= Attitudes, B=Beliefs

(Prompt: do you think you would do anything differently? *Change your medication? Take it differently? Stop your medication? Seek advice for Doctor or other HCP? Ask your family for advice? Look at the internet)*
A – What changes if any would you recommend to this section?
(Prompt: *explore issues with any concerns and anxieties, feeling reassured and informed)*

K, A, B – if you have the choice of having one of these formats which one would you have and why?

(Refer to power point.)

There are two sentences in the orange and blue sections. One is a positive frame, telling you how likely it is the medicine will make you feel better/ prevent a heart attack. The other is negative frame, telling you how likely it is the medicine will not make you feel better/ not prevent a heart attack.

K, A, B- Do you have any preference for either of these sentences? Or do you prefer the combined format that is on the leaflet?

SIDE EFFECT information Questions (10-15 mins)

(Refer to leaflet and highlight the side effect information.)

Finally, I'd like to talk to you briefly about the side effects section. Currently the side effects of this medicine are described using both verbal descriptors and frequencies. These are the terms 'common, uncommon and very rare' and the numbers may affect up to 1 in 10, 1 in 100

A – What do you think about the way the side effect information is presented in this leaflet?
A -Would you like to see side effect information presented in a different way?
(Prompt: *using percentages, graphical formats, consider the presentation of side effect information separately)*

A -What do you think about the balance of information (about the benefits and harms) in the leaflet?

Closing Questions

- Any other comments about the leaflets you get with medicines?
- Any other suggestions about ways in which medicine leaflets can be improved?

Thank you for all your help

Appendix 6: Participant information sheet for the focus groups (chapter 3/ study 2)

Participant Information Sheet

Title of Study: Improving the Content and Format of Medicines Leaflets (CoFoMeL)

We would like to invite you to take part in the above named study but before you decide, please read the following information.
You can choose not to take part without having to give a reason and without penalty.

What is the purpose of this study?

When a new medicine is prescribed all patients receive an information leaflet in the medicine box. We would like to find out more about what people think about the information provided with medicines. We would like to ask your opinions about different ways of presenting information that could be provided with the leaflet in boxes of medicine.

Some of the issues we would like to find out about include:

- Including positive information in medicine leaflets, this includes information on how the medicine works, what it does and what are its benefits?
- Using a summary box at the top of the medicines leaflet which contains important information of the medicine.

By doing so we hope to understand more about how we can improve the information provided with medication and help patients understand more about their medicines.

Who is doing the study?

The study is being done by researchers from the University of Leeds, Medicines Management Group. The study is being conducted as part of PhD, undertaken by Mrs. Rebecca Dickinson. The supervisor is Professor Theo Raynor.

Who is being asked to participate?

You have been invited to participate because you are over 50 years of age and are taking one or more long-term medicine (this can be a tablet, liquid or inhaler). If you would like to take part you must be able to speak and read English.

What will be involved if I take part in this study?

- If you are interested you will be invited to take part in a discussion with some other people taking long-term medicines. You will be given some medicine leaflets to look at and asked for your opinions.
- A researcher will ask a few questions and you will be free to talk with other group members about the subject.
- The discussion will take no more than 2 hours in total and refreshments will be provided.

What are the advantages and disadvantages of taking part?

There are few disadvantages of taking part in this study, although you may find the task tiring. You will be free to leave at any time. The group discussion will take two hours of your time. You may not get any personal medical benefits from agreeing to take part. However, the study may highlight better ways of proving information with long-term medicines. This could help patients in the future. If you do participate you will be given a £20 gift voucher at the end of the meeting to acknowledge the time you have given.

Can I withdraw from the study at any time?

You do not have to take part in the study, no-one will mind if you say no. You can say yes and then change your mind. You are free to withdraw from the study at any time and do not have to give a reason why. Once the focus groups have been undertaken then it will not be possible to exclude any information you have given from the research. However, any information will be made anonymous so you will not be identified in any way.

Will the information I give be kept confidential?

To keep an accurate record of what is discussed the meeting will be audio recorded. The recordings will be typed up and made anonymous. Then the recordings will then be destroyed. All information you offer during the research will be kept private and confidential. It will be stored for 4 years in a locked filing cabinet in a secure office. It will not be possible to identify you in any way from the publications, reports and guidelines that are produced.

What will happen to the results of the study?

The results from the study will form part of a PhD thesis. They will be written as a document and sent for publication in a medical journal. We will also present the results of the study to the Medicines and Healthcare products Regulatory Agency to help them improve the regulations about patient information leaflets.

Who has reviewed this study?

The University of Leeds School of Healthcare Research Ethics Committee has reviewed this study.

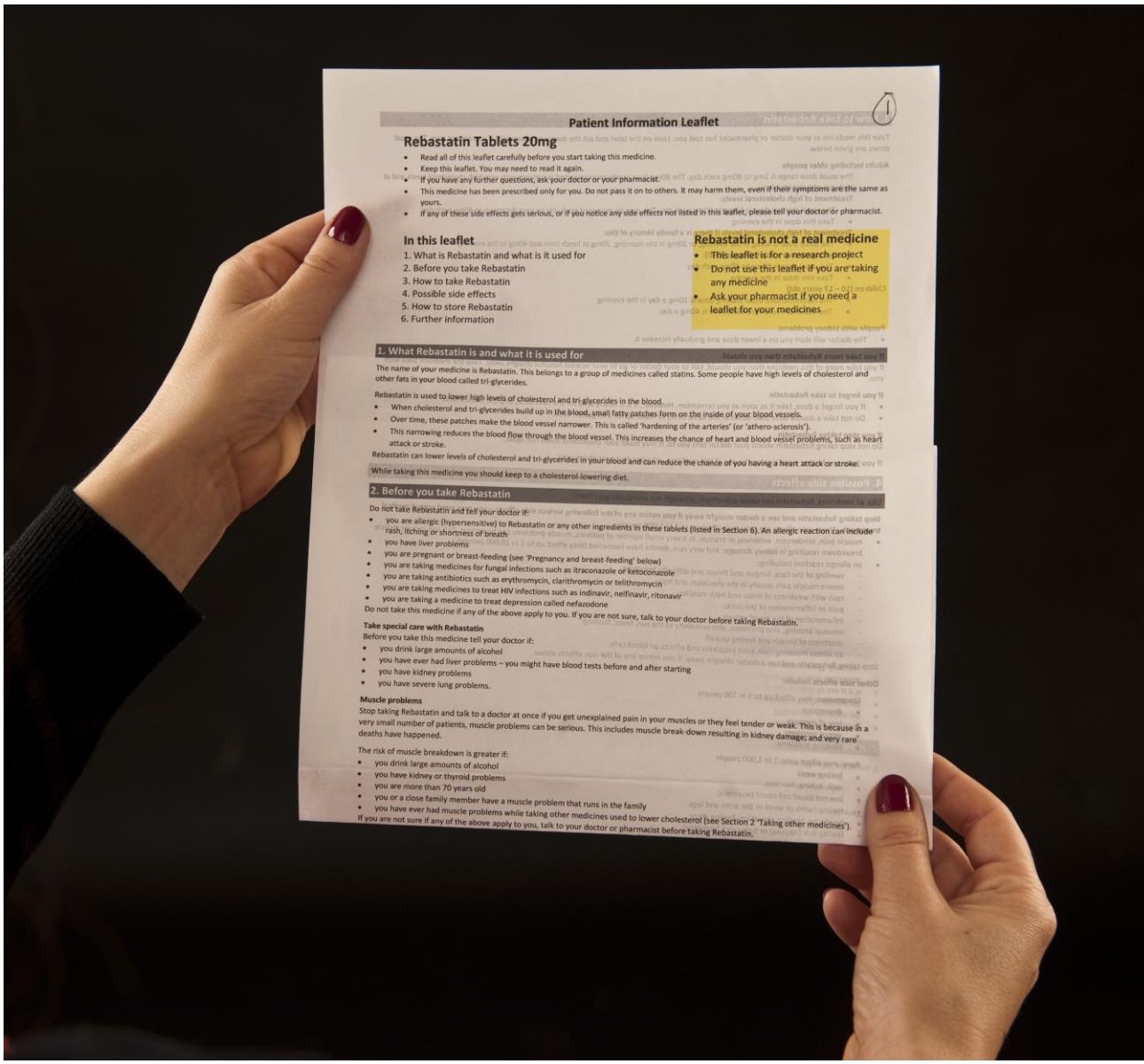
If you agree to take part, would like more information or have any questions or concerns about the study please contact:

Mrs Rebecca Dickinson,
Research Nurse, School of Healthcare, University of Leeds, LS2 9LN
Tel: **0113 3431190**
E-mail: **r.dickinson@leeds.ac.uk**

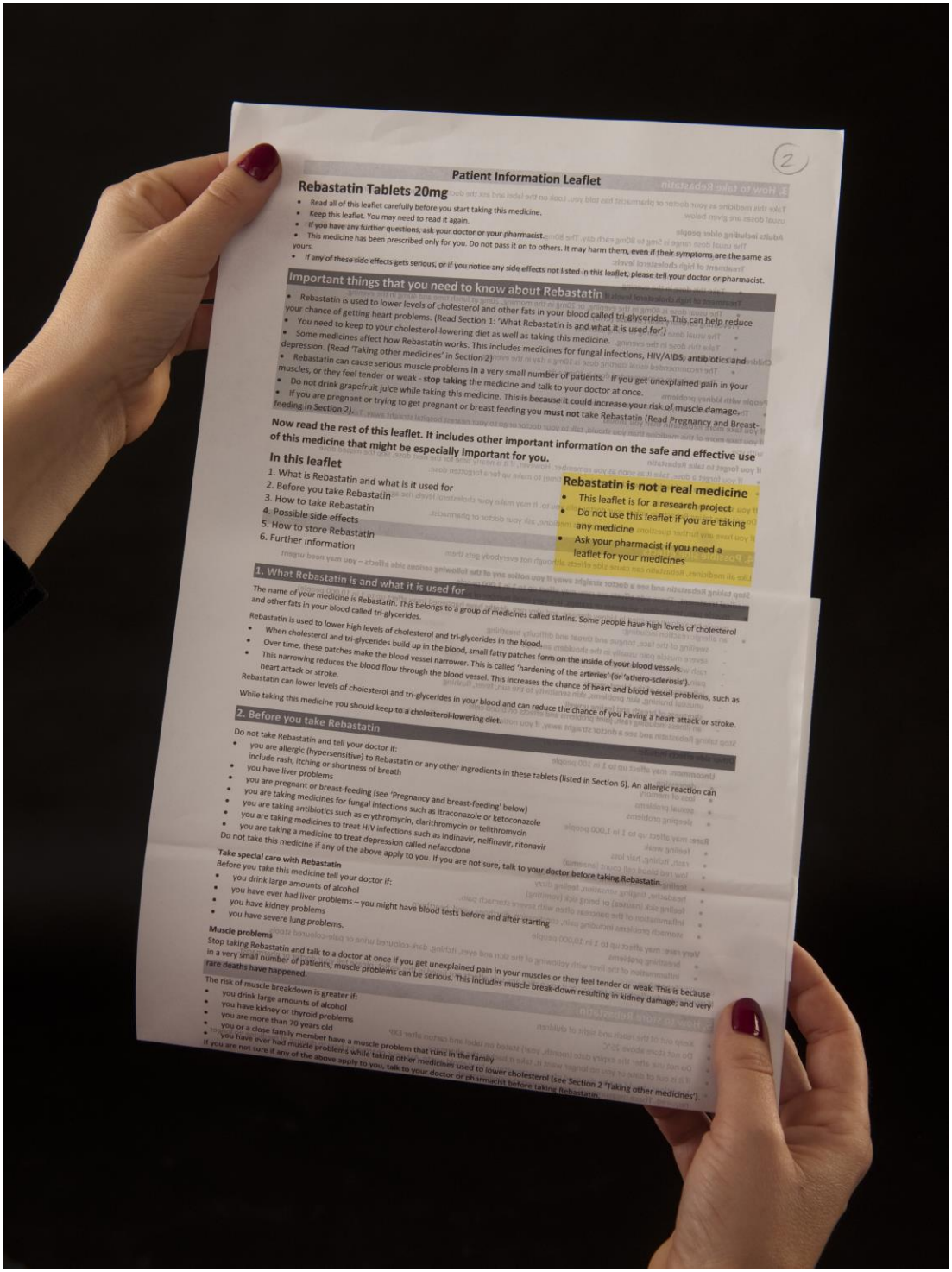
Thank you for taking the time to read this information sheet.

Appendix 7: Examples of the patient information leaflets shown to participants during the focus groups (chapter 3/ study 2)

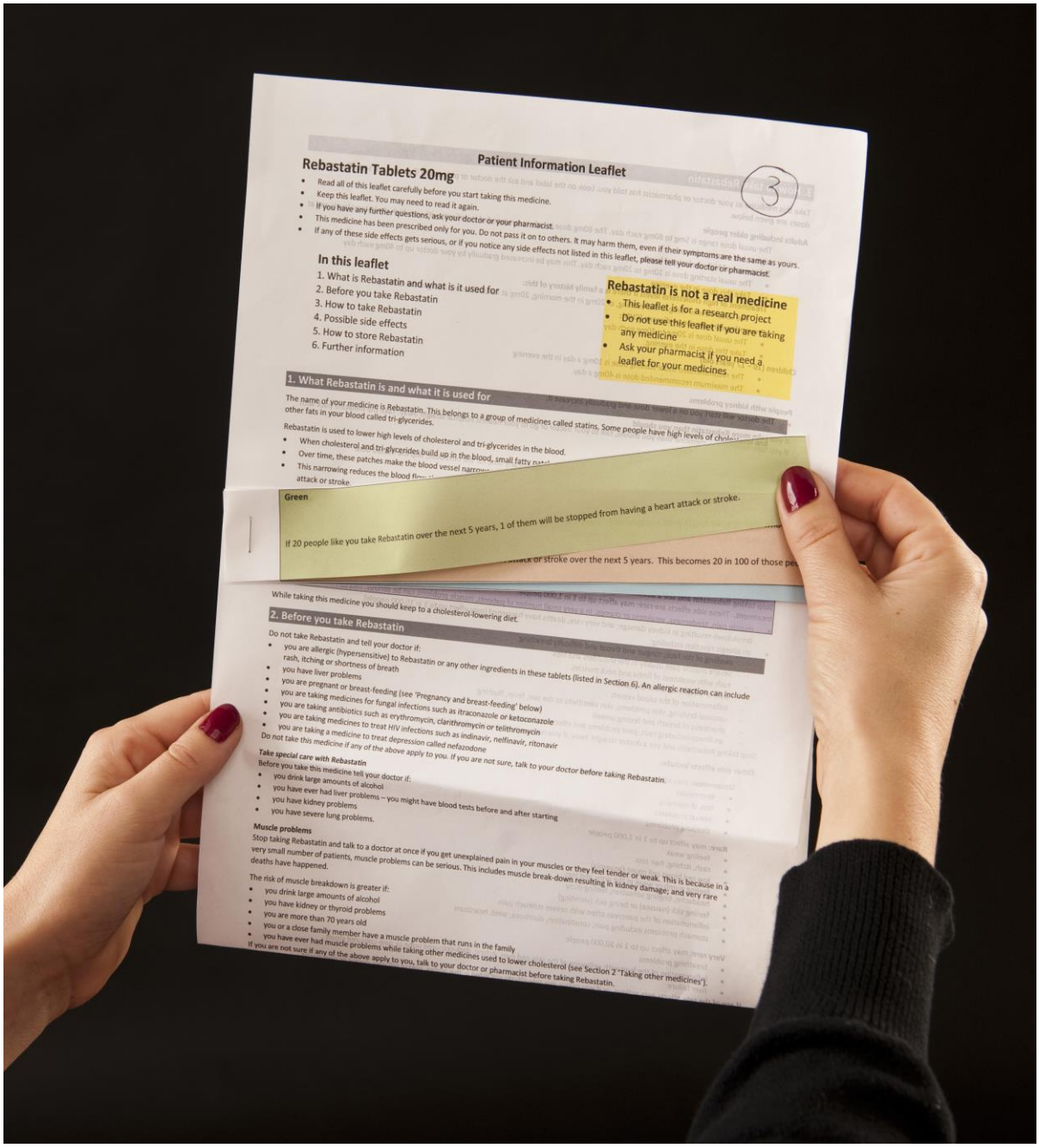
- **Example of typical leaflet**



- **Example of headline leaflet**



- **Example of benefit leaflet**



Appendix 8: Chart illustrating the development of the framework. This shows the process by which the initial transcript was indexed from the raw data into the index which was applied to analyse the rest of the focus groups.

Quote	Initial code	Preliminary thoughts	Initial themes	Categories
GENERAL LEAFLET				
So you get a lot of blurb, which doesn't tell you the basic thing and it's the one thing the pharmacists are constantly asked. 'How do I take them? When do I take them?' So there's just **far too much information.** LL	Too much information	Balance of information	Role of leaflet	Concerns about the leaflet
Well, I re-read mine because of this and I thought 'why am I taking this?' **because it was so negative** and **it never once said what the benefits were**. It was dreadful.JM	Negative message with leaflets	Desire for benefit information	Role of leaflet	Concerns about the leaflet
My mum was private person and **if that had happened to her** she would've never gone back to the doctors again, but they said to me 'persevere', I did. I think that kind of thing needs to be put in a leaflet, that you may feel like this for a couple of weeks because your body needs to adjust to taking it, and then if that doesn't happen then go back to your GP. But it didn't.JM	Type of person What needs to be in a leaflet	Role of leaflet	Patient Characteristics	Patient as an individual
When you get the leaflets, you open them up and **your heart literally sinks a**nd you think 'Oh!' All that verbiage and all that...small print. That's one thing, very small print... I mean you've highlighted some things, and highlighting in colour shows some things. It's much better the contrast. RG	Your heart sinks Small print and highlighting	Negative message with leaflets Design features of leaflets (format)	Role of leaflet	Concerns about the leaflet
And so the first thing I am going to look for is allergy	Priorities for	Role of leaflet (safety	Role of leaflet	Providing

advice. And the second thing is side effects because often those two are very closely linked, having said that I would sincerely hope that when I go to be GP I do not get prescribed something that is contra-indicated with my allergies.JP	information	net) Information needs		information and protecting
But the GP would then turn around and say that you haven't told us that you've had any reaction to this. You can give them back to the chemist, but then the chemist may not tell the GP that, so the GP's attitude is that you should've told me...LL	Chemist may not tell GP GP attitude	GP/HCP relationships	Role of healthcare professionals	Providing information and support
When I got the tablets from the pharmacist, the instructions I got from the pharmacist was don't take any antacids of the two hours after taking this tablet and on the leaflet it said just an hour each side. So they sort of contradicted each other... I just assume that is easy, quick and this refers to leaflets. I just assume they are in there for the litigation purposes. VW	Leaflet helped Leaflet for litigation purposes	Role of leaflet (litigation)	The role of the leaflet	Providing information and protecting Concerns about leaflet

Appendix 9: Thematic framework

The thematic framework was developed using the process above and was used to code the focus groups transcripts during the indexing stage of the analysis.

1. The role of the leaflet in providing Information (GENERAL)

1) Providing Information and protecting
2) Supporting HCP advice
3) Helping patient to make decisions
4) Patient engagement with the leaflet
5) Design of the leaflet (GENERAL)
6) Concerns about the leaflet

2. Using the HEADLINE section (HEADLINE)

1) Noticing the HEADLINE
2) Impact upon patient knowledge about medicines
3) Impact upon patient satisfaction about information and medicines
4) Impact upon behaviour
5) Concerns about HEADLINE section

3. Patient preference for the design of the leaflet (HEADLINE)

1) Content of the HEADLINE
2) Format of the HEADLINE

4. Talking about the different formats of information (BENEFIT)

1) Talking about TEXTUAL information
2) Talking about PERCENTAGES
3) Talking about NATURAL FREQUENCIES
4) Talking about NNTs
5) Talking about FRAMING
6) Talking about alternative formats

5. Impact of BENEFIT information (BENEFIT)

1) on knowledge and understanding of medicines
2) on satisfaction with information
3) on information seeking behaviour
4) on health behaviours
5) on making decisions

6) on medicine-taking
7) Anxieties and concerns about benefit information
8) other

6. Numeracy and numbers

1) Attitudes to numerical information
2) Context of numerical information
3) Accuracy of information
4) Trustworthiness of information

7. Talking about side effect information

1) Concerns about side effect information
2) Talking about balance of information
3) Impact of side effect information on knowledge and understanding
4) Satisfaction with side effect information

8. Patient characteristics

1) The patient as an individual
2) Experience of numbers
3) Ability to use information
4) Preferences for decision making
5) Personal health and condition
6) Family and friends (normative values)

9. Relationships with HCPs

1) Providing information and support
2) Trust

Appendix 10: Example of headline chart. Data were charted with each participant represented as a row and the data from each index represented by a column. This facilitated cross-case comparison of any emerging themes.

Participants	Noticing the HEADLINE	Impact upon patient knowledge about medicines	Impact upon satisfaction about information and medicines	Impact upon behaviour	Concerns about headline section.	Researcher comments
MF, 68, F FG1 JANA 4 items of meds Advanced White British	Thinks maybe a different colour tint might make it more legible. (179)			Thinks you might be less likely to read the leaflet _ people would only read that part…. (393)	Less concerned about repetition. Don't repeat things that don't need repeating! (517)	Good quote on behaviour.
PM, 56, M FG1 JANA 5 items Advanced White British				Feels that to stimulate behaviour change and get people to notice the section it needs to be more frightening.(327) Thinks that the précis means it relates more to the reader and	Thinks the whole leaflet could be more simple and the headline changed to be more in your face and simplistic. (257) Thinks it is too verbose. Wants in your face danger warnings. (319)	

				that is more tempting to read and it encourages you to read more (because you don't have to go through the whole leaflet).(419)		
Participants	**Noticing the HEADLINE**	**Impact upon patient knowledge about medicines**	**Impact upon satisfaction about information and medicines**	**Impact upon behaviour**	**Concerns about headline section.**	**Researcher comments**
BJ, 78, F FG1 JANA 12 items intermediate White British	It does catch your eye immediately and makes it readable. (305)		It's a good idea It's quite short in comparison to the rest of it. (367)	Thinks that if the leaflet is too frightening it will put people off and cause them to just throw away their tablets. (325)	Thinks it should be cross-referenced, but there is a lot of repetition. (191) Doesn't want to be frightened (in response to PM). (321) (325)	

I S,76, M FG1 JANA Three items advanced White British	It is an improvement, it catches your eye. Thought it was noticeable and a good idea. (97)		It's a good idea. (93)	Thinks it might make people read just that bit. The only thing is that some, who would not ordinarily read the leaflet if they think that the rest doesn't matter/ it's possible. (343)	Is concerned it might make people read just that bit. (343) Also expresses concerns about the leaflet being too big and repetitive. (456) Expresses concerns that others might not read the rest of the leaflet, just the Headline. Concerned about superfluous words and length making the font too small. (484) The HEADLINE is boring! (484)	

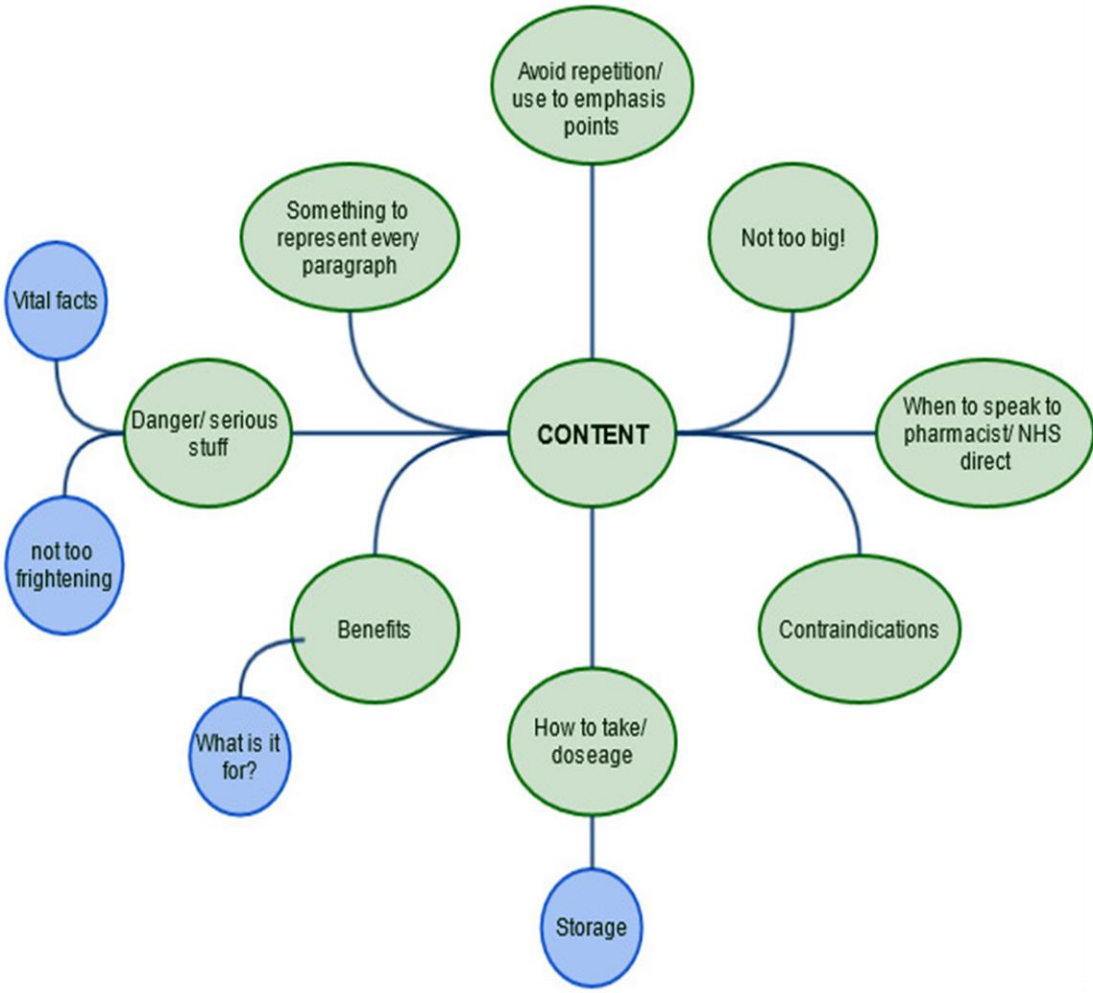
Appendix 12: Example of benefit chart							
Participants	On knowledge and understanding	On satisfaction	On information seeking behaviour	On health behaviours	On making decisions	On medicine taking	Anxieties and concerns
MF, 68, F FG1 JANA 4 items of meds Advanced White British	It needs simplifying. You do need the info, but it needs to be simpler. (611) The leaflet is too difficult to convey its main message (that the medicine doesn't work for everyone) The figures distract from this message. (629) MF also explains the baseline information to IS and stresses it's importance. The medicine isn't as good as expected. (865) People need to be given the		If the info is too difficult probably wouldn't seek it out. (735) Having the benefit info isn't relevant. Most people would skip over if they didn't have any problems or they would go see their GP. (975)		There is general principle to being given information, we need all the information to make a decision, the more information you have helps you make an informed decision. (869) It's too complicated and needs simplifying because it says a 1 in 4 chance, which isn't very high and might affect how people take their medicines. (611) The info is relevant to people hanging to make decisions	It might make a difference to how she feels about her medicines. (667) It's relevant info and might help people to make a choice. (857) If it's prescribed by a dr. most people would skim the leaflet and take the tablet if their dr. told them to. (967)	People do need to know that their medicine might not work…they need to know it happens to other people, but I don't think that is what this is trying to do. (585) It needs simplifying; people need to know that the medicine isn't going to work for everyone. It needs to be simpler. (611)

	information so they can make an informed choice. The more information you have the better. (869) Understand the context information and is able to explain it to her fellow participants. (881)				about taking lots of medicines – do they want to take more. The benefit info is useful in providing the chances of improvements. (853) Helps people make balanced decisions. (857) There is general principle at stake. People need this info to make informed decisions. (869)	Some people (my husband) would say 'I'm not taking those' because of what they have read. A lot will just take it. (975) It wouldn't stop you taking it, but it might make you think 'is it worth it'. (677)	Voices concerns that this info would encourage her husband to not take his medicines or to go back to see his GP (971)

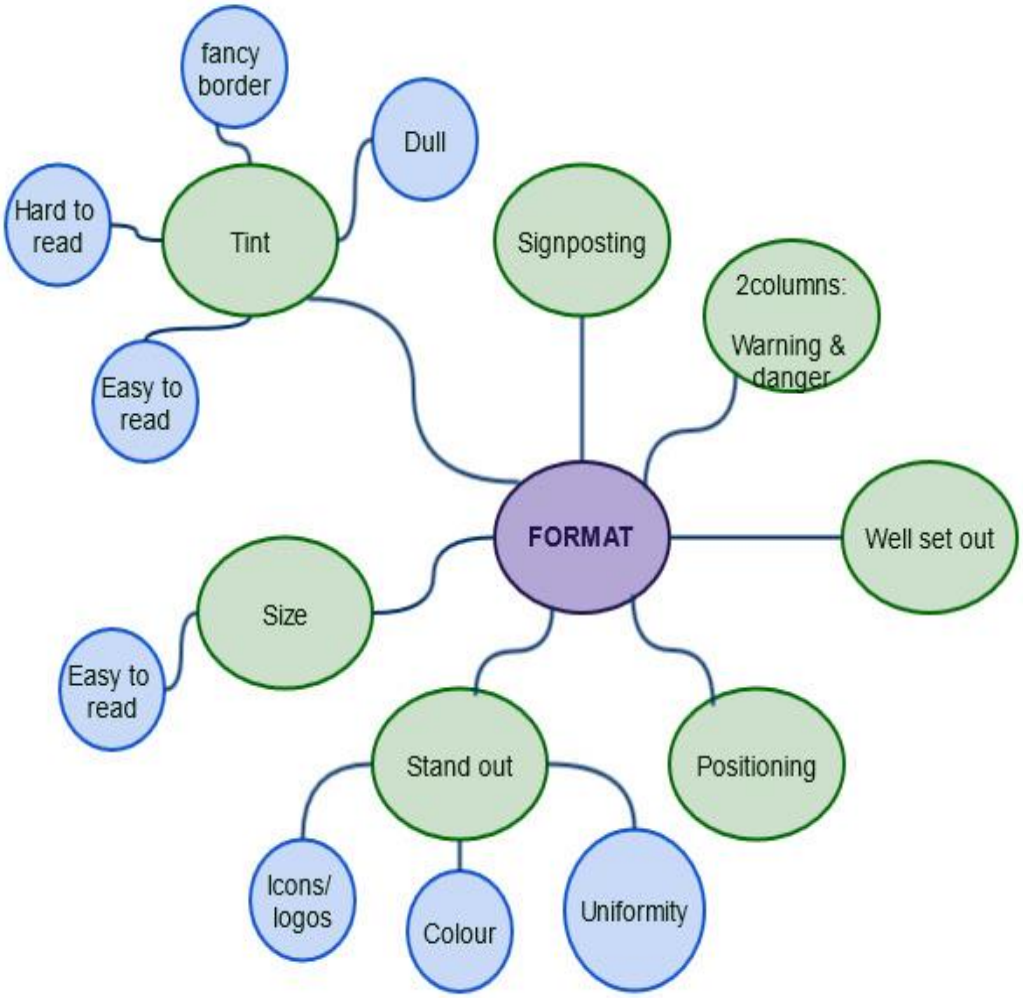
Participants	On knowledge and understanding	On satisfaction	On information seeking behaviour	On health behaviours	On making decisions	On medicine taking	Anxieties and concerns
PM, 56, M FG1 JANA 5 items Advanced White British	Struggles to understand the maths in all the examples. (589) Finds it very confusing. The double negative is confusing. (601) I would be so confused by them I wouldn't bother (631) You are giving me very little hope and telling me things I don't want to know. I'm supposed to be intelligent but I'm bamboozled. I can't get me head around them and I have no real indication of anything. (687)	Wants encouragement to be more satisfied with the information. Wants rewording of the statement to include the word 'rises' or 'increases' to emphasise the benefit. (707)	Likes the second half of the purple. (651) You are giving me very little hope and I don't want to know. And you are bamboozling me. (687)		He wouldn't take this medicine.(although it's difficult to know whether this is due to the info). (613)		Is the maths right? It doesn't make sense. Struggle to understand how all the stats related. Wants it to say doubling of chances instead (as it is more positive). Hates the double negative. (593) The numbers are confusing and I's think 'what's the point'? (631) You are giving

	Wants positive encouragement as this simplifies things. (713) Understands the context of the baseline information and explains it to other participant. (819) Acknowledges this is important information. Suggests the numerical information could say it doubles your chance and this is explained as inaccurate						me very little hope and telling me what is going to happen to me and I don't want to know. The ones with confusion in, I can't get my head around (and I'm supposed to be scientific and logical) they are confusing.

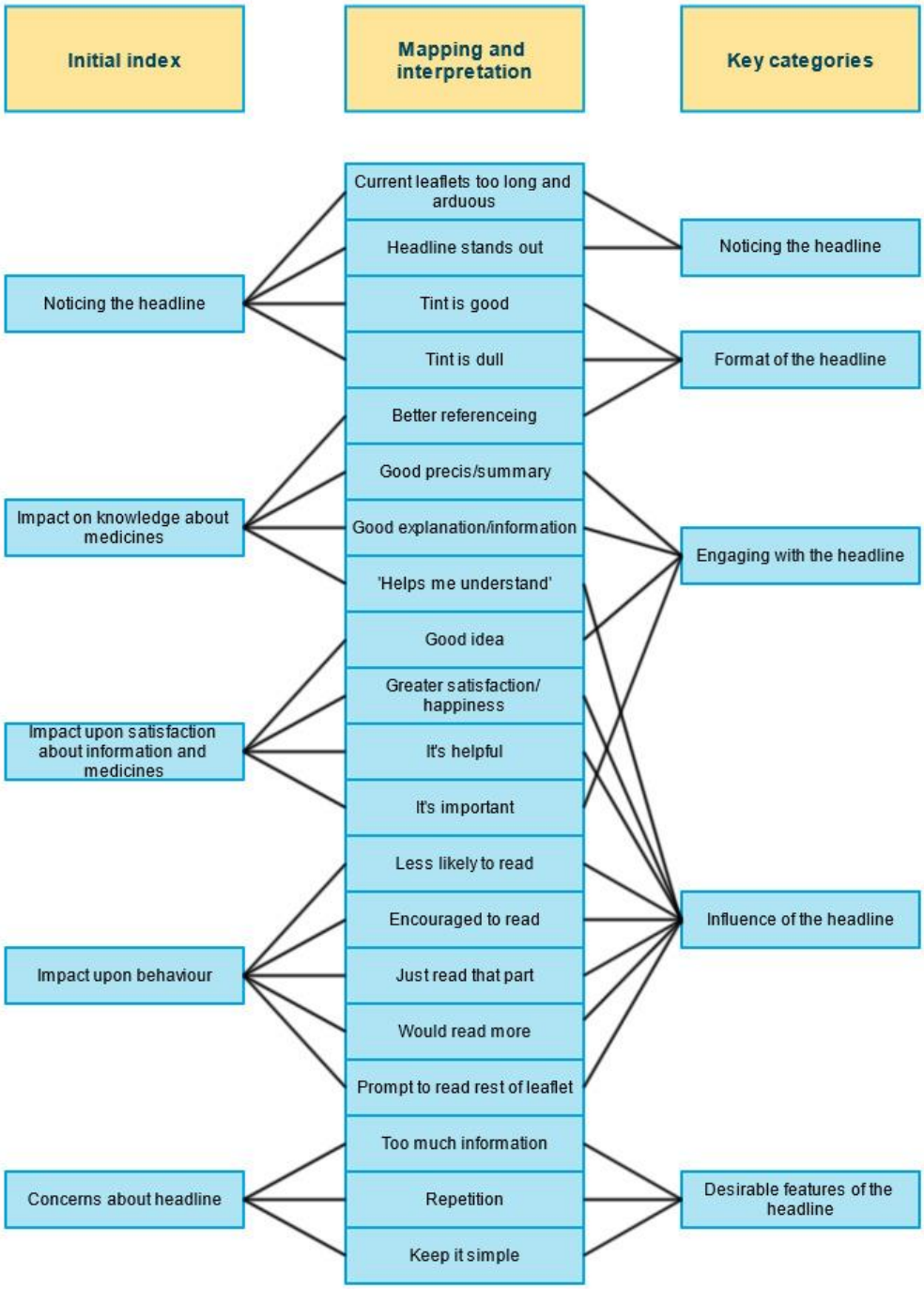
Appendix 11: Mapping and interpretation: Headline – content



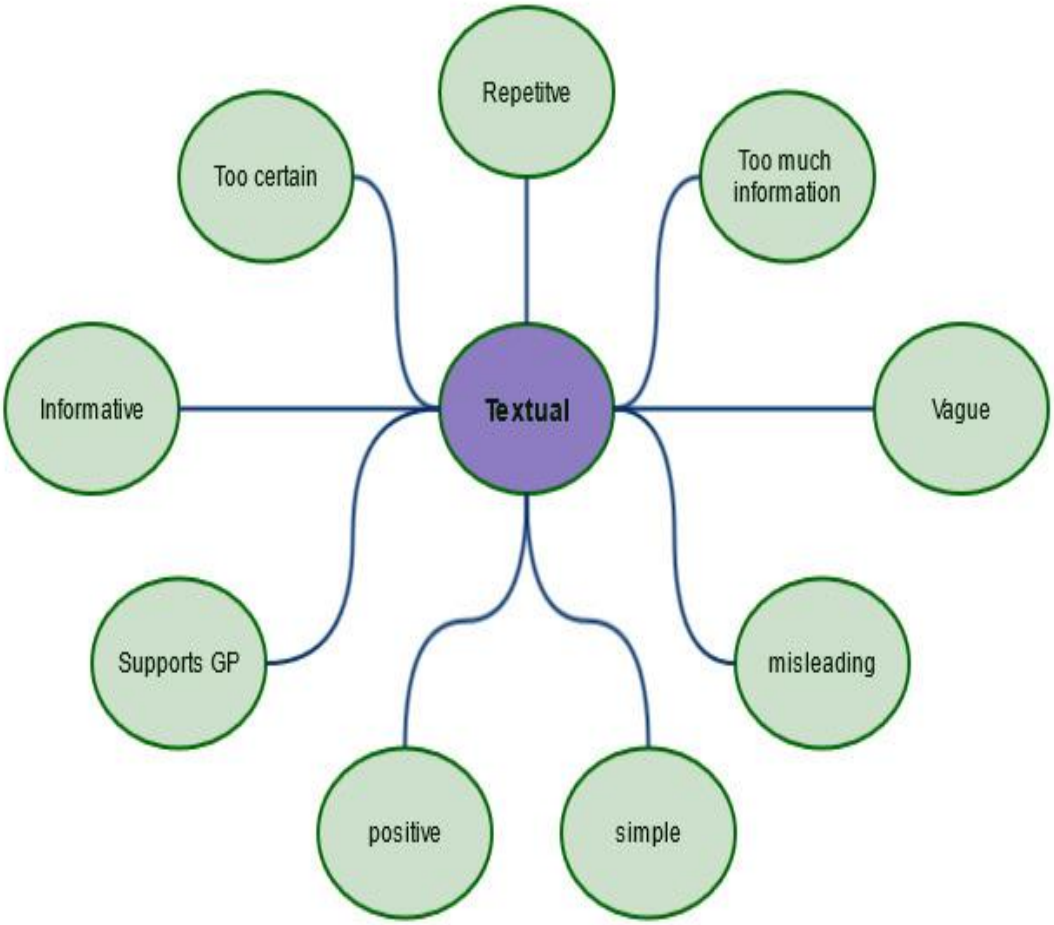
Appendix 12: Mapping and interpretation: Headline – format



Appendix 13: Indexing diagram for using the headline section. This diagram shows the development of the key categories from the initial index (chapter 3/ study 2)



Appendix 14: Example of Mapping and interpretation for the descriptive analysis of the 'preference for format' (chapter 3/ study 2)



Appendix 15: An example of the patient information leaflet for the user-testing study (chapter 4/ study 3)
Name of Centre: University of Leeds, Academic Unit of Medicines Management

Participant Information Sheet

Title of Study: Improving the Content and Format of Medicines Leaflets (CoFoMeL)

We would like to invite you to take part in the above named study but before you decide, please read the following information.
You can choose not to take part without having to give a reason and without penalty.

What is the purpose of this study?

When a new medicine is prescribed all patients receive information about the medicine in the form of a leaflet in the medicine box. A criticism of this information is that it is too complex and difficult to read. The aim of this research is to improve the quality of the leaflets provided with medicines.

We want to ask people who are likely to receive a leaflet like this in the future to test this information and see how easy it is to read and understand. The test is not an assessment of your memory, as you will have the leaflet to refer to throughout the interview. It is a test of how well the manufacturer has written and presented the information on the leaflet.

Who is doing the study?

The study is being done by researchers from the University of Leeds, Medicines Management Academic Unit. The study is being conducted as part of a PhD, undertaken by Mrs. Rebecca Dickinson. The supervisor is Professor Theo Raynor.

Who is being asked to participate?

You have been invited to participate because you are over 50 years of age and are taking one or more long-term medicines (this can be a tablet, capsule, liquid or inhaler). If you would like to take part you must be able to speak and read English.

What will be involved if I take part in this study?

- If you are interested you will be invited to take part in a User Test
- A User Test involves reading a Patient Information Leaflet and answering a few simple questions about the leaflet during an informal interview.
- Interviews typically take around 1 hour. You will receive a small token of £20 as thanks for your participation.
- The interview is not a test of your memory, as you will have the leaflet to refer to throughout the interview. It is a test of how well the leaflet is written and presented.

What are the advantages and disadvantages of taking part?

There are few disadvantages of taking part in this study, although you may find the task tiring. You will be free to leave at any time. The user-testing will take approximately an hour of your time. You may not get any personal medical benefits from agreeing to take part. However, the study may highlight better ways of proving information with long-term medicines. This could help patients in the future. If you do participate you will be given £20 at the end of the meeting to acknowledge the time you have given.

Can I withdraw from the study at any time?

You do not have to take part in the study, no-one will mind if you say no. You can say yes and then change your mind. You are free to withdraw from the study at any time.

Will the information I give be kept confidential?

To keep an accurate record of what is discussed the interview will be audio recorded. The recordings will be typed up and made anonymous. Then the recordings will be destroyed. All information you offer during the research will be kept private and confidential, in accordance with the Data Protection Act.

What will happen to the results of the study?

The result of the study will be used as part of a PhD thesis. They will be written as a document and sent for publication in a medical journal. We will also present the results of the study to the Medicines and Healthcare products Regulatory Agency to help them improve the regulations about patient information leaflets.

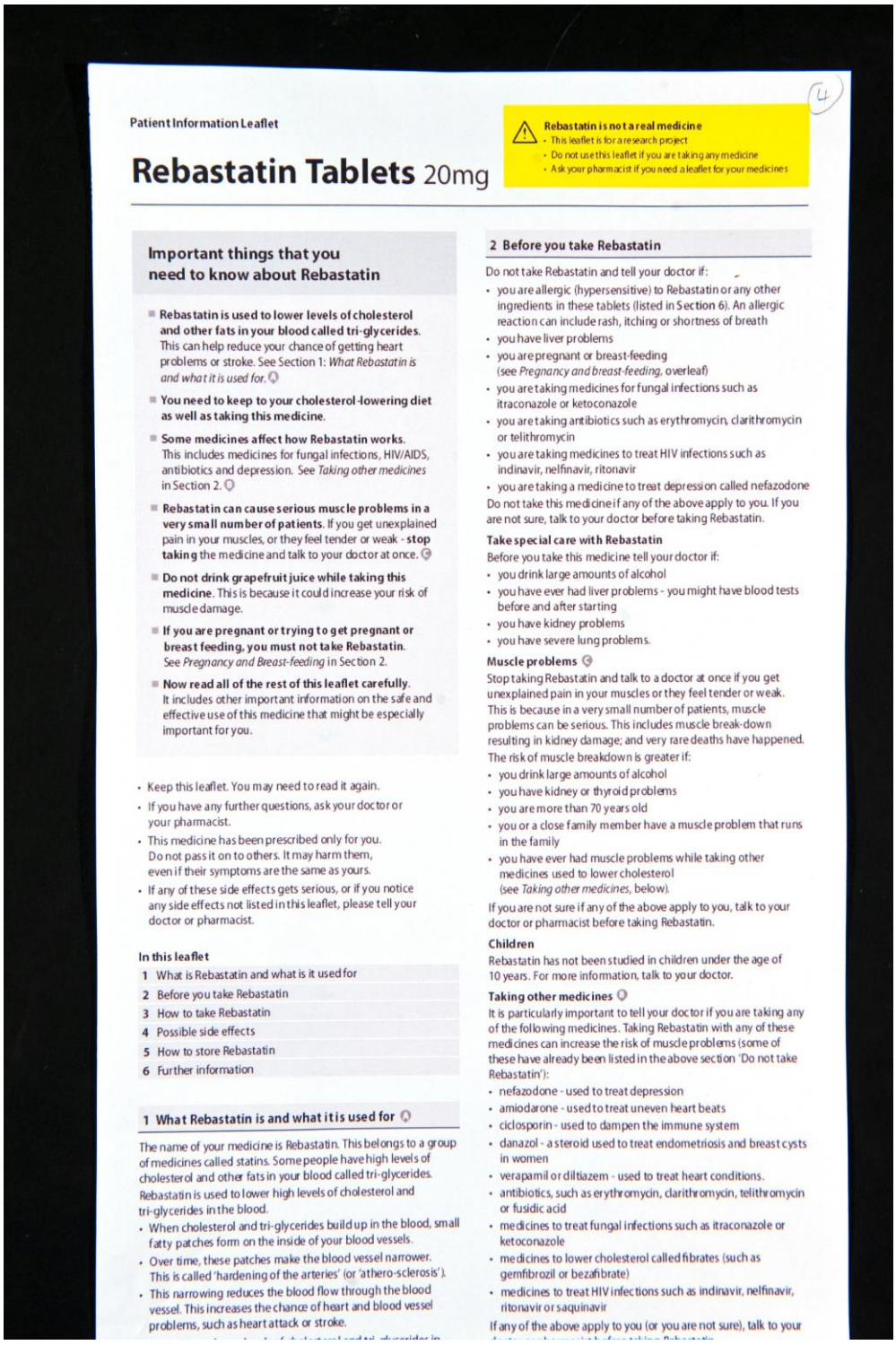
Who has reviewed this study?

The University of Leeds School of Healthcare Research Ethics Committee has reviewed this study.

If you agree to take part, would like more information or have any questions or concerns about the study please contact:

Mrs Rebecca Dickinson,
Research Nurse, School of Healthcare, University of Leeds, LS2 9LN
Tel: **0113 3431190,** E-mail: **r.dickinson@leeds.ac.uk**.

Appendix 16: Photograph of the leaflet used for the user-testing study (chapter 4/ study 3)



Patient Information Leaflet

Rebastatin Tablets 20mg

Rebastatin is not a real medicine
- This leaflet is for a research project
- Do not use this leaflet if you are taking any medicine
- Ask your pharmacist if you need a leaflet for your medicines

Important things that you need to know about Rebastatin

- **Rebastatin is used to lower levels of cholesterol and other fats in your blood called tri-glycerides.** This can help reduce your chance of getting heart problems or stroke. See Section 1: *What Rebastatin is and what it is used for.*
- **You need to keep to your cholesterol-lowering diet as well as taking this medicine.**
- **Some medicines affect how Rebastatin works.** This includes medicines for fungal infections, HIV/AIDS, antibiotics and depression. See *Taking other medicines* in Section 2.
- **Rebastatin can cause serious muscle problems in a very small number of patients.** If you get unexplained pain in your muscles, or they feel tender or weak - **stop taking** the medicine and talk to your doctor at once.
- **Do not drink grapefruit juice while taking this medicine.** This is because it could increase your risk of muscle damage.
- **If you are pregnant or trying to get pregnant or breast feeding, you must not take Rebastatin.** See *Pregnancy and Breast-feeding* in Section 2.
- **Now read all of the rest of this leaflet carefully.** It includes other important information on the safe and effective use of this medicine that might be especially important for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This medicine has been prescribed only for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of these side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet

1 What is Rebastatin and what is it used for
2 Before you take Rebastatin
3 How to take Rebastatin
4 Possible side effects
5 How to store Rebastatin
6 Further information

1 What Rebastatin is and what it is used for

The name of your medicine is Rebastatin. This belongs to a group of medicines called statins. Some people have high levels of cholesterol and other fats in your blood called tri-glycerides. Rebastatin is used to lower high levels of cholesterol and tri-glycerides in the blood.
- When cholesterol and tri-glycerides build up in the blood, small fatty patches form on the inside of your blood vessels.
- Over time, these patches make the blood vessel narrower. This is called 'hardening of the arteries' (or 'athero-sclerosis').
- This narrowing reduces the blood flow through the blood vessel. This increases the chance of heart and blood vessel problems, such as heart attack or stroke.

2 Before you take Rebastatin

Do not take Rebastatin and tell your doctor if:
- you are allergic (hypersensitive) to Rebastatin or any other ingredients in these tablets (listed in Section 6). An allergic reaction can include rash, itching or shortness of breath
- you have liver problems
- you are pregnant or breast-feeding (see *Pregnancy and breast-feeding*, overleaf)
- you are taking medicines for fungal infections such as itraconazole or ketoconazole
- you are taking antibiotics such as erythromycin, clarithromycin or telithromycin
- you are taking medicines to treat HIV infections such as indinavir, nelfinavir, ritonavir
- you are taking a medicine to treat depression called nefazodone

Do not take this medicine if any of the above apply to you. If you are not sure, talk to your doctor before taking Rebastatin.

Take special care with Rebastatin

Before you take this medicine tell your doctor if:
- you drink large amounts of alcohol
- you have ever had liver problems - you might have blood tests before and after starting
- you have kidney problems
- you have severe lung problems.

Muscle problems

Stop taking Rebastatin and talk to a doctor at once if you get unexplained pain in your muscles or they feel tender or weak. This is because in a very small number of patients, muscle problems can be serious. This includes muscle break-down resulting in kidney damage; and very rare deaths have happened. The risk of muscle breakdown is greater if:
- you drink large amounts of alcohol
- you have kidney or thyroid problems
- you are more than 70 years old
- you or a close family member have a muscle problem that runs in the family
- you have ever had muscle problems while taking other medicines used to lower cholesterol (see *Taking other medicines*, below).

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking Rebastatin.

Children

Rebastatin has not been studied in children under the age of 10 years. For more information, talk to your doctor.

Taking other medicines

It is particularly important to tell your doctor if you are taking any of the following medicines. Taking Rebastatin with any of these medicines can increase the risk of muscle problems (some of these have already been listed in the above section 'Do not take Rebastatin'):
- nefazodone - used to treat depression
- amiodarone - used to treat uneven heart beats
- ciclosporin - used to dampen the immune system
- danazol - a steroid used to treat endometriosis and breast cysts in women
- verapamil or diltiazem - used to treat heart conditions.
- antibiotics, such as erythromycin, clarithromycin, telithromycin or fusidic acid
- medicines to treat fungal infections such as itraconazole or ketoconazole
- medicines to lower cholesterol called fibrates (such as gemfibrozil or bezafibrate)
- medicines to treat HIV infections such as indinavir, nelfinavir, ritonavir or saquinavir

If any of the above apply to you (or you are not sure), talk to your

Appendix 17: Results of the pilot user-test (chapter 4/ study 3)

P	Criteria	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15
1	Found	FD	F	F	F	F	F	FD	F	FD	F	F	F	FD	F	FD
	Unders	U	U	U	U	U	U	U	U	NU	U	U	U	U	U	U
	Headline	Yes	Yes	Yes	NA	No	No	No	NA	No	No	NA	NA	NA	NA	NA
	Signpost	NA	NA	NA	NA	No	No	NA	NA	NA	NA	NA	NA	NA	NA	NA
2	Found	F	F	F	F	F	NF	F	F	F	F	F	F	F	F	F
	Unders	U	U	U	U	U	NU	U	U	U	U	U	U	U	U	U
	Headline	Yes	Yes	No	NA	NA	No	Yes	NA	No	No	NA	NA	NA	NA	NA
	Signpost	NA	NA	NA	NA	NA	No	NA	NA	NA	No	NA	NA	NA	NA	NA

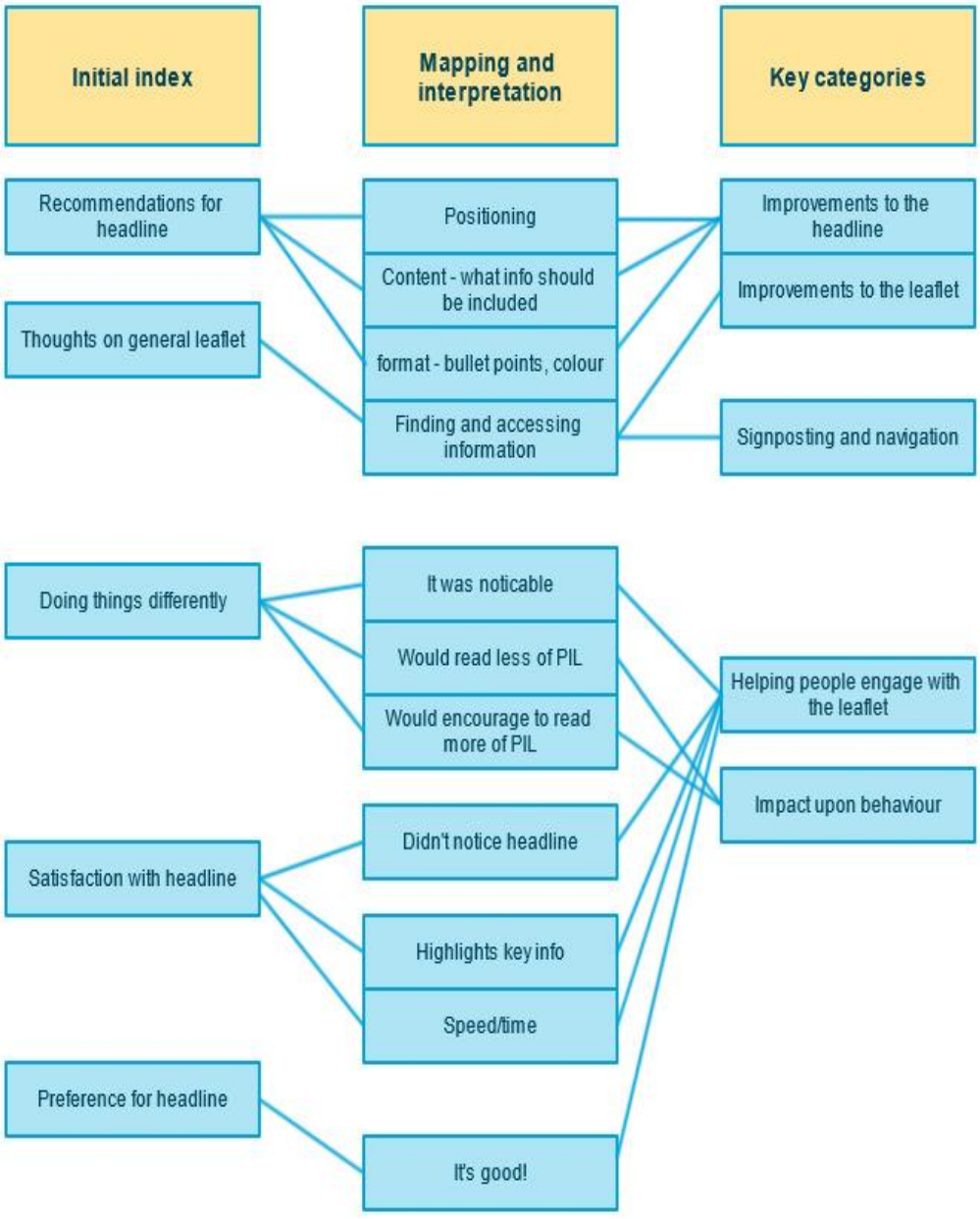
*Highlighted columns are indicative of questions which test the headline section

Appendix 18: Example of charting for thematic analysis (chapter 4/ study 3)

Participant	Can you recommend any improvements	Would you do anything differently if you leaflet came with HEADLINE	Signposting.	Other comments
01PM F, 52, 1, no lit. Difficult interview/ found it difficult to read.	No noted	When people are on medicines they read the most important things and the side effects, not everything. I don't look for everything, But what it is with me is that it takes me a while to register things and I think I would go for the most important things and I think it tells you on there, and what it's used for	You'll understand it better and you'll find all the rest of it when you are looking for it. It's like a book and then you look for that number, like on here (refers to signpost?) What did I think of what... Oh like A, B and C, Oh yeah I didn't notice them. I didn't see them and I should've and I didn't. I didn't see them. I didn't take any notice. think a lot of people are like me though. Aha, like A goes with A. Yeah. No, I didn't see them, I didn't take any notice of them or I would have found them answers quicker…	None noted

			Yes and It would have helped me find them quicker. But I didn't notice and that's what took my time. Stupid that… I would have found them answers quicker.	
Participant	Can you recommend any improvements	Would you do anything differently if you leaflet came with HEADLINE	Signposting.	Other comments
02 SW F, 56, 1, no lit, Took a while with the interview, but was slow and systematic. Struggled in parts but understood that layout of the leaflet in general.	None noted	I think I would be more liable to read that bit and not any of the other, just read the important things bit and not read any of the other	No, I didn't. I never used them once and I'd only noticed them now. That is very good really. That would have saved me having to go all the way through it. I think they should be underlined a bit more though. Cause when I was reading that it never dawned on me, until you said now. And I probably would have found it a lot quicker. That is definitely a good way	None noted

Appendix 19: Example of the mapping and interpretation diagram for qualitative element of the user-testing study (chapter 4/ study 3)



Appendix 20: List of leaflets surveyed indicating generic or brand and manufacturers (chapter 5/ study 4)

Medicine	Top 50 or newly licensed	Branded/generic	Listed manufacturers	Chosen manufacturers	Date chosen
Ramipril	Top 50	Generic	Accord, Zentiva, Rosemount, Pfizer, Aurobindo, Actavis, Winthrop	Winthrop Pharmaceuticals	07.01.13
Simvastatin	Top 50	Generic	Dexcel, Actavis, Zentiva, Kent Pharmaceuticals, Aurobindo, Rosemont, Accord	Zentiva	07.01.12
Amitriptyline Hydrochloride	Top 50	Generic	Accord, Mercury, Avantis	Accord	07.01.13
Tramadol	Top 50	Generic	Mercury, Actavis, Kent, Accord	Accord	09.01.13
Metformin	Top 50	Generic	Pfizer, Zentiva, Wockhardt, Winthrop	Winthrop Pharmaceuticals	09.01.13
Omeprazole	Top 50	Generic	Zentiva, Dexcel, Actavis	Zentiva	07.01.13
Hydrocortisone	Top 50	Generic	Actavis	Actavis	07.01.13
Alendronic acid	Top 50	Generic	Actavis, Rosemont, Accord, Zentive	Rosemont	07.01.13
Lactulose	Top 50	Generic	Intrapharm laboratories	Intrapharm	07.01.13

				Lamoratories	
Atenolol	Top 50	Generic	Wockhardt, Actavis, Accord	Wockhardt	07.01.12
Co-codamol	Top 50	Generic	Boots, Zentiva, Mercury Pharma Group, Actavis, Bayer	Boots	07.01.12
Levothyroxine	Top 50	Generic	Wockhardt, Mercury, Actavis	Mercury Pharam Group	07.01.12
Beclamethosone	Top 50	Generic	Orion Pharma	Orion Pharma	07.01.12
Losartan	Top 50	Generic	Dexcel, Kent Pharmaceuticals Ltd., Zentiva, Actavis, Accord	Kent Pharmaceuticals Ltd.	09.01.13
Lisinopril	Top 50	Generic	Zentive, Accord, Aurobind, Milpharm Ltd., Actavis	Actavis	09.01.13
Zopiclone	Top 50	Generic	Kent pharmaceuticals Ltd., Actavis	Kent Pharmaceuticals Ltd.	09.01.13
Naproxen	Top 50	Generic	Actavis, Accord, Aurobind pharm - Milpharm Ltd.	Actavis	09.01.12
Flucloxacillin	Top 50	Generic	Actavis, Kent Pharmaceuticals, Aurobind pharm –Milpharm ltd.	Kent pharmaceuticals	09.01.13
Aspirin	Top 50	Generic	Actavis, Wockhardt, Interpharm, The Boots Company Plc.,	The Boots Company Plc.	09.01.13
Folic Acid	Top 50	Generic	Wockhardt, Intrapharm, Actavis	Wockhardt	09.01.13

Isosorbide Mononitrate	Top 50	Generic	Accord, Actavis	Actavis	09.01.13
Furosemide (injection)	Top 50	Generic	Hameln pharmaceuticals Ltd., Accord, Actavis, Mercury Pharma Group, International Medication Systems (UK) Ltd., Wockhardt UK Ltd.	Hameln Pharmaceuticals Ltd.	09.01.13
Amoxicillin	Top 50	Generic	Accord, Kent Pharmaceuticals Ltd., Aurobind Pharm - Milpharm	Accord	09.01.12
Bendroflumethiazide	Top 50	Generic	Actavis	Actavis	09.01.13
Diazepam	Top 50	Generic	Actavis, Desitin Pharma Ltd, Hameln Pharmaceuticals,	Desitin Pharma Ltd.	09.01.13
Ibuprofen	Top 50	Branded - Brufen	Brand identified in BNF Sept 2012	Abbot Healthcare products	07.01.13
Warfarin sodium	Top 50	Branded - Marevan	Brand identified in BNF Sept 2012	Mercury Pharma Group	07.01.13
Tamsulosin Hydrochloride	Top 50	Branded - Flomaxtra	Brand identified in BNF Sept 2012	Astellas	07.01.13
Amlodipine	Top 50	Branded - Isitin	Brand identified in BNF Sept 2012	Pfizer	07.01.13
Perindopril	Top 50	Branded – Coversyl Arginine	Brand identified in BNF Sept 2012	Servier	07.01.13

Bisoprolol	Top 50	Branded - Cardicor	Brand identified in BNF Sept 2012	Merck Serono	07.01.13
Diclofenac	Top 50	Branded - Volterol	Brand identified in BNF Sept 2012	Novartis	07.01.13
Fluoxetine	Top 50	Branded - Prozac	Brand identified in BNF Sept 2012	Lilly	07.01.13
Alfa-calciferol *	Top 50	Branded – One-Alpha	Brand identified in BNF Sept 2012	Leo Pharma	26.03.13
Citalopram	Top 50	Branded - Cipramil	Brand identified in BNF Sept 2012	Lundbeck	07.01.13
Doxazosin	Top 50	Branded - Cardura	Brand identified in BNF Sept 2012	Pfizer	07.01.13
Paracetamol	Top 50	Branded - Panadol	Brand identified in BNF Sept 2012	GSK	07.01.13
Lansoprazole	Top 50	Branded - Zoton	Brand identified in BNF Sept 2012	Wyeth	07.01.13
Atorvastatin	Top 50	Branded - Lipitor	Brand identified in BNF Sept 2012	Pfizer	07.01.13
Cetirizine	Top 50	Branded - Pollenshield	Brand chosen at random from eMC	Actavis	07.01.13
Digoxin	Top 50	Branded - Lanoxin	Brand identified in BNF Sept 2012	Aspen	07.01.13
Prednisolone	Top 50	Branded - Deltacortril	Brand identified in BNF Sept 2012	Alliance	07.01.13
Candesartan Cilexetil	Top 50	Branded - Amais	Brand identified in BNF Sept 2012	Takeda	07.01.13
Senna	Top 50	Branded - Senokot	Brand identified in BNF Sept 2012	Reckitt Benckiser	07.01.13

Gliclazide	Top 50	Branded - Diamicron	Brand identified in BNF Sept 2012	Servier	07.01.13
Clopidogrel	Top 50	Branded - Plavix	Brand identified in BNF Sept 2012	SANOFI	07.01.13
Fluticasone	Top 50	Branded - Flixotide	Brand identified in BNF Sept 2012	Allen and Hanbury's	09.01.13
Tiotropium	Top 50	Branded - Spiriva	Brand identified in BNF Sept 2012	Boehringer Ingleheim	09.01.13
Salbutamol	Top 50	Branded - Pulvinal	Brand identified in BNF Sept 2012	Chiesi Limited	09.01.13
Felodipine	Top 50	Branded - Plendil	Brand identified in BNF Sept 2012	AstraZenica	09.01.13
Deferasirox	Black triangle	Beanded - EXJADE	NA	Novartis	19.02.13
Pasireotide	Black triangle	Branded - Signifor	NA	Novartis	19.01.13
Fampridine	Black triangle	Branded - Fampyra	NA	Biogen Idec	19.02.13
Perampanel	Black triangle	Branded - Fycompa	NA	Eisai Europe Limited	19.02.13
Canakinumab	Black triangle	Beanded - Ilaris	NA	Novartis	19.02.13
Mifamurtide	Black triangle	Branded - MEPACT	NA	Takeda	19.01.13
Bromfenac	Black triangle	Branded - Yellox	NA	Bausch and Lomb	19.02.13
Velaglucerase	Black triangle	Branded - VPRIV	NA	Shire Human Genetics	19.02.13
Palifermin	Black triangle	Branded - Keipvance	NA	Swedish Orphan Biovitrum	19.02.13

Ticagrelor	Black triangle	Branded- Brilique	NA	AstraZenica	19.02.13
Natalizumab	Black triangle	Branded - TYSABRI	NA	Biogen Idec	19.02.12
Fingolimod	Black triangle	Branded - Gilenya	NA	Novartis	19.02.13
Indacaterol	Black triangle	Branded – Onzbrez inhaler	NA	Novartis	19.02.13
Belimumab	Black triangle	Branded - Benlysta	NA	GSK	19.02.13
Idursulfase	Black triangle	Branded - Elaprase	NA	Shire Human Genetics	19.02.13
Exenatide	Black triangle	Branded - BYDUREON	NA	Bristol Myers Squibb Astra Zenica	19.02.13
Telaprevir	Black triangle	Branded - INCIVO	NA	Jannsen Cilag	19.02.13
Temsirolimus	Black triangle	Branded - Torisel	NA	Pfizer	19.02.13
Ruxolitinib	Black triangle	Branded - Jakavi	NA	Novartis	19.02.13
Pazopanib	Black triangle	Branded - Votrient	NA	GlaxoSmithKlein	19.02.13
Boceprevir	Black triangle	Branded - Victrelis	NA	Merck, Sharpe and Dohme	19.02.13
Rifaximin	Black triangle	Branded - Xifaxanta	NA	Norgine	19.02.13
Prucalopride	Black triangle	Branded - Resolor	NA	Shire Pharmaceuticals	19.02.13

Bivalirudin	Black triangle	Branded - Angiox	NA	The Medicines Company	19.02.13
Vinflunine	Black triangle	Branded - Javlor	NA	Pierre Fabin	19.02.13
C1 Inhibitor (Human)	Black triangle	Branded - Cinryze	NA	ViroPharma	19.02.13
Cannabidiol	Black triangle	Branded - Savitex	NA	GW Pharma (Bayer)	19.02.13
Erdosteine	Black triangle	Branded - Erdosteine	NA	Galen Limited	19.02.13
Ranolazine	Black triangle	Branded - Ranexa	NA	A. Menarini Farmaceutica Internazionale SRL	19.01.13
Bendamustine	Black triangle	Bradned - Levact	NA	Napp Pharmacueticals	19.02.13
Conestat Alfa	Black triangle	Branded - Ruconest	NA	Swedish Orphan Biovirtum	19.02.13
Axitinib	Black triangle	Branded - Inlyta	NA	Pfizer	19.02.13
Fondaparinux	Black triangle	Branded - Arixitra	NA	GlaxoSmithKlein	19.02.13
Tolcapone	Black triangle	Branded - Tasmar	NA	Meda Pharmaceuticals	19.02.13
Tocilizumab	Black triangle	Branded -	NA	Roche Products	19.02.12

		RoActemra		Limited	
Agomelatine	Black triangle	Branded - Valdoxan	NA	Les Laboratoires Servier	
Certolizumab	Black triangle	Branded - Cimzia	NA	UCN Pharma Limited	20.02.13
Ferumoxytol	Black triangle	Branded - Rienso	NA	Takeda	20.02.13
Aclidinium	Black triangle	Branded – Eklira Genuair	NA	Almirall	20.02.13
Tapentadol	Black triangle	Branded - Palexia	NA	Grunenthal	20.02.13
Rilpivirine	Black triangle	Branded - EDURANT	NA	Jannsen Cilag	20.02.13
Ofatumumab	Black triangle	Branded - Arzerra	NA	GlaxoSmithKlein	20.02.13
Fidaxomicin	Black triangle	Branded - Dificlir	NA	Astellas Pharma	20.02.13
Asenapine	Black triangle	Branded - Sycrest	NA	Lundbeck	20.02.13
Apixaban	Black triangle	Branded - Eliquis	NA	Bristol-Myers Squibb Pfizer	20.02.13
Cabazitaxel	Black triangle	Branded - JEVTANA	NA	Sanofi	20.02.13
Bevacizumab	Black triangle	Branded - Avastin	NA	Roche Products Limited	20.02.13
Abiraterone	Black triangle	Branded – Zytiga	NA	Jannsen Cilag	20.02.13

Varenicline	Black triangle	Branded - Champix	NA	Pfizer	20.02.13
Dronedarone	Black triangle	Branded - Multaq	NA	Sanofi	20.02.13

*No Ergocalciferol PIL was available on the eMC, therefore we chose the nearest pharmacological equivalent which is alfacalciferol.

Appendix 21: Example of patient information sheet used for study 5

Participant Information Sheet

Title of Study: The impact of benefit information in medicines leaflets.

We would like to invite you to take part in this study but before you decide, please read the following information.

You can choose not to take part without having to give a reason and without penalty.

What is the purpose of this study?

When a medicine is prescribed all patients receive an information leaflet in the medicine box. We would like to find out more about what people think about this information. We would like to ask your views on different ways of presenting some of the information that could be provided.

One important issue we would like to find out about looks at including **benefit information** in medicine leaflets. Benefit information includes information on how the medicine works, what it does and its possible benefits. We would like to find out what patients who take medicines think about the inclusion of this information in their medicines leaflets.

By doing so we hope to understand more about how we can improve the information provided with medicines and help patients understand more about their medicines.

Who is doing the study?

Researchers from the University of Leeds are doing the study. Mrs. Rebecca Dickinson is doing the study as part of her PhD. The supervisor is Professor Theo Raynor.

Who is being asked to participate?

You have been invited to participate because you are currently receiving a prescription for **simvastatin**. If you would like to take part you must be able to speak and read English. Your GP will be aware of your invitation to participate in this study.

What will be involved if I take part in this study?

- If you are interested we will invite you to take part in an interview. You will be given some medicine leaflets which contain information about the benefits of your medicine to look at and we will ask for your views.
- A researcher will ask questions and you will be free to talk about your views on the medicines leaflets and the benefit information.
- The interview will take approximately 1 hour in total and can be done somewhere convenient for you, this could be at your own home, or if you prefer an alternative location such as Leeds University or the GP practice.

What are the advantages and disadvantages of taking part?

There are few disadvantages of taking part in this study. You may find the task tiring but you will be free to stop the interview at any time without giving a reason. You may not get any personal medical benefits from agreeing to take part. However, the study may highlight better ways of providing information with medicines.

Some of the benefit information provided about your medicines might be surprising or difficult to understand and reading about it might raise some new questions about your medicines. If you have any questions about your medicines as a result of taking part in this research, and which cannot be addressed by the researcher, you should speak with your GP or pharmacist. If you do participate you will be given a £20 gift voucher at the end of the meeting to acknowledge the time you have given.

Can I withdraw from the study at any time?

You do not have to take part in the study, no-one will mind if you say no. You can say yes and then change your mind. You are free to withdraw from the study at any time and do not have to give a reason why. If you do change your mind please let Rebecca Dickinson know within 1 month of participation. After this time it might be difficult to remove any data you provide from the research reports, although this data will be anonymous.

Will the information I give be kept confidential?

To keep an accurate record of what is discussed the meeting will be audio recorded. The recordings will be typed up and made anonymous. Then the recordings will be destroyed. All information you offer during the research will be kept private and confidential. It will be stored for 4 years in a locked filing cabinet in a secure office. It will not be possible to identify you in any way from the publications, reports and guidelines that are produced. There is a duty to disclose to a relevant person if a risk of harm to self or others is disclosed during the interview.

What will happen to the results of the study?

The results from the study will form part of a PhD thesis. They will be written as a document and sent for publication in a medical journal. We will also present the results of the study to the Medicines and Healthcare products Regulatory Agency to help them improve the regulations about patient information leaflets.

Who has reviewed this study?

The National Research Ethics Service has reviewed this application. Reference: 13/YH/0180

If you agree to take part, would like more information or have any questions or concerns about the study please contact:

Mrs Rebecca Dickinson
Research Nurse, School of Healthcare, University of Leeds, LS2 9LN.

Tel: **0113 3431190.** E-mail: **r.dickinson@leeds.ac.uk**

Appendix 22: Illustrative topic guide used to guide the interviews for study 5 (chapter 6). The topic guide was adapted for each interview.

Research study: The impact of benefit information in medicine leaflets

Historical questions

- Can you tell me about the information you got when you were first prescribed simvastatin?
  (Prompts: Who was this from? Was it spoken or in writing?)
- Have you ever seen an information leaflet like this inside your packet of medicine? What have you done with this information?
  (Prompts: Do you read it? When? Do you refer to it? How often? Do you keep the leaflets? How do you use the information?)

- In the last month, have there been any times where you have not taken your medicines as prescribed?

Benefit information

I'm going to show you 3 versions of a leaflet about your medicine which talks about the benefits of the medicine in different ways:

Refer to:

1) General description in words
2) In a 100 people like you who do not take this medicine, 22 will have a heart attack or stroke over the next five years. But if they all take Rebastatin over the next 5 years, 22 will have a heart attack or stroke.(NEGATIVE - no treatment first)
3) If 17 people like you take simvastatin over the next 5 years, 1 of them will be stopped having a heart attack or stroke.

- What did you think of this information?
- Have you ever seen or been told information like this before?

  *(**Prompt:** in another leaflet? Website? Has a doctor or pharmacist ever discussed this type of information with you?)*
- Which one of these did you prefer? Why?
- What changes if any would you recommend to this section?

  ***(Prompt:** explore issues with any concerns and anxieties, feeling reassured and informed. Also other types of benefit, for example revascularisation and lowering of cholesterol as benefits to be included? More or less benefit information?)*
- Can I ask some questions specifically about the **orange** statement?
- Here is a statement similar to first orange statement, only it is put in a **positive** way, that is it tells you how likely you are to not have a heart attack. Which of these statements do you prefer and can you tell me why. (Present positive on a slip of paper)

- This statement could be organised in a different way, with the numbers of those taking the medicine put before those who don't take the medicine, so it might say (read below). Can you tell me which of these you prefer and why?

3. ORANGE

In 100 people like you who take this medicine, 22 will have a heart attack or stroke. But if they do not take Rebastatin over the next 5 years, 28 will have a heart attack or stroke.

- Finally, can I ask what do you think about the phrase 'people like you'? *(Prompt: can you think of any alternatives?*

These leaflets already contain numbers about the chance of side effects of the medicine. Having these numbers would also tell you about the chance of benefit.

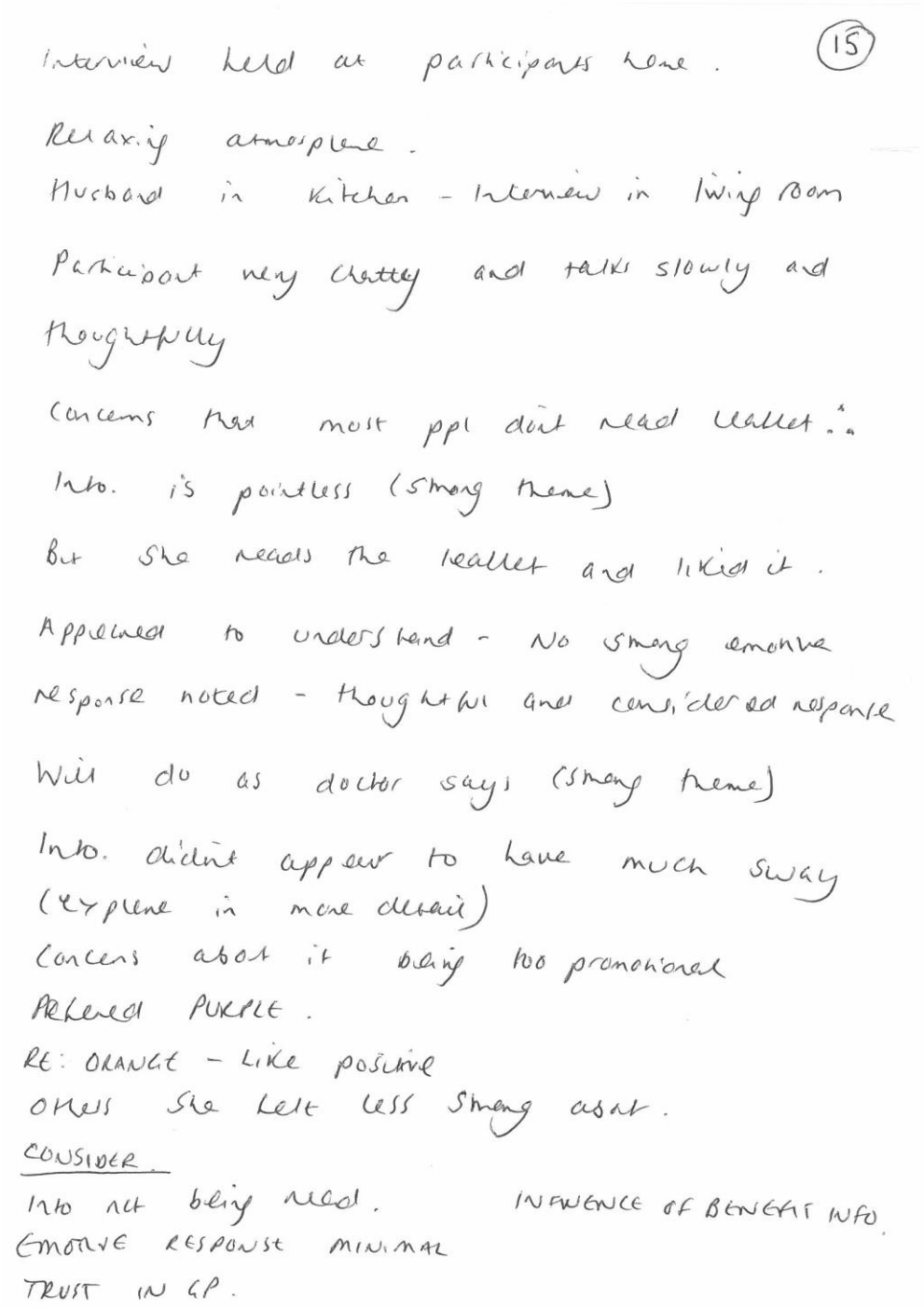
- Do you think that having this information about the chance of benefit and the chance of side effects helps you make a decision about whether the medicine is right for you?
- Imagine you received this information when you were first prescribed this medicine, what difference do you think this would have made to what you did and thought about the medicine?

  (Prompt: do you think you would do anything differently? *Change your medication? Take it differently? Stop your medication? Seek advice for Doctor or other HCP? Ask your family for advice? Look at the internet)*
- Do you think, if this type of information was commonplace in the leaflets, it would make people to do anything differently with their medicines?
- Having has our discussion, if you have the choice of having one of these formats which one would you have and why?

Additional questions (time permitting):

• Would you be interested in reading benefit information in other medicines leaflets? (Prompt: what about OTC medicines? Or medicines for a different condition? Or if you had a choice about different medicines to take? Prompt: about whether numbers or texts would be preferred in other medicines leaflets

Appendix 23: Example of field note written after benefit interview (chapter 6/ study 5)



Interview held at participants home. (15)

Relaxing atmosphere.
Husband in kitchen - Interview in living room

Participant very chatty and talks slowly and thoughtfully

Concerns that most ppl don't read leaflet.

Info. is pointless (strong theme)

But she reads the leaflet and likied it.

Appeared to understand - No strong emotive response noted - thoughtful and considered response

Will do as doctor says (strong theme)

Info. didn't appear to have much sway (explore in more detail)

Concern about it being too promotional

PREFERED PURPLE.

RE: ORANGE - Like positive

OTHERS She felt less strong about.

CONSIDER.

Info not being read. INFLUENCE OF BENEFIT INFO.

EMOTIVE RESPONSE MINIMAL

TRUST IN GP.

Appendix 24: Example of framework development for the interview stage (chapter 6/ study 5)

Quote	In-vivo code	Preliminary thoughts	Initial themes	Categories
Well, they just told us it was for lowering cholesterol. Erm… and you can read the leaflet, like you say, cos there's that much long words and you think, "What does that mean? What does that mean?" some of em are confusing but, and when I looked at the LDL and the HDL thing and I'm thinking, "Well, L for lardy, fats and stuff, those are bad ones", that's the way I looked at it. And the H ones, those are the happy ones, so they're good ones. And that's the way I saw the LDL [*laughs*].	• **The doctors told me it was for cholesterol.** • **The leaflet is too long… too long words. Confusing**	• **Source of information: written 'v' verbal** • **Reading the leaflet is difficult**	**Typical information behaviour.** **Typical leaflet-use**	**Typical Patient actions** • **Typical leaflet use.** **Barriers to benefit info.**
Oh, yeah, she told me everything, yeah, yeah, she was really good, because I take the heart medicines as well, as I say, I had two heart attacks, one in the classroom…And one in hospital when I got there, yeah, so, and I've got COPD as well. So I've got medication for that and sprays, so really, I'm a wreck [*laughs*]. So the tablets actually keep me going, basically, yeah.	• **Doctor told me everything** • **Heart attack, COPD,** • **The tablets keep me going**	• **Source of information: written 'v' verbal** • **Multiple health conditions** • **Positive medicine associations**	**Role of leaflet** **Health** **Experience with medicines**	**Typical patient actions**
After I got the letter from you, I'd just got a new month's supply, so I actually read them all, and I was bog-eyed by the by the end of it… you know!	• **I was bog-eyed by the end of it**	**Reading the leaflets is difficult**	**Perceptions of typical leaflet**	**Typical patient actions** • **Leaflet use and thoughts**
I:Do you normally read them or…? P:No. I:Do you read any of them?	• **Doesn't normally read leaflets unless**	• **Engagement with leaflet** • **Reading the leaflet**	**Engagement with leaflet**	**Typical patient actions** • **Leaflet use**

P:Sometimes, well, if it's a new one, yeah, but, like you say, sometimes you're reading and you don't know what you've read, you don't really understand what you've read.	**new medicine** • **You don't really understand what you have read**	**is difficult**		**and thoughts**
Yeah, exactly, yeah, yeah. I know what doesn't mix with this and you can't take this if you're taking that and it's… so you look through, "Do I take them? No, I don't" so you're alright, you can take em, but, yeah, sometimes they are a little bit confusing, especially as you're getting older as well	• I know what doesn't mix with this and you can't take this if you're taking that • "Do I take them? No, I don't" so you're alright, you can take em • sometimes they are a little bit confusing, especially as you're getting older as well	• **Leaflet tells her how to take/ what she can take them with** • **Reading the leaflet is difficult - AGE**	**Typical leaflet use** **Barriers to reading leaflet**	**Typical patient actions** • **Leaflet use and thoughts** **Barriers to benefit info**
Yes, a hundred people like you do not take, twenty eight will have a heart attack or a stroke but if they all take Rebastatin over the next five years, twenty	**Reads the leaflet** • Right, it only	• **Surprise at the benefit**	**Affect/ emotional responses**	**Initial response to benefit info**

two will have a heart attack. Right, it only lowers it by six, doesn't it?	lowers it by six, doesn't it?			
Well, it's clear enough but is it genuine, this, or not? Is it just like a make up type thing, say, if they hear what you're doing?	• **It's clear enough but is it genuine?** • **Is it just make-up type thing?**	• **Surprise at the benefit** • **Scepticism/ mistrust…**	**Initial response concerns**	**Initial response to benefit info**
Right. Mmm, yeah, it's clear enough, int it, like I say.	• it's clear enough,	• **understanding of information**	**Knowledge and understanding**	**Knowledge and understanding**
No, well, it, like I say, here where twenty eight will have an heart attack or stroke, but if they all take Rebastatin over the next five years, twenty two will have, well, yes, it does have a number but…	Reads the leaflet	Does not require coding		Does not require coding
It's, yeah, it's helpful, I suppose, yeah, but, I mean, what's the other one? Seventeen people over the next five years, one extra person will be prevented from having a heart attack or a stroke. There is, but there again, you don't know what lifestyle they were, what type of folk they, all these other things what come into it. Erm… yeah, they'd have to higher level of it to take statins anyway, don't they, they have to have a higher level of cholesterol.	• It's helpful I suppose [not convinced] • You don't know what the lifestyle is • They'd have to have high levels of it to take statins	• Some uncertainty about the benefit statement • How relevant is this information to me! • Who are these people? Are they similar to me?	• Barriers to benefit info	Impact of benefits • Barriers/ facilitators to benefit info

Appendix 25: Example of index applied to each interview (chapter 6/ study 5)

Typical patient actions

- Medicine-taking and beliefs about medicines
- Relationship with GP
- Decision-making
- Leaflet use and thoughts on the role of the leaflet
- Health and well-being
- Personal characteristics
- Experience with numbers
- Information seeking
- Initial information

Impact of benefit info

- Positives about benefit
- Concerns about benefit info
- Barriers to benefit info
- Impact on decision-making and medicine taking
- Impact on other behaviours
- Knowledge and understanding
- Initial response to benefit info
- Balance of harm and benefits.
- Timing of delivery of benefit info.
- On others

Talking about format

- NNT
- NF
- TEXTUAL
- Framing
- Other formats

- Wording of benefit info
- Desirable attributes of benefit info
- Numbers in general

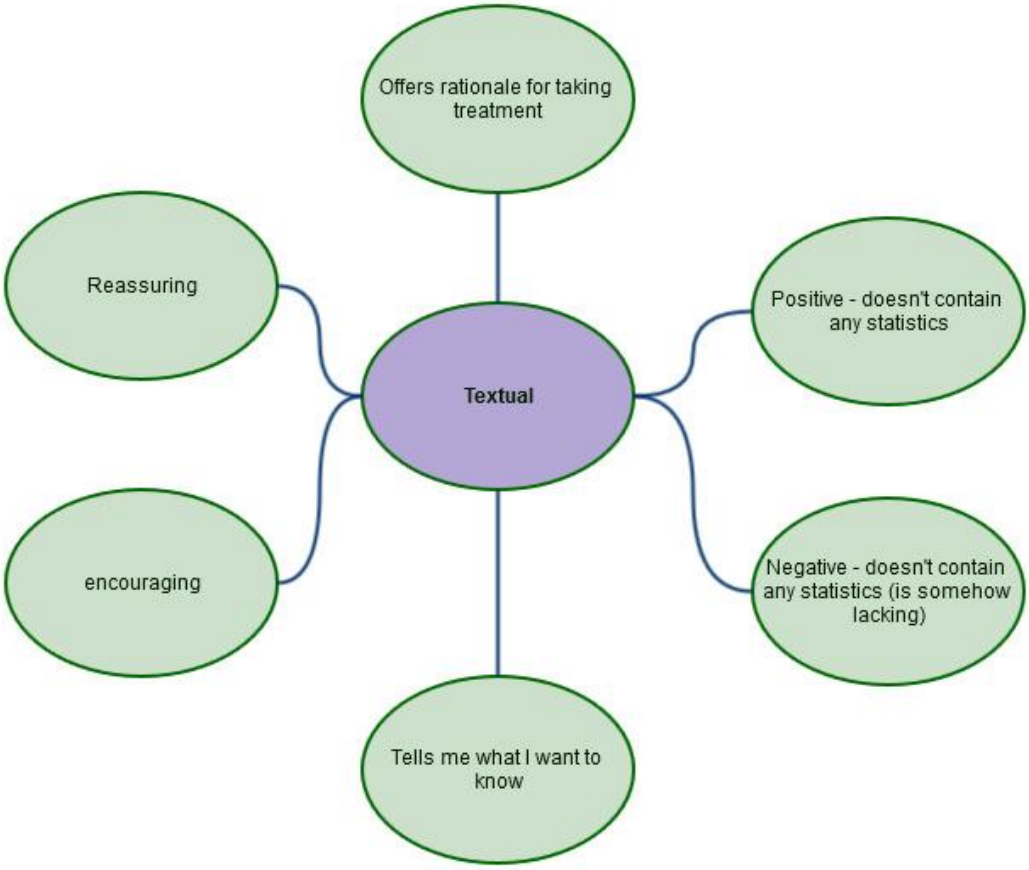
Talking about uncertainty

- Chance
- Risk

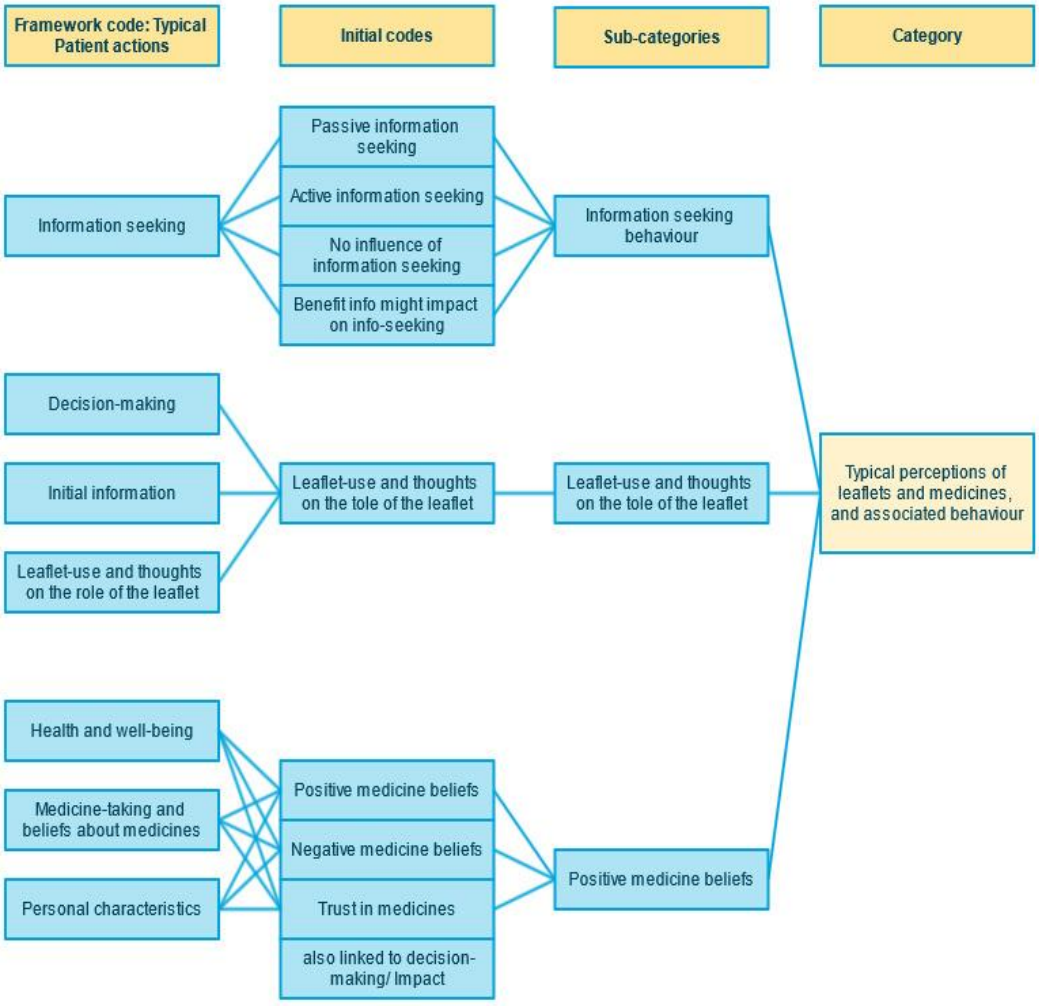
Talking about HCP relationships

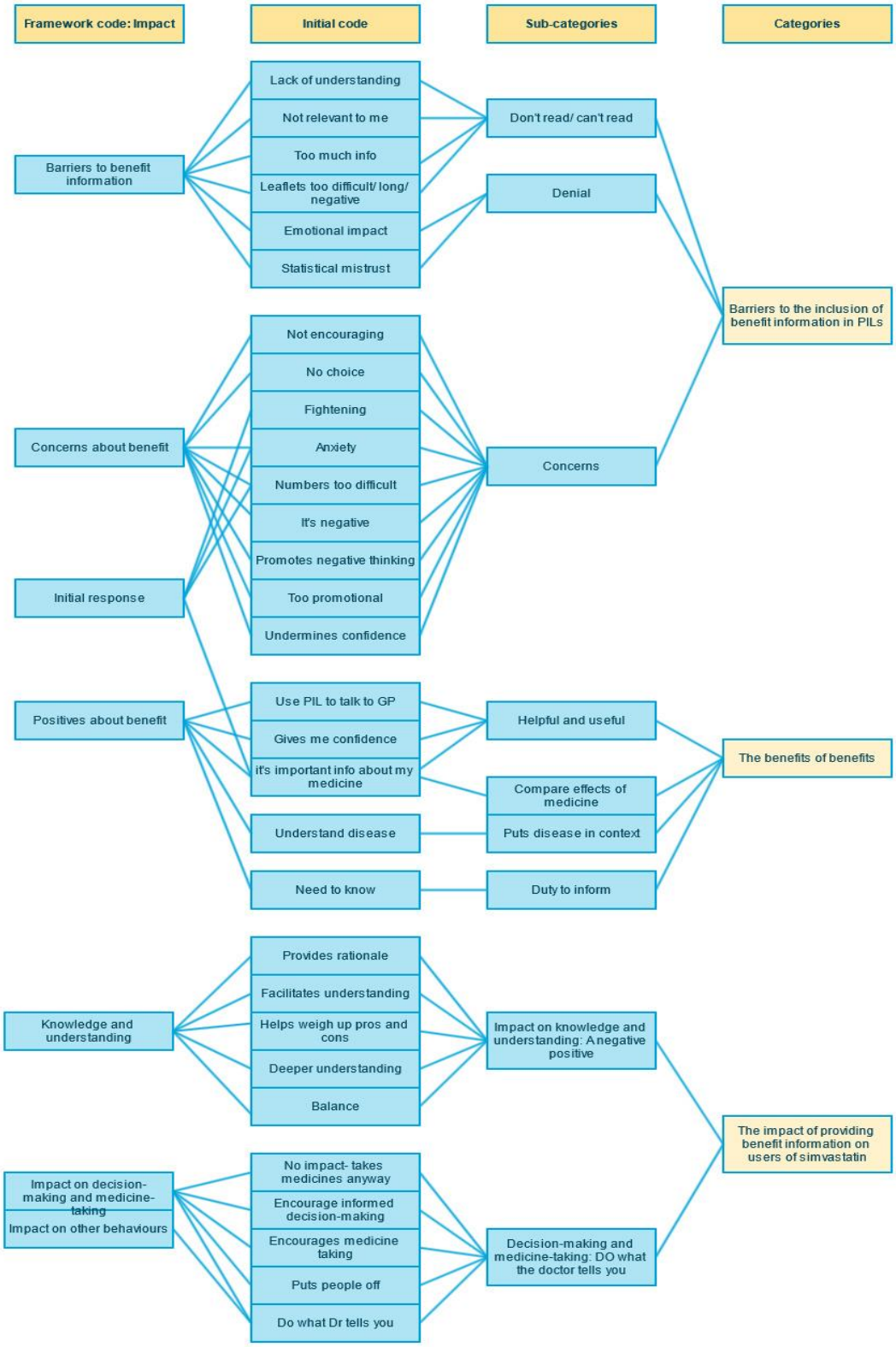
Other influences on medicine taking

Appendix 26: Example of mapping and interpretation for the descriptive analysis of the 'preference for format': Textual (Chapter 6/ study 5)



Appendix 27: Example of the mapping and interpretation stage of the framework analysis for the interview stage of the research (chapter 6/ study 5)




Framework code: Impact
Initial code
Sub-categories
Categories
Barriers to benefit information
Lack of understanding
Not relevant to me
Too much info
Leaflets too difficult/ long/ negative
Emotional impact
Statistical mistrust
Don't read/ can't read
Denial
Barriers to the inclusion of benefit information in PILs
Concerns about benefit
Initial response
Not encouraging
No choice
Fightening
Anxiety
Numbers too difficult
It's negative
Promotes negative thinking
Too promotional
Undermines confidence
Concerns
Positives about benefit
Use PIL to talk to GP
Gives me confidence
it's important info about my medicine
Understand disease
Need to know
Helpful and useful
Compare effects of medicine
Puts disease in context
Duty to inform
The benefits of benefits
Knowledge and understanding
Provides rationale
Facilitates understanding
Helps weigh up pros and cons
Deeper understanding
Balance
Impact on knowledge and understanding: A negative positive
Impact on decision-making and medicine-taking
Impact on other behaviours
No impact- takes medicines anyway
Encourage informed decision-making
Encourages medicine taking
Puts people off
Do what Dr tells you
Decision-making and medicine-taking: DO what the doctor tells you
The impact of providing benefit information on users of simvastatin