DEVELOPMENT AND VALIDATION OF A NEW INSTRUMENT TO MEASURE THE SOCIOECONOMIC IMPACT OF MEDICATION-RELATED PROBLEMS IN COMMUNITY PHARMACY SETTING

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'To err is human' is an old statement; however, human error can be stopped.

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ABSTRACT

The social and economic impact of medication-related problems (MRPs) of cardiovascular drugs has been under-reported in the community setting. Cardiovascular patients on multiple drug therapy do not know whether side-effects they experience are medication-related or due to their condition. The aim of this study was therefore to develop a system to detect medication side-effects of cardiovascular drugs and their impact on patients' social and economic wellbeing. The problem was overcome by developing a Socioeconomic Impact Profile (SEIP) questionnaire in which patients were asked if they experienced medication side-effects and what impact these MRPs have on their ability to work, socialise or use healthcare services.

The Socioeconomic Impact Profile (SEIP) consisted of 19 items in three domains. Each item was scored from 1 to 5 (1=all of the time, 2=most of the time, 3=some of the time, 4=a little of the time, 5=never). Higher scores indicated better socioeconomic wellbeing. Psychometric evaluation of the SEIP was carried out in 348 patients with cardiovascular disease (mean age=58.8; median=58.5; age range=37-84; male=175; female=173) recruited from five pharmacies across South West England and South Wales. The SEIP was generally acceptable to most patients with a mean completion time of 5.7 minutes. A high level of agreement among expert panel members on all items of the SEIP was achieved during content validation (Kappa coefficient "k"= 0.85). Factor analysis was used to identify redundant items and also provide initial evidence of construct validity. Evidence supporting internal consistency reliability was excellent (Cronbach's α =0.77-0.95).

To further examine the reliability of the SEIP, test-retest reliability was carried out in 92 patients with cardiovascular disease [50 (42.3%) males; mean age= 57.7; median=57.0; range=39-78] from five community pharmacies in South Wales and the reliability coefficient was high (r_s= 0.91-0.93). Evidence supporting the validity of the SEIP was also shown in 96 patients [49 (51.0%) males; mean age=63.1; median=63.0; age range=39-84] with a cardiovascular condition from the community pharmacy setting. Convergent validity was demonstrated as SEIP patient scores showed moderate to good correlation with the patient MIDAS (Myocardial Infarction Dimensional Assessment Scale) scores. Divergent validity was established as the

Short Form-12 health survey (SF-12) overall score demonstrated weak to moderate correlation with the SEIP scores. This study has established the practicality, reliability and validity of the SEIP as a promising socioeconomic related tool, especially in cardiovascular patients with medication-related problems in the community setting. Future work needs to focus on promoting use of the SEIP as part of the new community pharmacy initiatives in the UK for evaluation of treatment outcomes in patients with medication-related side-effects.

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ABBREVIATIONS

ACE	Angiotensin Converting Enzymes
ADR	Adverse Drug Reactions
ANOVA	Analysis of Variance
APQLQ	Angina Pectoris Quality of Life Questionnaire
ASCP	American Society of Consultant Pharmacists
ASHP	American Society of Hospital Pharmacists
CFA	Confirmatory Factor Analysis
CHD	Coronary Heart Disease
CHF	Congestive Heart Failure
DRPs	Drug Related Problems
EFA	Exploratory Factor Analysis
HMS	Health Measurement Scale
IF	Image Factoring
IHD	Ischaemic Heart Disease
MAI	Medication Appropriateness Index
MAP	Minimum Average Partial
MAR	Missing At Random
MCAR	Missing Completely At Random
MCS	Mental Component Summary
MIDAS	Myocardial Infarction Dimensional Assessment Scale
MILQ	Multidimensional Index of Life Questionnaire

MLHF	Minnesota Living with Heart Failure Questionnaire
MRPs	Medication Related Problems
MUR	Medicine Use Review
NCC-MERP	National Co-ordinating Council for Medication Error Reporting & Prevention
PAF	Principal Axis Factoring
PAS	Problem Analysis Solution
PCA	Principal Component Analysis
PCI	Pharmaceutical Care Issue
PCS	Physical Component Summary
PCNE	Pharmaceutical Care Network Europe
PF	Principal Factor
PDA	Personal Digital Assistant
PI-DOC	Problem Intervention Documentation
QLI-CV	Quality of Life Index Cardiac Version
QLMI	Quality of Life after Myocardial Infarction
QOL	Quality Of Life
QUM	Quality Use of Medicine
SAQ	Seattle Angina Questionnaire
SEIP-MRP	Socioeconomic Impact Profile Medication Related Problems
SF-12	Short Form-12
SI	Summary Index
TOM	Therapeutic Outcome Monitoring

GLOSSARY OF TERMS

Applicability	Describes the content and emphasis of an instrument in terms of appropriateness of wording, clarity and simplicity of language.
Construct Validity	Describes the extent to which a measure behaves in a manner consistent with its referent theoretical or logical properties by comparison with other measures and population characteristics.
Content Validity	Describes how adequately the items sampled represent the range of each domain assessed by an instrument.
Convergent Validity	Describes the extent of agreement between the instrument and measures of related and similar constructs.
Comprehensiveness	Describes how thoroughly the domain(s) of interest in a measure are sampled by the items or questions included in that measure.
Criterion Validity	Describes the extent of agreement between the instrument and a designed gold standard or 'criterion'.
Discriminative Validity	Describes the ability of an instrument to distinguish between different populations with different health-related characteristics.

Divergent Validity	Describes the extent of agreement between the instrument and measures of related yet different constructs.
Face Validity	Describes the extent to which the items, on the face of it, appear to be measuring the variables they claim to measure.
Internal Consistency	Describes the average degree of association or homogeneity between the items in the test.
Inter-Rater Reliability	Describes the degree of concordance shown between two or more raters in assessing the HRQOL of a common cohort of subjects using the same HRQOL instrument.
Practicality	Describes the feasibility of using an instrument in its intended population and clinical setting.
Responsiveness	Describes an equivalent term to sensitivity.
Sensitivity	Describes an instrument's sensitivity to small clinically important changes in an individual's HRQOL
Test-Retest Reliability	Describes the stability of an instrument over time by assessing the extent to which a score can be replicated under constant conditions or equivalent testing situations.

CHAPTER 1

General Introduction

BACKGROUND

Cardiovascular disease

Cardiovascular disease is the number one cause of death globally, according to the World Health Organisation's report (Gaziano, 2007). It is the leading cause of death in developed countries such as the UK and the US today, despite the fact that many of the major risk factors for coronary disease have been identified (Hobbs and Boyle, 2004). An estimated 17.5 million people died from cardiovascular disease in 2005, representing 30% of all global deaths (Figure 1). It is the number one cause of death in America, responsible for more than 40% of annual deaths (Van den bemt et al., 2000) and has remained the leading cause of death in the UK responsible for about 20% of deaths in 2001. 85% of those deaths occurred in people aged over 65 years, although the disease remains a significant cause of premature mortality, particularly amongst men aged 45-64 years (Yuen, 2003).

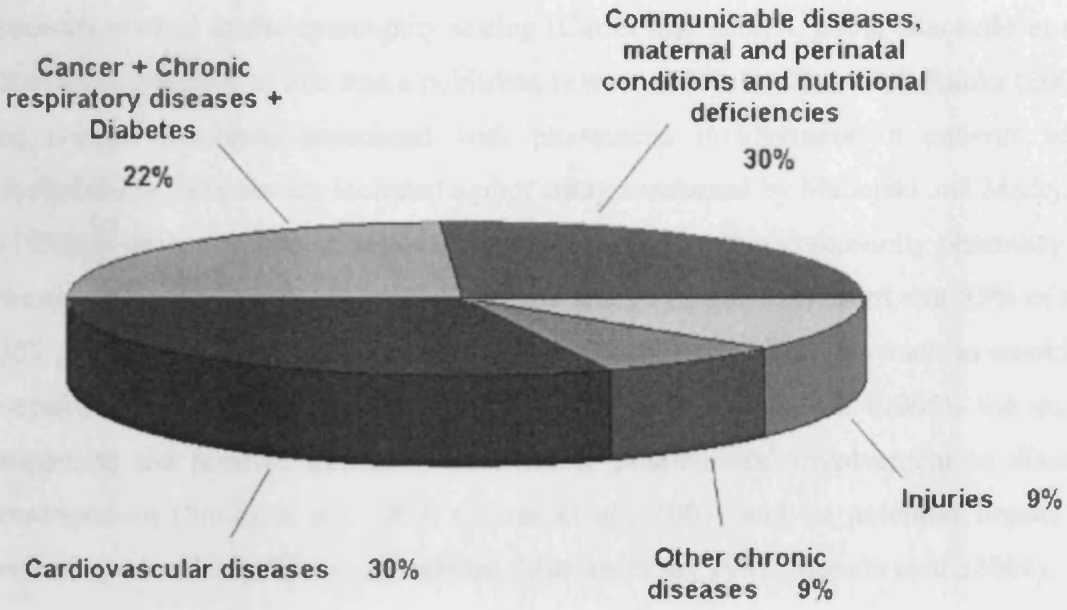
Cardiovascular diseases include myocardial infarction, angina, hypertension, congestive heart failure (CHF), stroke, atherosclerosis and other diseases of the circulatory system. The chronic nature of cardiovascular disease and its contribution to high medical resource utilisation, costs and high rates of morbidity and mortality make it an ideal disease category upon which managed care organisations may focus (Kaiser, 2002). In the recent Health Statistics report published by the UK office of Health Economics (Hawe, 2008), coronary heart disease (CHD) was the most prevalent fatal disease amongst the UK male working population and is responsible for about 14% of working years of life lost for men. Ischaemic heart disease (IHD) remains the most common cause of death in adults and accounts for some 200,000 deaths per year in the UK including 70% of sudden natural deaths and 127,000 infarct deaths (Scott, 1999). Around one-third of 50- to 59-year old men have evidence of IHD, and this proportion increases with age (Scott, 1999).

Economic burden of cardiovascular disease

Studies have shown that cardiovascular diseases impose a significant economic and humanistic burden on patients and society (Johnson and Bootman, 1997; Mackay and Mensah, 2004; Leal et al., 2006; Haase et al., 2006; Gaziano, 2007). In the United

States of America (USA) for example, the total annual expenditure for treating heart failure in 1991 was estimated to cost around $38 billion, with the majority of spending related to direct hospital costs (O'Connell, 2000). A similar study carried out in 2002 showed that the annual estimation of the medical and disability costs of cardiovascular disease-related disorders was $330 billion (Sheta, 2004). In 2003, cardiovascular disease cost the European Union €169 billion (Leal et al., 2006) and the most up to date data from the United States of America shows that cardiovascular disease costs nearly €310.23 billion in direct and indirect annual costs (Haase et al., 2006). In China, annual direct costs are estimated at €30.76 billion or 4% of gross national income (Gaziano, 2007). In South Africa, 25% of the country's health care spending is devoted to cardiovascular disease (The Centre for Global Health and Economic Development, 2004).

Figure 1 WHO findings on cardiovascular diseases (2005)



Apart from the direct costs of the disease, loss of work time and decreased productivity account for a substantial amount of the indirect costs. More recently, there has been much interest in systematically improving the quality and reducing the cost of caring for patients with chronic illnesses such as cardiovascular disease (Weingarten et al., 2002). At present, emphasis has been placed on disease management as part of the programmes initiated to improve the quality and efficiency

of care for patients with chronic illness. Disease management is a multidisciplinary approach to care for chronic diseases that coordinates comprehensive care along the disease continuum across healthcare delivery systems (Ellrodt et al., 1997; Allenet et al., 2006).

Role of pharmacists in disease management

In most countries, community pharmacists are the most accessible healthcare professionals. Pharmacists have developed primary care roles in the management of chronic diseases among which cardiovascular diseases such as hypertension, ischaemic heart disease and congestive heart failure are the common area of focus (Allenet et al., 2006). Studies have shown that community pharmacists' involvement in disease management often lead to early intervention for drug-related problems (Munroe et al., 1997). More recent evidence also suggests that interventions of community pharmacists in patient management has led to improvement of blood pressure control in the community setting (Carter and Zillich, 2003; Machado et al., 2007). An example of this was a published review article by Cross and Franks (2005) on clinical outcomes associated with pharmacist involvement in patients with dyslipidemia. The review included a pilot study conducted by Madejski and Madejski (1996) to determine the effect of cholesterol screening in a community pharmacy in western New York, USA. The results of the study (Table1.1) showed that 83% of the 359 patients who were interviewed reported lifestyle modifications such as smoking cessation and dietary changes. According to Cross and Franks (2005), the study supported the positive impact of community pharmacists' involvement in disease management (Smith et al., 1999; Cranor et al., 2003) and its potential impact in reducing overall healthcare expenditure (Munroe et al., 1997; Menzin et al., 2004).

Cardiovascular disease patients are often on multiple drug therapy for their disease management. They are in most cases prone to medication–related problems such as adverse drug reactions, inappropriate medication use, non-compliance due to side-effects of certain prescribed drugs and problems with over/under dosage (Morrow et al., 2004). According to Munroe et al (1997), "a major goal of disease management programmes is to combat drug-related morbidity and mortality to improve outcomes and decrease health care costs". The economic burden of medication-related problems

in the society has been well documented in the literature (Johnson and Bootman, 1997; Ernst and Grizzle, 2001; Mullins et al., 2004). However a gap remains in the literature regarding the impact of medication-related problems on the health-related quality of life of cardiovascular patients, especially in a community setting.

Role of community pharmacists in medication management

Pharmacists have been involved in the development and implementation of validated methods and services aimed at preventing, detecting, and solving actual or potential drug-related problems in patients and overall to assist patient needs in community settings (Patel and Zed, 2002; Machado et al., 2007). As part of the pharmaceutical care process, community pharmacists dispense the vast majority of prescriptions on a daily basis. Based on their depth of drug knowledge and their accessibility to patients on a regular basis, pharmacists are in a unique position, in collaboration with other healthcare professionals (general practitioners, nurses etc) to improve therapeutic outcomes from medication by reducing adverse events, increasing medication appropriateness and improving medication adherence (Hugtenburg et al., 2004; Viktil et al., 2004; Zehnder et al., 2004).

Previous studies have also shown that involvement of hospital-based ambulatory clinic pharmacists has led to improvement of all-cause mortality and reduced non-fatal heart failure events in heart failure and improved signs and symptoms and reduced hospitalizations for individuals with asthma (Gourley et al., 1998; Solomon et al., 1998; Gattis et al., 1999; Vik et al., 2006). In addition, studies in the US have shown that pharmacists working in general practitioners' offices contributed to a reduction in adverse drug events and improvements in medication adherence (Hanlon et al., 1996; Jameson and VanNoord, 2001; Petrilla et al., 2005). In the United States of America for example, observational studies have shown that community pharmacists identify problems in two percent of new prescriptions, avoiding adverse consequences in 21% of cases (Rupp 1992; Rupp et al., 1992). These studies also estimated that savings attributable to resolved medication problems ranged from

Table 1.1 Studies evaluating pharmacists role in disease management

Reference	Setting	Target population	Evaluable sample size	Interventions	Effect
Madejski and Madejski, 1996	One community pharmacy, USA	Patients with hypercholesterolaemia	539 patients	Phone interviews of patients; recommendation /reference to physicians; advice on diet education	Enhanced patient awareness of hypercholesterolaemia and other associated cardiovascular risk; Positive lifestyle changes achieved in some patients.
Munroe et al,1997	Multicentre community pharmacies, USA	Patients with asthma, hypertension, diabetes, and / or hypercholesterolaemia	188 patients at three intervention pharmacies; 401 patients for control study at five non-participating pharmacies	Assessment of patients' adherence to medication & non-drug therapies; education of patients about their medical conditions; medication administration, self-monitoring & adverse effects. Assessment of drug therapy efficacy by subjective & objective monitoring of blood pressure, blood cholesterol, blood glucose, & peak flow rate, weight, pulse & respiratory rate. Regular communication with physicians of any information obtained to serve as early warning system to negative clinical trends.	Total monthly costs for healthcare use were lower for the intervention than for the control.
Malone and Alger-Mayer, 2003	One community pharmacy, USA	Obese patients attending an outpatient nutritional programme	Pilot study; 15 intervention and 15 control patients.	Patients were prescribed orlistat;	Patients receiving pharmaceutical care had improved outcome with orlistat therapy. The intervention patient group had significantly greater persistence with orlistat therapy; no significant difference in the percentage of weight loss between groups.

$3.50 per prescription to $122 per intervention (Loh et al., 1996; Christensen and Hansen, 1999; Westerlund et al., 2003).

In the United Kingdom, a new initiative was introduced in 2005 to improve the quality and range of services that community pharmacies offer. It is expected that this New Community Pharmacy Contractual Framework will help to support people with long-term conditions such as cardiovascular disease and promote health improvement. As part of this new initiative, Medicine Use Review (MUR) was introduced to help people, especially on multiple drug therapy, to improve their knowledge and understanding of what their prescribed medications are for and also how to use their medicines. MUR, according to the UK Department of Health, will also help to reduce the number of hospital admissions caused by inappropriate use of medicines.

MEDICATION-RELATED PROBLEMS (MRPs) - A REVIEW OF THE LITERATURE

Scientific literature can be described as a bibliography of events describing the truth (Gaudet, 1998). According to William James, the pioneering American psychologist and philosopher in the $19^{th}/20^{th}$ century, "Truth happens to an idea; it becomes true, and is made true by events". A literature review enlightens researchers about the work of other colleagues and encourages researchers to develop new hypotheses to confirm what is already believed to be true.

This chapter will be divided into three sections. These sections will focus on a literature review in the area of medication-related problems of cardiovascular drug therapy, its economic and societal impacts and its impacts on cardiovascular patients' quality of life. A literature search was performed in Medline, and Embase using keywords such as drug-related problems, antihypertensive and side effects, beta-blockers and depression, antihypertensive and anxiety. These terms were also combined with other keywords such as quality of life, evaluation, economic outcomes, and socioeconomic status. Although a large percentage of studies have been published on the concept of medication-related problems and different

instruments of assessment of medication-related problems, fewer studies have focused on a specific area of drug therapy where there is a high rate of these problems, for example in cardiovascular drug therapy. Further, there were few studies in the published literature evaluating the economic impact and quality of life in people with medication-related problems of cardiovascular drug therapy. Section I of this literature review will focus on 1) the concept of medication-related problems; 2) the impact of cardiovascular drugs-related side effects on patients' quality of life; and 3) different instruments for assessing medication-related problems. Section II will focus on a critical appraisal of the published literature on both the societal and economic burdens of medication-related problems. Section III will review some of the existing cardiovascular disease-specific quality of life instruments to detect whether they can be used in the present study.

SECTION I

Concept of Medication-Related Problems- Historical Review

Different terminologies have been used to describe the concept of a medication-related problem. The term "medication error" is widely used in clinical settings to describe cases involving administration errors and those errors that involve drug dispensing (Van Mil et al., 2003). In the United States of America, where most of the research studies in this area have been carried out, The National Co-ordinating Council for Medication Error Reporting and Prevention (NCC-MERP) in 1998 used the term "medication error" to describe any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of a health care professional, patient or consumer (Shaw –Phillips, 2002).

In the United Kingdom, Krska et al. (2001) used the term "pharmaceutical care issue (PCI)" to describe problems which are either preventable or can be solved with the application of the pharmaceutical care process. During a conference in pharmaceutical care in 1998 in the United States of America, the American Society of Hospital Pharmacists (ASHP) adopted the term "medication-related problem" to describe "any event or circumstances involving medication therapy that actually or potentially interferes with an optimum outcome for a specific patient" and Cipolle et al (1998) described "drug therapy problem" as "any undesirable event experienced by

the patient that involves or is suspected to involve drug therapy and that actually or potentially interferes with a desired patient outcome". Other notable definitions include: the 1998 Granada I (group of Spanish experts) drug-related problem concept as a "health problem of the patient which provokes the action of any health provider as a consequence of drug therapy". This definition was in contrast to the 2002 Granada II definition of the concept as "a negative clinical outcome of pharmacotherapy" (Alvarez-de-Toledo, 2004). All the above definitions are patient-focused with a common interest in the patient's health outcome. Johnson and Bootman (1997) in their article on a model of drug-related morbidity and mortality considered drug-related problems as a negative therapeutic outcome upon which the Granada II concept of drug-related problems could have been based.

Classification of medication-related problems

Since the beginning of the classification system of drug-related problems in 1975, its concept description and the first establishment of classification categories in 1990, various researchers in the pharmaceutical care process across the world have developed, used and validated various classification systems of drug-related issues based on the area of focus and their research purpose (Fernandez-Llimos et al., 2004). These risk assessment tools were developed for reasons such as prescribing improvement, reduction in medication-related problems and improved outcomes (Buerger, 1999). Some of these risk assessment tools have been applied in clinical practices to identify and document medication errors, some have also been used in both community settings and care homes to identify and resolve medication-related problems. The overall goal and objective of documenting drug-related problems that a patient experiences is to improve the quality of pharmaceutical care offered to them in order to ensure continuity of positive outcomes of drug therapy.

Van Mill et al (2004) published a review article on drug-related problem documentation tools and based on various criteria of their evaluation such as usability in pharmaceutical care practice, validation method and its hierarchical structure, only one out of fourteen documentation tools was found to fulfil the pharmaceutical care practice objective (Table 1.2). This section of the thesis is therefore focused on the implementation of these existing tools in various healthcare settings. The terms

"Medication-related problem" and "drug-related problem" will be used interchangeably, however they are actually explaining the same concept. Drug-related problems can generally be described as the negative impact of a drug therapy on a patient's desired health outcomes.

Hepler and Strand classification

During the early stages of the pharmaceutical care concept and developments in the United States of America, Helper and Strand (1990) grouped drug-related problems into eight main categories, namely:

- Untreated indications;
- Improper drug selection;
- Sub therapeutic dosage;
- Failure to receive drugs;
- Over-dosage
- Adverse drug reactions;
- Drug interactions;
- And drug use without indication

However, according to some published studies (Van Mill et al., 2004), this first classification system had some limitations. Nevertheless, it did form the cornerstone of today's pharmaceutical care research and a starting point for many of the existing classification systems (Strand et al, 1990). The system was widely used in the early 1990s and reported in many institutional and community settings (Briceland et al., 1993; Ho, 1994; Curie et al., 1997)

Minnesota Pharmaceutical Care Project Classification

Due to a lack of robustness associated with the Hepler and Strand DRP classification system at the 1995 Minnesota Pharmaceutical Care Project, an improvement was made upon this previous work. The eight original DRP categories were reassessed and grouped into five domains:

- Drug Indication;
- Effectiveness;
- Safety;

- Compliance,
- And Untreated indication.

These five groups could be considered as the standardised guidelines for tackling most pharmaceutical care issues today. They are more distinct than the previous categories because the drug-related problems and their causes were separated. However, this new classification was considered to be limited in its usability as neither the process nor the outcomes of any intervention attempted to resolve the problems were included in this new system (Van Mil, 1999). This was later challenged by Cipolle et al (1998) when they published a classification system of DRP called "Drug Therapy Problems Coding System".

Drug Therapy Problems Coding System

This system was a modification of the 1995 Minnesota system with the original five approaches to the drug–related needs reduced to four (Santos and Madeira, 2003). These are:

- Drug Indication;
- Effectiveness;
- Safety,
- And compliance.

Although the Drug Therapy Problems classification scheme has been widely tested and used in practice in several studies in community settings both in Europe and America, the system lacked robustness because its authors did not attempt to include either interventions or the outcomes of intervention in the system (Van Mill, 2004).

The Problem-Analysis-Solution Coding System (PAS-Coding System)

The Problem-Analysis-Solution system (PAS-coding system) was developed primarily to quantify oral communication processes during counselling in pharmacy practice (Van Mil et al., 1999). The system was community pharmacy practice-oriented and had been used to document DRPs in various studies involving therapeutic outcome monitoring (TOM). Although the PAS system is community pharmacy oriented, its limited usability in practice might have been due to the following factors:

- Time required for its use in community practice;
- Too elaborate and more research based,
- No distinct clarity between the main headings, thereby making the coding of some of the problems experienced by patients difficult (Van Mil et al., 2004).

Problem-Intervention Documentation (PI-Doc)

The development of the Problem-Intervention-Documentation (PI-Doc) system was based on the need for a broader implementation of pharmaceutical care in the pharmacy (Schaefer, 2002). Before its development, the following criteria, as described by the author, were taken into consideration:

- Suitability for both scientific studies and pharmacy practice;
- User friendliness in routine practice;
- Consist of three parts: problem code, intervention code and outcome of intervention code;
- Structured like a decision tree with main groups and sub-groups supporting computer aided use;
- Open structure enabling introduction of additional coding levels without changing the basic structure;
- Clear and defined problems leading to one choice of coding only;
- Coding should focus on the problem itself and not on its cause or consequence,
- Suitability for documentation necessary for the remuneration of cognitive services.

The PI-Doc system by far is the most widely used risk assessment tool for comprehensive documentation of interventions occurring in community pharmacy, especially in Germany and Denmark (Schaefer, 2002). There was, however, no clear distinction between the various problems and the cause. Indeed, according to the author, the system was not developed to explore the origin of drug-related problems but to give insight into how the problems could be tackled, and intervention undertaken by pharmacists in practice (Ellison, 2003).

Other existing systems that have been used in many studies include: National Coordinating Council for Medication Error Reporting and Prevention (NCC-MERP) taxonomy of medication errors, Hanlon's Medication Appropriateness Index (MAI), and the Pharmaceutical Care Network Europe system (PCNE).

National Coordinating Council for Medication Error Reporting and Prevention (NCC-MERP)

In respect of the guidance issued by the NCC-MERP council after its development, the taxonomy was designed not as a reporting form of medication errors but as a tool for medication error analysis and categorisation (NCC-MERP, 1998). The NCC-MERP taxonomy has been used widely in North America especially the USA where, apart from the existence of such a system for DRP analysis and documentation, there have been in place other established systems for medication error reporting, such as the Joint Commission on Accreditation of Healthcare Organisation (JCAHO), FDA's Med Watch, and USP's MedMARx. Although the taxonomy has many practical benefits such as its possibility to code reported medication errors with the aid of the other systems cited above, and the possibility of classifying errors according to the level of severity (Shaw –Phillips, 2002), it has some limitations, such as inability to document interventions and outcomes using the system. However, it provides a system of documenting the type of medication errors involved and their causes.

Medication Appropriateness Index (MAI)

The Medication Appropriateness Index (MAI) was designed in 1992 with the aim of creating an instrument that could address multiple elements of drug therapy prescribing, applicable to a variety of medications, clinical conditions and settings (Hanlon et al., 1992). The authors of this risk assessment tool took into consideration three of the key pharmaceutical issues (drug indication, effectiveness and safety) in addition to the cost-effectiveness of a drug in order to decide its appropriateness (METRIC, 2005). The authors also used implicit criteria to judge the appropriateness of medication prescribing and also to measure the magnitude of inappropriate prescribing for most dimensions of drug use that are clinically relevant. The MAI implicit criteria include:

- Medication Indication;

- Effectiveness;
- Dosage;
- Correct directions;
- Drug-drug interactions;
- Drug-disease interactions;
- Expense;
- Practical directions;
- Therapeutic duplication,
- Duration

The Medication Appropriateness Index has been used in many studies by the same group of researchers (Hanlon et al., 1992; Samsa et al., 1994; Schmader et al., 1994; Hanlon et al., 1996; Murray, 1997; Schmader et al., 1997), and also in medication reviews in clinical settings (Sorensen et al., 2003). However, the question about its reliability remains unanswered. Studies examining the reliability of the MAI produced inconclusive results, due to involving a small sample size. The authors summarised the MAI as follows: *"while broadly applicable and easy to use, the MAI does not address several important medication use issues, including the causality of adverse drug reactions and variable patient compliance"*. The MAI instrument provides a foundation for identifying areas that need appropriateness in prescribing and is also useful in drug treatment decision- making. However, more evidence will be needed to establish the stability and acceptability of the instrument in other settings and populations (Fitzgerald et al., 1997).

Modified Medication Appropriateness Index (MMAI)

The Modified Medication Appropriateness Index (MMAI) was designed to examine the practicality /applicability of the original version in the community setting. As implied from the name, the tool is a modification of some of the items in Hanlon's MAI (1992) implicit criteria. These modifications included a revised definition for "ineffective" and refined directions for instructions, procedures to assess drug interactions, and methods to determine medication expense (Fitzgerald et al., 1997). However, few published studies have used this tool to document drug appropriateness/ inappropriateness in the community setting (Fitzgerald et al., 1997;

Kassam et al., 2003) and similar limitations to the original version were detected such as small sample sizes used in reliability tests. The instrument therefore needs validation in order to increase its reliability and wider acceptability.

Pharmaceutical Care Network Europe Drug-Related Problems System (PCNE_DRP)

The Pharmaceutical Care Network Europe Drug-Related Problems System (PCNE_DRP) was developed with its first version in 1999. The system was initially developed for research purposes internationally (Ellison, 2003). However, after various conferences, the authors arrived at a consensus to develop a system that would be used in community pharmacies to document drug-related problems identified during pharmaceutical care processes in routine practice and practice research (McElnay, 2004). The system, according to the authors, has both the problems and causes separated, has an intervention section and outcome of intervention section. Also it has been hierarchically structured and has undergone several validation tests since its development in 1999 (Van Mil, 2003). Nevertheless, its validity is still questionable (Fernandez-Llimos et al., 2004; Farris et al., 2005). Some of the limitations of this system identified elsewhere include:

- Low usability and acceptability;
- Poor internal consistency;
- Continued overlap between some problems and cause,
- Problems with its construct validity

According to some authors, if the PCNE-DRP system is to be considered as European consensus for a drug-related problem coding system, it needs to undergo a thorough validation process in order to increase its usability and wider acceptability, not only in Europe but across the world.

Personal Digital Assistant (PDA)

The Personal Digital Assistant (PDA) is a risk assessment documentation tool developed in Canada as a drug-related problem and pharmacist-intervention documentation system in hospital pharmacies (Raybardhan et al., 2005). The drug-related problems classification scheme used in this system was modification of the

eight pharmaceutical care model described earlier by Hepler and Strand (1990). Although the system was described as a very useful documentation tool, especially in clinical settings, its applicability in community settings has not been tested. Its use is limited to hospital settings and there is no published evidence of its validation process and usability rates.

Quality Use of medicines (QUM) coding system

Another drug-related problem documentation tool identified in this review is the Quality Use of Medicines (QUM) Coding System. This tool was developed by a group of experts in Australia to assess the quality and impact of pharmacists' medication review (Sorensen et al., 2003). Its usability has been tested mainly in hospital settings with satisfactory inter-rater reliability. However, the system suffers from a number of limitations. For example, lack of intra-rater reliability test as pointed out by the authors themselves, and no published studies to examine its usefulness in other settings such as nursing homes, community settings etc.

For consistency in a suitable DRP coding system to be achievable, it is important that there should be guidelines and agreements to be followed during its development. Schaefer (2002) has proposed some criteria for consideration during such processes. In addition to these, Van Mil et al (2003) have defined five requirements for a drug-related problems classification system. Taking into consideration the eight criteria and these five requirements, a universally acceptable, comprehensive drug-related problem classification scheme can be developed. Adoption of the criteria proposed by Schaefer (2002) will ensure a well-defined system without overlap in problem codes and usable both in pharmaceutical care practice and practice research scenarios.

According to Buerger (1999), developing, refining and validating medication-related problem risk assessment tools is one thing; their implementation in real-world clinical situations to drive better prescribing and improved outcomes is another thing. There is also a need for more incorporation of some of the community-oriented risk assessment tools in community pharmacy practice. Most community pharmacists are not aware of such risk assessment tools. With the introduction of medication review as part of advanced services in the new pharmacy contracts in the United Kingdom,

community pharmacists are now in a better position to access these tools to document medication-related side effects they come across while performing medicine use reviews for their patients. However, in order for pharmacists to familiarise themselves with these risk assessment tools, there is a need to develop pharmacists' version of some of the existing DRP classification schemes in order to increase their accessibility, comprehensiveness and acceptability.

Medication-related problems and HRQoL

While efficacy and safety of drug therapy have been documented extensively, much less emphasis has been placed on assessment of the patient's own perception of treatment and its impact on his/her quality of life. Studies have shown that cardiovascular drug treatment may have a negative impact on patient's HRQoL (Bardage, 2000). Studies have also shown that there is low concordance between patient and physician regarding drug treatment and health evaluations due to distressing medication side-effects (Testa et al., 1993). In many cases, these side-effects have resulted in drug treatment withdrawal or low compliance (Buurma et al., 2007). Burke, et al. (1997) estimated that 20-80% of patients prescribed cardiovascular drugs fail to adhere to a drug treatment regimen sufficiently to realise full therapeutic benefits. Antihypertensive drug therapy, for example, is often associated with side-effects such as tiredness, mood change, sleep disturbances, impotence, dry mouth, and blurred vision, to mention a few (Table 1.3).

A patient's perception of these side effects therefore plays an important role in the success of the therapeutic regimen (Bardage, 2000). Some patients perceive the use of their medications to be more troublesome than their seemingly asymptomatic disease (Battersby et al., 1995). It is universally accepted that "No drug is absolutely free from side effects". An essential element of pharmaceutical care is that pharmacists should accept responsibility for the patient's pharmacotherapeutic outcomes (ASHP, 1993). ASHP (1993) suggested that part of pharmacists' responsibility is to provide mechanisms for monitoring, detecting, evaluating, documenting and reporting adverse drug reactions and other medication-related problems. These also include intervention and provision of educational feedback to prescribers and other healthcare professionals and patients (ASHP, 1993).

Table 1.2 Drug-Related Problem Classification Systems

DRP System	Main Categories	Based on Clear Definition	Hierarchical Problem Classification	Causes Classification	Intervention Classifications	Validation published	Used in Published Study
Meyboom ABC of DRP (2000)	3	No	No	Integrated	No	No	No
ASHP (1996)	13	Yes	No	Integrated	No	No	Yes
Cipolle et al (1998)	7	Yes	No	No	Yes	No	Yes
Granada Consensus (2002)	6	Yes	No	Integrated	No	No	Yes
Hanlon (MAI) (1992)	10	No	No	Integrated	No	No	Yes
Helper and Strand (1990)	8	Yes	No	No	No	No	Yes
Krska et al (2002)	13	Yes	No	No	integrated	No	Yes
Mackie (2002)	13	Yes	No	No	No	No	Yes
NCC-MERP (2003)	14	Yes	No	Integrated	Yes	No	Yes
PAS (1997)	5	No	Yes	Yes	Yes	Yes	No
PCNE (2003)	6	Yes	Yes	Yes	Yes	Yes	Yes
PI-Doc (2002)	6	No	Yes	Integrated	Yes	No	Yes
SHB-SEP (2003)	10	No	Yes	Yes	Yes	No	No
Westerlund (2002)	13	Yes	No	Integrated	Yes	Yes	Yes

ASHP = American Society of Health-System Pharmacists. PCNE = Pharmaceutical Care Network Europe.

"Integrated" = cause integrated in the problem description. PI-Doc = Problem Intervention Documentation.

NCC-MERP = National Coordinating Council for Medication Error Reporting and Prevention.

PAS = Problems, Assessment, and Solutions. SHB-SEP = Health Base Foundation Subjective Evaluation Plan

Source: JWF Van Mil et al., (2004). The Annals of Pharmacotherapy, 38, 8

Table 1.3 Antihypertensive drugs and frequency of adverse drug reactions

Class of drug	Adverse drug reactions (ADRs) and frequency of ADR (%)		
	< 1%	1% - 10%	> 10%
Beta – blockers e.g. Atenolol,	Chest pain, hypotension nightmares, vivid dreams, cold extremities	Confusion, dizziness, insomnia, fatigue, rash, diarrhoea, nausea, wheezing	Mental depression, decreased sexual ability, bradycardia
Bumetanide (diuretic)	Hypotension, rash, cramps, pruritus, nausea, vomiting	Dizziness, headache, muscle cramps, weakness etc.	Hyperuricemia, hypokalemia etc.
Captopril	Hypotension, angioedema, etc.	Chest pain, tachycardia, insomnia, headache, rash, dizziness, fatigue, cough	None
Clonidine	Insomnia, vivid dream, fever, pruritus, blurred vision, weight gain etc.	Mental depression, headache, fatigue, pain, rash, loss of libido, decreased sexual activity, impotence, weakness	Anxiety, confusion, orthostatic hypotension, drowsiness, dizziness,
Enalapril	Insomnia, drowsiness, confusion, depression, nervousness, impotence, blurred vision etc.	Chest pain (2%), hypotension (6.7%), headache (2-5%), rash, dizziness (4-8%), cough	None
Furosemide	Rash, nausea, gout, etc.	Headache, diarrhoea, photosensitivity, loss of appetite, blurred vision.	Dizziness, orthostatic hypotension etc.
Hydralazine	Dizziness, fever, rash, weakness, malaise etc.	Hypotension, redness or flushing of face, nasal congestion etc.	Angina pectoris, Flushing, headache, nausea, vomiting.
Moexipril	Angina, chest pain, sleep disturbances, mood changes, anxiety etc.	Headache, dizziness, fatigue, rash, diarrhoea, non productive cough (6%)	none
Perindopril	Hypotension, psoriasis, impotence, dry eyes, blurred vision, taste disturbances.	Headache, dizziness, rash, mood and sleep disorder, fatigue, cough (incidence greater in women, 3:1), nausea and vomiting etc.	None.
Ramipril	Hypotension, headache, dizziness, fatigue, insomnia, drowsiness, depression, nervousness, rash, weight gain, impotence etc.	None.	Cough (12%).
Trandolapril	Insomnia, rash, sleep disturbances, anxiety, decreased libido, diarrhoea, vomiting, constipation, impotence	Chest pain, fatigue, myalgia, cough (1.9-35%) etc.	None.

Source: Excerpts from Drug-Induced Nutrient Depletion Handbook 1999-2000; Pelton, R et al.

Antihypertensive drugs and patients' HRQOL

The effects of antihypertensive treatments on patients' HRQOL have been described in published studies to be complex, with persistence in a negative perception of drug treatment due to their side-effects (Mayou, 1990; Bremner, 2003; Aqil et al., 2006). For example, calcium channel blockers such as felodipine or isradipine can cause severe ankle swelling as a late–onset side effect (Douglas and McLay, 1996), resulting in poor HRQOL of patients (Testa et al., 1998). Dry, persistent cough commonly associated with ACE inhibitors such as enalapril, has been demonstrated to have a negative influence on sleep patterns and in many cases has lead to either low concordance among patients or discontinuation from ACE inhibitor therapy (Israili and Hall, 1992; Fletcher et al., 1994). Studies have also shown that beta-blockers have an immediate negative impact on patients' well being and therefore need to be carefully titrated with low doses when initiating treatment (Tregaskis and McDevitt, 1990; Thomsen et al., 2007).

In the United Kingdom in 2006, use of beta–blockers came under scrutiny following a publication on re-evaluation of the benefits of beta-blockers (Carlberg et al., 2004). As a result of this, the British National Formulary (BNF) 51 suggested reconsideration of use of this class of antihypertensive drugs as a first choice in routine initial therapy for hypertension. In addition, studies have associated beta blockers with side-effects such as impotence (Ostergren et al., 1996), depression and decreased life satisfaction (Breckenridge, 1991), and an assessment of the impact of these side effects on such areas as emotional well being, performance at work and overall perception of well being needs a constant focus and attention (Karimova and Martin, 2003).

Cardiovascular drugs and fatigue

Cardiovascular drugs such as beta blockers and ACE inhibitors have been proved to reduce the mortality rate by 20% (Ko et al., 2002) in patients after myocardial infarction, heart failure etc. However, studies have shown that physicians do feel reluctant to prescribe these agents partly due to concerns about patients developing side-effects such as fatigue, depression, sexual dysfunction and tiredness (Koch-Weser and Frishman, 1981; Brouwer et al., 2005).

Fatigue has been frequently reported as a side effect in patients on beta-blockers. Fletcher et al (1992) published the results of a major trial using QOL evaluation methods; this was a multicentre, double–blind study of six months duration in 540 patients with mild to moderate essential hypertension randomly assigned to cilazapril, atenolol and nifedipine retard. Spontaneous reports revealed occurrence of fatigue in 10% of patients in the atenolol group compared with 4% in both the cilazapril and nifedipine retard group. In another published study of 10 trials that included 17682 patients with 33.4% on beta–blockers and 30.4 % on placebo, there was a substantial reported incidence of fatigue among the beta–blockers group with a significantly increased risk of withdrawal from the trials due to fatigue (Julian et al., 1982).

Cardiovascular drugs and depression

Case reports linking beta-blockers with incidence of depression have been published in the literature; however there are not enough published studies to clarify the association between beta-blockers and depression. Despite this, a study carried out by Gerstman et al (1996) demonstrated a low incidence of depression among patients on beta-blockers. Not surprisingly, Wang et al (2002) in a cross–sectional study comparing utilisation of antihypertensive prescriptions with patients' responses to a structured interview concluded that depressive symptoms may be an under recognised but modifiable risk factor for compliance with antihypertensive medications.

SECTION II

Economic impact of medication-related problems

The costs of medication-related problems cannot be overestimated. In addition to the direct costs such as laboratory tests and hospital admissions, there are also indirect costs, such as loss of productivity and treatment of ADRs (Lassetter and Warnick, 2003). The most comprehensive analyses of the economic burden of medication–related mortality and morbidity in the US were conducted by Johnson and Bootman (1997); and Ernst and Grizzle (2001). Johnson and Bootman (1997) in a study on the cost of drug-related morbidity and mortality in the USA estimated that the annual cost of drug-related morbidity and mortality as a result of medication–related problems in

the ambulatory setting in the United States was $76.6 billion. Five years later, a similar study carried out by Ernst and Grizzle (2001) to update the previous findings of Johnson and Bootman (1997) found out that the cost of drug-related morbidity and mortality had more than doubled, exceeding $177.4 billion in 2000, with hospital admissions accounting for nearly 70% ($121.5 billion) of total costs, followed by long-term-care admissions, which accounted for 18% ($32.8 billion). Ernst and Grizzle (2001) also found that costs associated with medication-related problems exceeded the expenditure for initial drug therapy. According to the annual report of the American Society of Consultant Pharmacists (ASCP), the economic impact of medication-related problems in persons over the age of 65 in the USA now rivals that of Alzheimer's disease, cancer, cardiovascular disease, and diabetes (ASCP, 2002).

The economic burden of medication-related problems is a global issue (Lassetter and Warnick, 2003; Stroupe et al., 2004). Studies have demonstrated the significance of medication-related problems on both direct and indirect healthcare costs in various countries of the world (Plumridge and Wojnar-Horton, 1998; Van den bemt et al., 2000). In the Netherlands in 2002, the annual estimation was 186-430 million Euro (Beijer and Blaey, 2002) while some estimates put the annual cost of medication-related problems to the UK at more than £380 million a year (Wiffen, 2002).

Direct medical costs of medication-related problems

Medication–related complications, as a major cause of hospitalisations, have lead to a huge economic burden and significant human suffering (Palaian et al., 2006; Becker et al., 2006). A large proportion of studies so far have estimated direct costs of ADRs, such as the impact on hospital admissions, emergency room visits and also outpatient general practitioner visits. When estimating the direct costs of medication-related problems, especially adverse drug reactions, researchers frequently take into consideration the following: length of stay in hospitals, medical costs related to the treatment of ADRs, and in some cases, the non-medical costs related to travel expenditure (Lacoste-Roussillon et al., 2001; Becker et al., 2006). In 2002, ASCP estimated the total annual direct medical cost of medication-related problems at around $104.2 billion (ASCP, 2002). ADRs for example, are one of the leading causes of morbidity and mortality (Lazarou et al., 1998) and in some studies, were

shown to be responsible for a significant number of hospital admissions, with reported cases ranging from 0.3% to as high as 11% (Beard, 1992). In 1993, it was estimated that approximately 2.9% to 5.6% of all hospital admissions were caused by ADRs and as many as 35% of the hospitalized patients experienced an ADR during their hospital stay (Murphy and Frigo, 1993; Pirmohamed et al., 2004; Thomsen et al., 2007).

Another study conducted at two prestigious teaching hospitals in the US found that almost two percent of admissions experienced a preventable adverse drug event, resulting in an average increased length of stay of 4.6 days and an average increased hospital cost of nearly $4,700 per admission (Ernst and Grizzle, 2001) amounting to about $2.8 million annually for a 700-bed teaching hospital (Fernandez-Llimos et al., 2004). Krska et al. (2001) reported that 12-14 percent of hospital admissions in Scotland were as a result of medication-related problems such as adverse drug reactions, and poor compliance with therapy among others. Several other studies have also shown low concordance and compliance with treatments as a result of distressing medication–related side effects experienced by patients during drug therapy (Cline et al., 1999; Jackevicius et al., 2002).

In another study, Yee et al (1997) reported that inappropriate drug treatment, another aspect of medication-related problems could have cost a hospital setting extra health care expenses if it had not had the benefit of a pharmacist's intervention and his participation in clinical rounds that saved that institution an estimated $523,907.

Higher costs have also been observed in medical errors. Medical errors cost the U.S. approximately $37.6 billion each year. $17 billion of those costs are associated with preventable errors. About 50% of the expenditures for preventable medical errors are for direct health care costs (approximately four percent and two percent, respectively, of national health expenditure in 1996 or slightly higher than the direct and indirect costs of caring for people with HIV and AIDS). It has been estimated that for every dollar spent on ambulatory medication, another dollar is spent to treat new health problems caused by the same medication.

SECTION III

Review of Cardio-Specific Quality of Life Instruments

Medication-related problems are not a disease but the outcome of drug treatment of any disease. A question arises: are existing cardio-specific HRQOL instruments sufficient to measure the impact of medication-related problems on patients' quality of life? To answer this question, there is a need to review these instruments in order to identify gaps in any already existing knowledge in this area. It is also important to bear in mind that MRPs are not comparable with disease as stated earlier but are the outcomes of drug therapy. The existing cardio-specific quality of life instruments focus on the quality of life of patients in a certain disease state of cardiovascular disorder (Table 1.5). An example of what could be considered a core coronary heart disease (CHD) specific HRQOL instrument has been published, however, its psychometric properties such as validity and reliability have not been fully established (Avis et al., 1996).

The following disease specific and generic instruments have been used in various studies to measure HRQOL in cardiovascular disease. Table 1.5 describes their origin, weaknesses and strengths as well as their psychometric properties.

- Quality of Life after Myocardial Infarction (QLMI-2)
- The Seattle Angina Questionnaire (SAQ)
- The Quality of Life Index-Cardiac Version (QLI-CV)
- The Angina Pectoris Quality of Life Questionnaire (APQLQ)
- The Summary Index (SI)
- The Myocardial Infarction Dimensional Assessment scale (MIDAS)
- Minnesota Living with Heart Failure Questionnaire (MLHF)
- Multidimensional Index of Life Quality (MILQ)
- The Short Form-12 Health Survey Questionnaire (SF-12)

Quality of life after Myocardial Infarction (QLMI-2)

The QLMI-2 has been considered to be the best known and most widely used disease-specific measure for the myocardial infarction patient group (Thompson et al., 2002;

Asadi-Lari et al., 2003). This is a refined 27-item version of the original 26-item QLMI instrument otherwise known as MacNew Heart Disease Questionnaire. The 27-item instrument is grouped into three non-exclusive domains: emotional, physical and social (Lim et al., 1993; Valenti, et al., 1996). Each item has a 7-point Likert response scale scored from one to seven, where a higher score represents a better QOL; domain scores are taken as the average score of responded items in the domain.

The QLMI-2 has been validated and found to have better psychometric properties than the original QLMI with higher internal consistency (Hillers et al., 1994; Dempster and Donnelly, 2000). The instrument has been widely used in Australia and Canada, however, it is not in widespread use in the UK or the rest of Europe (Thompson and Jenkinson, 2002). According to these authors, although QLMI-2 has established psychometric property, its evaluative properties have yet to be investigated despite the fact that most of the domains of the original QLMI displayed a moderate to strong evaluative dimension (Ribera et al., 2006), high estimates of test-retest reliability and a moderate to high responsiveness (Dempster and Donnelly 2000; De Gucht et al., 2004).

The Seattle Angina Questionnaire (SAQ)

This is a psychometrically solid and one of the most widely used patient–assessed disease-specific health outcome measures developed to assess the functional status of patients with angina (Garratt et al., 2001; Thompson and Jenkinson, 2002). The SAQ has been tested for the measurement properties of reliability, validity and responsiveness in a US population (Spertus et al., 1994; Spertus et al., 1995; Pettersen et al., 2005). The SAQ is a 19-item questionnaire grouped into five domains: physical limitation, anginal stability, anginal frequency, treatment satisfaction, and disease perception. All five domains displayed sound psychometric properties (Dempster and Donnelly, 2000).

The physical limitation scale measures how daily activities are limited by symptoms of coronary artery disease; the anginal stability scale assesses change over the prior month in the frequency of angina at the patient's most strenuous level of activity, while the anginal frequency scale quantifies the number of anginal episodes. The

treatment satisfaction scale quantifies satisfaction with current treatment of angina (Dougherty et al., 1998).

There is a varying level of agreement on some of its psychometric properties by different authors. While Stewart (1992) stated that each domain of the SAQ has been independently validated and shown to be reliable and responsive to clinical change (Dougherty et al., 1998), Thompson and Jenkinson (2002) on the other hand, reported that two of the domains (treatment satisfaction and anginal stability) are unsuitable for evaluative purposes for the following reasons:

- Low responsiveness estimate of the treatment satisfaction.
- Low test-retest reliability estimate of the anginal stability domain.

In addition, Thompson and Jenkinson (2002) revealed that the SAQ was neither developed for use in MI patients nor as a health-related quality of life measure, although it has been used in MI patients (Garratt et al., 2001) because seven of its 19 items were found to relate to emotional health (Thompson and Jenkinson, 2002). Some advantages of using SAQ are that it takes less than 5 minutes to complete, it is brief and easily self-administered.

The Quality of Life Index-Cardiac Version (QoLI-CV)

This is a self administered, modified version of a renal-specific quality of life instrument. It was first designed for use with dialysis patients (Ferrans and Powers 1985; Dougherty et al., 1998; Thompson and Jenkinson, 2002; Lee et al., 2004). The QLI-CV III contains 72 items equally divided into two parts. Part 1 measures the satisfaction of patients with various domains of life and part 2 measures the importance of those domains to the individual (Dougherty et al., 1998; Dempster and Donnelly, 2000). The content validity of the QLI-CV was established by an extensive review of published reports on issues related to quality of life and on reports from cardiac patients concerning their quality of life (Ferrans and Powers, 1985).

Both the satisfaction and the importance part contain 36 items covering five domains: overall life satisfaction; health and functionin;, socioeconomic; psychosocial and spiritual; and family and relationships (Dempster and Donnelly, 2000). Its limitation

includes low usability in cardiac patients and its limited discriminative and evaluative value (Dempster and Donnelly, 2000; Smith et al., 2000).

Angina Pectoris Quality of Life Questionnaire (APQLQ)

This is a 22-item instrument divided into four domains: physical activities, somatic symptoms; emotional distress; and life satisfaction (Smith et al., 2000). The instrument has established good psychometric properties for discriminative purposes. However, its limitation includes low test-retest reliability estimates and low responsiveness estimates.

The Summary Index (SI)

The Summary Index is a product of a combination of three health-related quality of life instruments (Dempster and Donnelly, 2000). The three combined instruments are: the Angina pectoris Quality of Life Questionnaire (APQLQ); the anginal impact questionnaire (Wilson et al., 1991); and the psychological general well being scale (Dupuy, 1984). The SI is a 51-item questionnaire, divided into six sections: impact of angina on daily life; physical exertion; vitality; alertness; self-control; and emotional function (Dempster and Donnelly, 2000). Although the instrument displayed good reliability and responsiveness properties, its use in clinical practice is limited because it is lengthy and not user friendly.

The Myocardial Infarction Dimensional Assessment Scale (MIDAS)

This is a 35-item myocardial infarction specific instrument measuring seven areas of health status: physical activity, insecurity, emotional reaction, dependency, diet, concerns over medication, and side effects (Thompson and Jenkinson, 2002). Although, according to the authors, MIDAS has high face, internal and constructs validity, the instrument still needs to undergo further psychometric evaluation in order to establish its wider usability in clinical practice.

Minnesota Living with Heart Failure Questionnaire (MLHF)

The MLHF is a 21-item widely used valid and reliable self-administered instrument. It has been recognised as one of the preferred health related quality of life instrument for patients with heart failure (Rector and Cohn, 1992; Berry and McMurray, 1999). It

is used to assess the physical, socioeconomic and psychological impairments of patients with heart failure. MLHF was originally adapted from the following three instruments: Duke Health profile (Guillemin et al., 1993); the Minnesota Quality of life Questionnaire in Cardiac failure (Leal et al., 2005); and the Goldman Specific Activity Questionnaire (Salek, 2004).

Multidimensional Index of Life Quality (MILQ)

This is the only existing single HRQoL measure for cardiovascular patients. It contains 35 items covering nine different domains: mental health; physical functioning; physical health; cognitive functioning; intimacy; social functioning; productivity; relationship with health professionals; and financial status (Avis et al., 1996). Although an article on its usability has been published, there is no empirical evidence of its use in patients with CHD other than the original manuscript describing its development and psychometric properties (Oldridge et al., 2002).

The Short Form -12 health survey (SF-12)

The Short Form-12 Health Survey measures generic health concepts relevant across age, disease, and treatment groups (Lim and Fisher, 1999). It was designed in responding to the need for development of a shorter instrument to the original SF-36 (Garratt et al., 2001). The SF-12 includes eight concepts commonly represented in health surveys: Physical Functioning (PF); Role Functioning Physical (RFP); Bodily Pain (BP); General Health (GH); Vitality (VT); Social Functioning (SF); Role Functioning Emotional (RFE); and Mental Health. Results are expressed in terms of two meta-scores: the Physical Component Summary (PCS); and the Mental Component Summary (MCS). SF-12 was designed for self-administration and has been used with a high degree of acceptability and data quality (Ware et al., 1995). The SF-12 uses two items each to estimate scores for four of the eight health concepts (physical functioning, role functioning physical, role functioning emotional, and mental health). Scores for the remaining four health concepts (bodily pain, general health, vitality, and social functioning) are estimated using one item each (Ware et al., 1995).

Table 1.4 Attributes of existing cardio-specific quality of life instruments

CARDIO-SPECIFIC HRQOL INSTRUMENT & SOURCE	COVERAGE	ITEMS	RATER (Time)	RESPONSE OPTIONS	Language Validation studies	PSYCHOMETRIC PROPERTIES		
						Reliability	Validity	Responsiveness
Quality of life after myocardial Infarction (QLMI-2)(revised version of MacNew quality of life (Hillers et al., 1994)	Emotional, physical & Social status	27	Self – administered 5-10 minutes Valenti et al, 1996; Interview-administered (Farsi version)	Score : 1-7	Iranian (Farsi) version (Asadi-Lari et al., 2003); Chinese version (Yu et al.,2007); Dutch version (De Gucht et al., 2004); German version (Hofer et al.,2003); English (US, Australian) version (Valenti et al.,1996; Hillers et al., 1994; Lim et al., 1993); Portuguese version (Leal et al.,2005); Spanish version (Brotons et al.,2000); Turkish version (Daskapan et al., 2007)	Pearson's correlation coefficient (0.75-0.87) Internal consistency (0.50-0.83), Intra class correlation (Farsi version) 0.92-0.95	Evaluative Validity; Discriminative validity	Not reported
MacNew quality of life (MacNew QLMI) (Dempster et al., 2004; Taylor et al., 2000)	Self-esteem, restriction, fatigue, emotional function & confidence	26	Self-administered	Score: 1-7	Not reported	Not reported	High inter- and intra reliability coefficient (Taylor et al., 2000)	Not reported

The Seattle angina questionnaire (SAQ) (Spertus et al.,1994)	**Coronary artery disease (CAD); Physical limitation, anginal stability, anginal frequency, treatment satisfaction, and disease perception.**	**19**	**Self-administered < 5 minutes**	**Scales: 0-100 Higher scores indicate Higher levels of Functioning.**	**UK version (Garratt et al., 2001); Norwegian version (Pettersen et al.,2005)**	**Internal consistency-Norwegian version (0.75-0.92); intra – class correlation-Norwegian version (0.29-0.84)**	**Construct validity between SAQ and SF-36; factor analysis (UK version)**	**Tested in 60 CAD patients, four of the five SAQ scales showed significant improvement in functional status (Spertus et al.,1994)**
Quality of life index-cardiac version (QOLI-CV) (Dougherty et al., 1998; Taylor et al, 2000)	Originally designed for dialysis patients. Five domains: overall life satisfaction, health & functioning, Socioeconomic, psychosocial & spiritual, family & relationships.	72	Self-administered	Likert scales: 0-30	Not reported	High reliability; internal consistency (0.86-0.96) in angioplasty patients & 0.70-0.93 in anginal patients (Dempster et al., 2007)	Construct validity (factor analysis)	Significant change in the health and functioning scale (Dougherty et al., 1998)
Angina pectoris quality of life (APQLO) (Dempster et al., 2007)	Physical activities, somatic symptoms, emotional distress, & life satisfaction.	22	Self - administered	Not reported	Original language= Swedish. Danish version, Dutch version, Finnish version, French version, German version etc.	Internal consistency (0.82-0.90)	Concurrent validity with SF-36; discriminant validity between APLQ scales & total APLQ scores in CAD patients	Not reported

Summary index (SI) (Dempster et al., 2007	Impact of anginal on daily life, physical exertion, vitality, alertness, self control, & emotional function.	51	Self-administered	Not reported	Not reported	Test-retest reliability (0.69-0.84) Internal consistency (0.91-0.98)	Discriminant validity	Responsiveness (0.25-0.44)
Myocardial infarction dimensional assessment scale (MIDAS) (Thompson and Jenkinson, 2002)	Physical activity, Insecurity, emotional reaction, dependency, diet, concerns over medication, side effects of medication.	35	Self-administered	Score: 1-5	Mandarin for China	Internal consistency (0.74-0.95)	Construct validity with SF-36	Not reported
Multidimensional index of life quality (MILQ) Avis et al., 1996	Mental health, physical health, physical functioning, cognitive functioning, social functioning, intimacy, productivity, financial status & health professional	35	Interview-administered	Score: 1-7 1= very dissatisfied 7= very satisfied	Spanish version	Internal consistency > 0.76; test-retest reliability > 0.73 (Avis et al., 1996)	Construct validity	Not reported
Minnesota living with heart failure questionnaire (MLHF) (Briancon et al., 1997)	Physical, mental, Socioeconomic, disability.	21	Interviewer-administered, self-administered, telephone-administered. 5-10 minutes for self-administered.	Scale: 0-5	French version, Czech version, Danish version, Croatian version, German version etc.	Test-retest correlation to 26 patients on a transplantation waiting list (Briancon et al., 1997)	Factor analysis.	Not reported

Aims of the present study

No published studies have investigated the social and economic implications of medication-related problems in people with chronic illness, such as cardiovascular, diabetes, asthma etc receiving long term multiple drug therapy. This study therefore aims to examine the impact of medication-related problems and medication side effects on socio-economic and quality of life of cardiovascular patients.

The majority of patients with chronic conditions are on repeat prescriptions of their medication provided their conditions are stable. Many of these patients do not see their general practitioners regularly. Community pharmacists are therefore in a unique position to identify medication-related problems in these patients through their pro-active involvement in pharmaceutical care services such as medicine use review (MUR) and prescription intervention procedure. Provision of pharmaceutical care services by community pharmacists have so far shown positive results in all the three components of health outcomes (economic, clinical and humanistic) with early prevention of potential harm to the patient. With the availability of a new instrument aimed at cardiovascular patients in the community setting, they will be able to ascertain whether side-effects patients experience are due to drug treatment. This instrument will also help community pharmacists to evaluate the impact of any reported cases of medication-related side effects on the quality of life of their patient.

Objectives:

- To determine frequency of medication-related problems of cardiovascular drugs in the community setting.
- To investigate the impact of medication-related problems on cardiovascular patients' quality of life.
- To develop an instrument to measure the socio-economic impact of medication-related problems of cardiovascular drugs.

- To evaluate the psychometric properties of this newly developed instrument such as content validity, factor analysis, practicality and applicability and test-retest reliability.
- And finally, to compare its validity with some of the existing cardio-specific and generic quality of life instruments.

CHAPTER 2

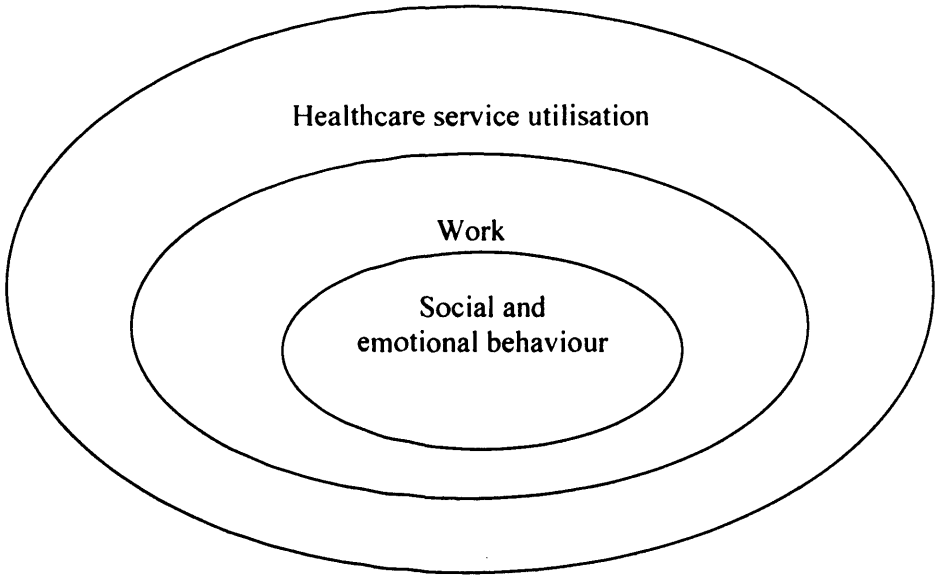
Study Rationale and Methodological Framework

INTRODUCTION

The general introduction to this thesis in chapter one outlined the lack of a socioeconomic measure that is tailor-made for use in assessing the socioeconomic impact of medication-related problems especially of cardiovascular drugs. Although some existing HRQOL instruments provide a comprehensive evaluation of the disease impact, they do not consider the influence of medication side-effect on a patient's physical and psychosocial functional behaviour. Therefore, there are still gaps in the knowledge of measures that provide treatment outcomes especially those of medication-related side-effects. Considering the socioeconomic concept as part of a wider component of HRQOL measures, the impact of medication side-effects often affect more than three of these HRQOL measure components such as emotional status, social activities and work. Medication-related problems can impact other important areas of a patient's life such as healthcare services utilisation (Figure 2.1).

In the absence of a validated instrument with which to measure the socioeconomic impact of the side-effects of cardiovascular drugs, this chapter will present the rationale for the development of such a measure and review the appropriate methodological framework.

Figure 2.1 Socioeconomic concepts and medication-related problems



STUDY RATIONALE

As shown in the introductory part of this chapter, the rationale behind undertaking this present study is multifarious. The main reasons can be summarised as: 1) unavailability of a validated socioeconomic instrument; 2) insufficient data to actually carry out research in this area; and 3) different opinions on what constitutes the socioeconomic impact of medication-related issues. The socioeconomic impact of medication-related problems (SEIP-MRP) encompasses a number of different domains such as the socio-emotional distress of MRP, impact on productivity, and use of healthcare services. The phrase "socioeconomic impact of medication-related problems" is a component of the health-related quality of life (HRQOL) concept. In this present study, it will be used interchangeably with "impact on patients' quality of life" as they are expressing the same meaning.

At present, there are no instruments that assessed the socioeconomic impact of medication-related problems in cardiovascular disease. The commonly used available scales for cardio-specific HRQOL measurement as detailed in chapter one which may be applicable to the socio-economic concept have little relevance. They are actually measuring a related outcome but different to the socioeconomic impact concept. There is therefore a need for the development of a valid and reliable instrument for measurement of socioeconomic impact of medication-related problems. Due to these shortcomings, the present study was undertaken to develop a socioeconomic measure that redressed some of these problems. The following suggestions were taken into consideration:

- To conceptualise a measure that will be universally accepted as a cardio-specific socioeconomic health status measure;
- To develop an instrument with a sound methodology and which will be based on constructs which the observed population consider to be important determinants of the socioeconomic effects of medication-related problems;
- To develop an instrument that will measure the socioeconomic impact of medication-related problems rather than a medical condition;
- The instrument developed will possess sound psychometric properties so that it will be widely acceptable in clinical research and health policy decision-making in the area of drug therapy.

This new instrument, in line with already established guidelines will undergo reliability and validity tests before it can be administered to patients with cardiovascular disease.

METHODOLOGICAL FRAMEWORK

Methodology is the navigator of research. It describes the process by which the researcher arrived at their results and conclusions. Methodology is important in determining whether the findings of a study can infer truth in the phenomena of interest (Gaudet, 1998).

Semantic issues

Semantic issues are those issues which arise when trying to implement new measure in a situation where there is non in existence to compare with. In this study, these issues relate to whose socioeconomic condition is affected, who provides the assessment and the type of instrument to be used.

Whose socioeconomic status is affected?

Despite the availability of effective drug therapy, many cardiovascular patients who are on long-term beta-blocker therapy may develop symptoms such as depression, fatigue, and sexual dysfunction. These conditions can be considered to be strong indicators of the social and emotional well being of a human being. Developing a socioeconomic instrument will therefore help to capture these negative outcomes of drug therapy.

In HRQOL studies for example, assessment of an individual is ideally obtained by a self-report method (Adair et al., 2007). However, the main problem with this method in the context of measuring the impact of medication-related problems may be in obtaining a reliable and accurate assessment. Cardiovascular patients, for example may not know whether the side-effects are medication-related or due to their condition. For example, fatigue- a common symptom of heart failure may be misinterpreted as a side-effect of a beta-blocker in a patient initiated with this drug. The items that form the basis of a socioeconomic measure may therefore be taken from patients' experiences of administration of a new drug to treat their condition.

Technical issues

These relate to the administration of a questionnaire, scaling of responses and documentation of measurement properties.

Administration of Questionnaires

Use of questionnaires in carrying out research is an inexpensive way to gather data from a potentially large number of respondents. A well-designed questionnaire that is used effectively can gather information on the overall performance of the observed measure (Bowling, 2005a). There are several different methods of data collection using questionnaires including postal, telephone interview, or face-to-face administration. When a questionnaire is administered, the researchers' control over the environment will be limited. This loss of control may have different effects on the quality of the data collected. Within different modes of questionnaire administration, there could be many biases influencing the accuracy of responses. Therefore knowledge of such factors in advance of data collection should enable the researcher to minimise their impact on the quality of the data.

Interviewer-administered

Interviewer-administered questionnaires involve the use of a trained interviewer, who administers the questionnaire on a one-to-one basis to ensure compliance, higher response rate and minimise the occurrence of missing items. According to Salek and Luscombe (1992), this method can be engaged in a situation where the respondent is illiterate, physically disabled or has visual problems. The interviewer must read aloud the questions and document responses without influencing the respondent's views (Salek and Luscombe, 1992). This mode of administration also allows clarification of ambiguity. According to Bowling (2005a), "a friendly motivating interviewer can increase response and item response rates, maintain motivation with longer questionnaires, probe for responses, clarify ambiguous questions, help respondents with enlarged show cards of response choice options, use memory jogging techniques for aiding recall of events and behaviour, and control the order of the questions" .

However, this mode of administration has its limitations. The disadvantages include longer completion time, higher cost, and occurrence of bias. In addition to these, its

use is limited when such issues such as privacy, quietness and confidentiality are taken into consideration in a situation where there is no consultation room to carry out this task.

Interviewer-delivered

This is a self-report mode of questionnaire administration. Interviewer-delivered questionnaires require direct and full-time involvement from the interviewer to provide an initial instruction, hand over the questionnaire and respond to any questions from the respondents (Lua, 2002). Its advantages include: time and resource reduction and fewer burdens to professionals. However, the disadvantages of this method include low response rate and the occurrence of bias as a result of unwillingness of respondents to acknowledge problems (Guyatt, 1993).

Mail-delivered

Mail-delivered mode of administration of questionnaires is less expensive and gives the respondents more privacy, confidentiality and time to complete the questionnaire (Lua, 2002). However, response rate with this mode of administration may be lower than expected with other modes of administration. This is the most burdensome mode as this demands that respondents are literate in reading the language of the survey, that they do not have visual impairments and have the dexterity (e.g. of wrist, fingers) to self-complete the questions (Bowling, 2005a). In addition, bias can arise as a result of differences between respondents and non-respondents, no assurance of completion from the intended person and no opportunity to supplement the patient's responses with observational data (Salek and Luscombe, 1992).

Telephone-administered

There is similarity between this mode of administration and interviewer-administered questionnaires. The only difference is that the interviewer is not physically involved face-to-face with the respondent throughout the process. In addition, it is less resource intensive (Guyatt, 1993). This mode of administration requires basic verbal and language skills. Its disadvantages include staff training requirement, limited coverage for only respondents in possession of a telephone facility. Also, telephone interviews make greater auditory demands and may be burdensome to some respondents (Bowling, 2005a).

Electronic questionnaire administration

This mode of administration requires access to a computer and /or Internet facilities (whether via an interviewer with a lap top personal computer (PC), or facilities in an office, clinic or home setting), basic computer literacy, and also familiarity with numbers and keyboards. They have literacy requirements in relation to reading the questions and replying, and can also have auditory requirements. However, electronic programmes can be designed to require a limited range of keys. They can also eliminate the problem of missing data (Drummond et al., 1995). Studies have also been documented in individual experiments and in reviews that this mode of administration has more complete item response rates than paper and pencil methods (Johnson et al., 2001). However, its drawbacks included its high cost and short battery life on the computer. In addition, populations in some cultures may be apprehensive to use such a method and be intimidated by technology (Lua, 2002). It is therefore clear that modes of questionnaire administration differ in many ways with regard to their strengths and weaknesses. In general, low education level, poor physical status and progressive disease can result in a low rate of completion (Kaasa et al., 1998).

Scaling of Responses

Scaling involves the construction of instruments for the purpose of measuring abstract concepts. A wide variety of response options are available and different options are suitable for different types of question and for different types of measure. Simple scales might consist of an affirmative response or the choice of dichotomous yes/no options. Evaluative instruments must be responsive to any important change, even if small. Scales are often chosen with multiple response options such as a 4 or 5-point Likert scale because of their easy administration and interpretation.

Frame of Reference

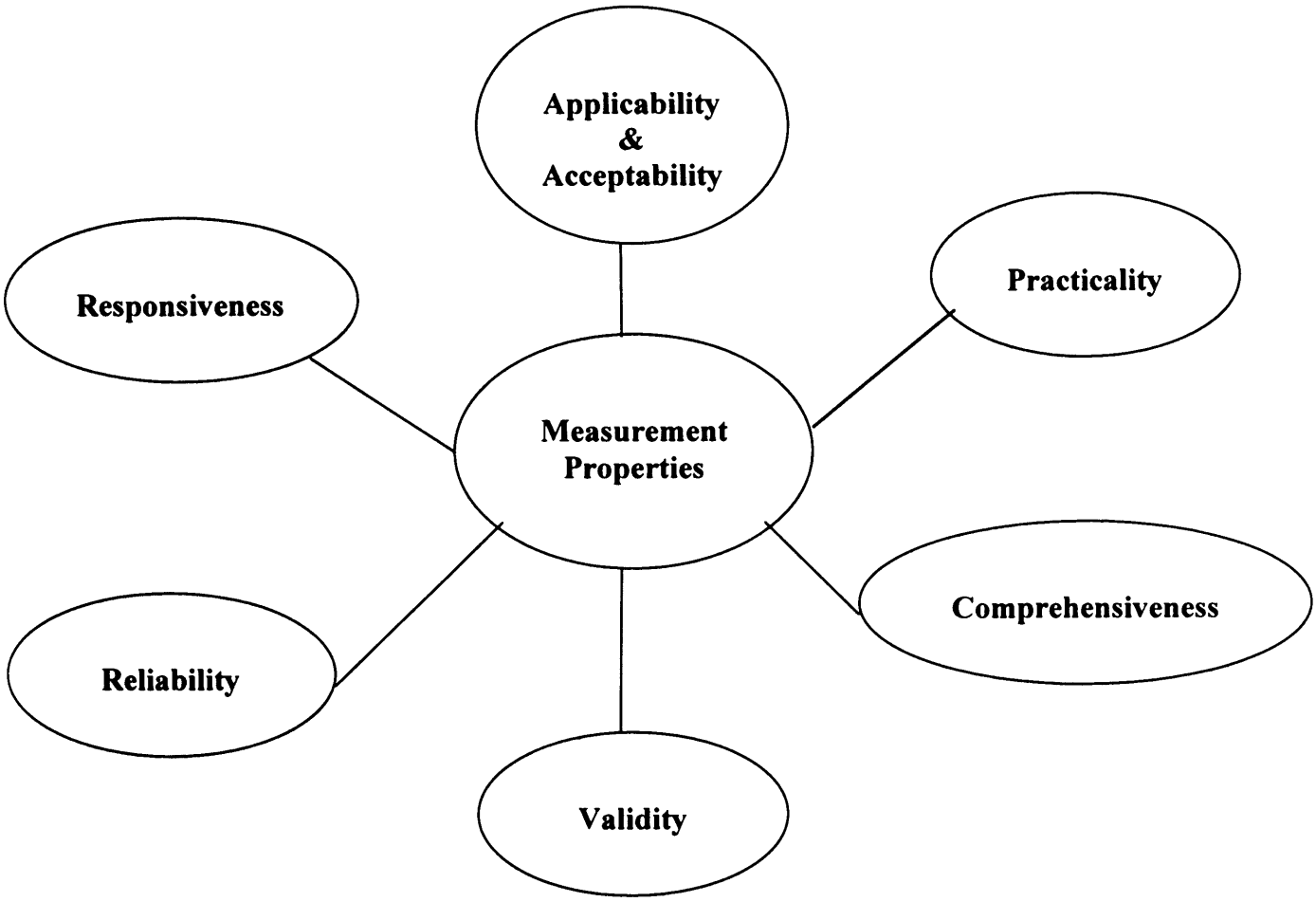
This is defined as a structure of concepts, values, customs, views, etc., by means of which an individual or group perceives or evaluates data, communicates ideas, and regulates behaviour. In questionnaire development, the items in a questionnaire should be asked in the context of a specific and well-defined period of time. The

frame of reference chosen must take into account the respondent's ability to recall information.

Measurement Properties

Various measurement properties need to be assessed when evaluating a new instrument/measure (Figure 2.2). According to Bungay et al (2005), there are two psychometric properties that any measurement scale must possess: reliability and validity (Bootman et al., 2005) and in addition to these, useful measuring scales must be sensitive to change and accepted by the investigators and respondents. Examples of such psychometric properties that will be assessed in this present study include applicability and acceptability, comprehensiveness, practicality, reliability, and validity.

Figure 2.2 Types of psychometric tests carried out in the evaluation of a new instrument



In addition to what Bootman et al. (2005) suggested above when deciding which measure to use, Bowling (2005b) also added that the investigator should establish: whether a disease-specific or broad-ranging (generic) instrument is required; the appropriateness of the instrument for the study population; and the acceptability of the instrument to the group under study (Hunt et al., 1980)

Applicability and acceptability for use

Applicability describes the content and emphasis of an instrument in terms of appropriateness of wording, clarity and simplicity of language (Lua, 2002). It must also be acceptable to the intended respondents (Salek and Luscombe, 1992). Both investigators and respondents will have valuable opinions about the acceptability of the instrument. How easy the measure is to use, score, and interpret are valid concerns. In addition, the completion rate, the extent of missing data, and the number and nature of complaints about the tool are clues about the acceptability of the measure for use in a research or clinical setting (Bootman et al., 2005). According to these authors, acceptability is also expressed as respondent burden. Regardless of the administration format (self-administered, telephone interview, personal interview, observation, or postal survey), Bootman et al. (2005) stated further that failure to consider respondent burden can doom any survey project.

Practicality

An instrument should be feasible in its intended population and clinical setting. The length of the questionnaire must be appropriate for the population and there should be minimal burden imposed on both the respondents and professionals during data collection and analysis (Salek and Luscombe, 1992). This is especially vital with regard to the cost and time consumed in the process (Deyo, 1984). Considerations must also be made in terms of the questionnaire mode of administration and whether it can be easily scored and understood. Questionnaire length, frequency of administration as well as staff and institutional burden would have to be taken into account. Patients would not generally tolerate lengthy and repeated measurement (Lua, 2002)

Comprehensiveness

Comprehensiveness describes how thoroughly the domains of interest in a measure are sampled by the items or questions included in that measure. The coverage of a tool needs to be comprehensive so that sufficient information can be gathered to justify the produced outcomes. According to Osoba (1994), in HRQOL for example, evidence has shown that one-dimensional instruments are not comprehensive enough to measure health-related quality of life and in essence, emphasises is placed on the need for a multidimensional, more comprehensive tool. Similar to this, a comprehensive socioeconomic measurement should include both objective and subjective issues in addition to other concerns such as spirituality and body image.

Validity

Validity is concerned with whether the indicator actually does measure the underlying attribute or not. As suggested by Bungay and Ware (1993), a number of key questions must be answered if researchers are to have confidence in the data captured with a newly developed health measure. These include:

- Do the questions in the instrument really measure the concept under study?
- Do respondents understand the questions being asked?
- Are the response categories appropriate for the questions?

Validity refers to the extent to which differences in test scores reflect the true differences in individuals under study (Bungay and Ware, 1993). Although it is the goal to elicit observed differences that are indeed true differences among respondents, factors such as how the measure is administered, who administers it, where it is administered, and when it is administered can affect responses across study participants. There are no standard guidelines for validating health measures, however, varying terminology has been used to assess validity of a measure such as content validity, criterion validity and construct validity (Bowling, 2005b). However, all types of validity are addressing the same issue of the degree of confidence that can be placed on the inferences drawn from scale scores.

According to the American Psychological Association (1974), the assessment of validity involves assessment against a standard criterion, however, due to unavailability of a "gold standard" of health against which health-status indices can be compared, the validation methods commonly used are the assessment of content and construct validity.

Content validity

Content validity of health measurement scales (HMS) has been described as how adequately the items sampled represent the range of each domain assessed by the instrument. Yaghmaie (2003) referred to the content validity of an instrument as the degree that the instrument covers the content that it is supposed to measure. Each item should fall into at least one of the content areas being measured. If it does not, then the item is not relevant to the scale's objectives. A scale with good content validity is one that covers all aspects of the concept being addressed. To establish content validity, Bungay et al (1993) suggested that a comparison needs to be made between the items included in a scale and some definitional standard for which there is general acceptance.

Content validity is related to face validity though content validity should not be confused with face validity. The latter is not validity in the technical sense; it refers, not to what the test actually measures, but to what it appears superficially to measure (Bowling, 2005b). Content validity is more systematic than face validity, and a panel following literature reviews, focus groups, and exploratory interviews with the target population usually makes judgements about these issues. It is generally agreed that the content validity of subjective indicators should be judged by members of the target group being assessed (Patrick, 2003)

Criterion validity

This refers to whether the variable can be measured with accuracy. Traditionally, criterion validity is defined as the correlation of a scale with some other "criterion" measure of the topic under study, ideally a "gold standard" (Bowling, 2005b). Criteria or concrete validity is the extent to which the measures are demonstrably related to concrete criteria in the "real" world (Pennington, 2003).

Criterion validity is divided into two types: concurrent and predictive validity. Concurrent validity is demonstrated where a test correlates well with a measure that has previously been validated. The two measures may be for the same construct, or for different, but presumably related, constructs (Pennington, 2003). Predictive validity in contrast is the extent to which a scale predicts scores on some criterion measure. Predictive validity shares similarities with concurrent validity in that both are generally measured as correlations between a test and some criterion measure.

Construct validity

Construct validity refers to whether a scale measures the unobservable construct that it purports to measure. A construct is not restricted to one set of observable indicators or attributes. It is common to a number of sets of indicators. Evaluation of construct validity requires examining the correlation of the measure being evaluated with variables that are known to be related to the construct purportedly measured by the instrument being evaluated or for which there are theoretical grounds for expecting it to be related (Campbell & Fiske, 1959). Unlike other types of validity testing, testing for construct validity involves assessing both theory and method simultaneously. It necessitates stating a conceptual definition of the construct to be measured, specifying its dimensions, hypothesising its theoretical relationship with other variables, and then testing it (Bowling, 2005b).

Convergent and discriminant validity are special types of construct validity. Convergent validity, is the degree to which an operation is similar to (converges on) other operations that it theoretically should also be similar to. For convergent validity, correlations should be high between similar or related measures of the same health concept (Bungay and Ware, 1993). For instance, to show the convergent validity of a cardio-specific HRQOL measure, the scores on the test can be correlated with scores on other tests that are also designed to measure quality of life in heart disease. High correlation between the test scores would be evidence of a convergent validity. Discriminant validity on the other hand describes the degree to which the operationalisation is not similar to (diverges from) other operationalisations that it theoretically should not be similar to. Campbell and Fiske (1959) introduced the concept of discriminant validity within their discussion on evaluating test validity. They stressed the importance of using both discriminant and convergent validation

techniques when assessing new tests. A successful evaluation of discriminant validity shows that a test of a concept is not highly correlated with other tests designed to measure theoretically different concepts. Construct validity can be evaluated by statistical methods that show whether or not a common factor can be shown to exist underlying several measurements using different observable indicators. In many research studies, factor analysis has been used to demonstrate evidence of construct validity.

Factor analysis

Factor analysis is one of numerous statistical techniques used to analyse data. It has been widely used by psychometricians as a construct validation tool (Gorsuch, 1983). This technique allows its user to condense a large set of variables or scale items down to a smaller, more manageable number of dimensions or factors. It is often used when developing scales and measures, to identify the underlying structure (Pallant, 2002). In research, factor analysis is primarily engaged to reduce a large number of variables to a smaller number of clusters while retaining maximum spread among experimental units (Pallant, 2002). Many researchers have shown that this method can be used to provide an operational definition for an unobserved, hypothetical construct by using observed variables, or to test a theory about the nature of underlying variables (Ang and Huan, 2006)

Exploratory factor analysis

Factor analysis can be either exploratory or confirmatory. Exploratory factor analysis (EFA) groups together variables that are intercorrelated. According to Finch (2006), EFA is used when the researcher is primarily interested in trying to identify potential factors underlying a set of items, but may not have a strong a priori model that he or she would like to test. Tabachnick and Fidell (2001) pointed out that EFA is usually used in the early stages of research when hypotheses about relationships in a reduced data set can be generated.

Confirmatory factor analysis

In contrast to EFA, Confirmatory factor analysis (CFA) is a more complex set of techniques used later in the research processes to confirm hypotheses about the

structure of underlying set of variables. In this case, variables are specifically chosen to reveal underlying structural processes. CFA can also be applied in a situation where specific model linking items to factors is to be tested (Finch, 2006). Sometimes, data used in confirmatory factor analysis can be different from those used in exploratory FA.

There are different opinions on what factor analysis and principal component analyses are. Pallant (2002) has pointed out that researchers often use the terms 'factor analyses' and 'principal components analyses' interchangeably. These two sets of techniques are similar in many ways since both attempt to produce a smaller number of linear combinations of the original variables in a way that captures most of the variability in the pattern of correlation. Some researchers argued that these two techniques do differ in a number of ways. For example, Tabachnick and Fidell (2001) suggested that in principal components analysis the original variables are transformed into a smaller set of linear combinations, with all of the variance in the variables being used whereas in factor analysis, factors are estimated using a mathematical model, where only the shared variance is analysed.

Suitability of data for factor analysis

Pallant (2002) suggested that 'sample size' and 'the strength of the relationship among variables should be taken into consideration before determining suitability of a particular data set for factor analysis. This was further elaborated by Hogarty et al., (2005) who suggested that researchers need to take into consideration among other factors the use of larger samples in the conduct of factor analysis and its provision of more precise and stable estimates of factor loadings in the observed population.

Many researchers have proposed a rough guide for rating adequate sample sizes (Hogarty et al., 2005). For example, sample sizes of 100 are considered to be poor, 200 sample size is fair, 300 = good, 500 = very good, and 1000 or more = excellent. Gorsuch (1983) recommended minimum sample sizes that vary between 100 to 250. Tabachnick and Fidell (2001) suggested that there should be 300 or more cases for factor-analytic purposes (Reio and Wiswell, 2006). However, Pallant (2002) stated that many authors do concede that a smaller sample size such as 150 cases should be

sufficient if solutions have several high loading marker variables such as 0.80 and above. In the light of these diverse recommendations, Hogarty et al. (2005) suggested that under certain conditions, smaller sample sizes than those generally recommended in the literature may be adequate to yield good recovery of factors.

Another issue that determines factorability of a data set is 'the ratio of sample size to the number of variable'. Although there is scholarly support for employing sample size-variable ratios as low as 5:1 for factor-analytic research, Gorsuch (1983) has recommended a 10:1 ratio; that is 10 cases for each item to be factor analysed; Cattell (1978) on the other hand has recommended a ratio ranging from 3:1 to 6:1; whereas Hair et al. (1995) have suggested a ratio of 20:1.

The strength of the inter-correlation among the items is another issue to take into consideration before determining factorability of a data set. Tabachnick and Fidell (2001) suggested that a correlation matrix should be inspected for coefficients greater than 0.30 and recommend factor analysis should not be considered as an appropriate technique for the given data set if few correlations above this level are found (Pallant, 2002). To support this recommendation, it has been suggested that loadings in excess of 0.71 are excellent, 0.63 are very good, 0.55 are good, 0.45 are fair, and 0.32 are poor (Hogarty et al., 2005).

However, researchers often choose different values based on other preferences as many consider these rules not to represent an undisputed choice. Other measures that have been frequently used to determine the use of factor analysis in a set of data are: the Bartlett's test of sphericity (Bartlett, 1954) and the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy (Kaiser, 1970; Kaiser, 1974). These two measures are common with SPSS- a statistical package that is often used in factor analytic purposes. Bartlett's test of sphericity should be significant with a p value less than 0.05 and the KMO index ranges 0 to 1, with 0.60 suggested as the minimum value for a good factor analysis (Tabachnick and Fidell, 2001).

Factor extraction

Factor extraction according to Pallant (2002) involves determination of the smallest number of factors suitable to represent the inter-relations among the set of variables. This method attempts to remove variance common to sets of variables from the original matrix of association. There are multiple ways to extract factors, these include methods such as principal components analysis (PCA), principal factors (PF); Image factoring (IF) and principal axis factoring (PAF). The most commonly used approach is PCA and PAF. Gorsuch (1983) suggested that the researcher should consider carefully which method to use because differences can be meaningful. On the other hand, Tabachnick and Fidell (1996) recommended that researchers should adopt an exploratory approach experimenting with different numbers of factors until a satisfactory solution is found (Pallant, 2002).

O'Connor, (2000) pointed out some potential problems that may emerge when non-optimal numbers of factors are extracted. For example, under-extraction can lead to compression of variables into a small factor space, which can result in a loss of important information, or neglect of potentially important factors, or distorted fusing of two or more factors, and above all, an increase in error in the loadings. O'Connor (2000) further elaborated that over-extraction on the other hand may lead to diffusion of variables across a large factor space, and this potentially may result in factor splitting, factors with few high loadings or in researchers' attributing excessive substantive importance to trivial factors.

Factor retention rules

According to Herson (2006), PCA is intended to simply summarise many variables into fewer components, and the latent constructs (i.e., factors) are not the focus of the analysis. This author explained further that when variables are factored, the total number of possible factors equal the number of variables factored; assuming all of the variance in the original variables is not reproduced. Because many of these factors may not contribute substantially to the overall solution or be interpretable, some of them are therefore considered not useful to retain in the analysis and as a result of this can generally constitute a noise or error (Henson, 2006).

Given that the goal of exploratory factor analysis (EFA) is to retain the fewest possible factors while explaining the most variance of the observed variables, Henson suggested that the researcher should extract the correct number of factors, as the decision will affect results directly. Many rules can be used to determine the number of factors to retain. These include: Kaiser's criterion or the Eigen value>1 rule; Catell's scree test; Bartlett's chi square test; minimum average partial (MAP) correlation; and parallel analysis (Turner, 1998). The most commonly used techniques is the eigenvalue > 1 rule and in most cases is the default option in most statistics packages (Thompson and Daniel, 1996). Henson (2006) therefore suggested that these rules do not necessarily lead to the same decision regarding the number of factors to retain

Kaiser's criterion or eigenvalue > 1 rule

This is one of the most commonly used extraction techniques. Using this rule, only factors with an eigenvalue of 1.0 or more are retained for further investigation (Pallant, 2002) and the eigenvalue of a factor actually represents the amount of the total variance explained by that factor. However, researchers have found that the use of this rule is problematic. Eigenvalue > 1 rule has been found to overestimates the number of components to retain (Pallant, 2002) and sometimes underestimates (Reio and Wiswell, 2006).

The use of eigenvalue > 1 rule has also been criticised however, as resulting in the retention of too many factors in some situations (Pallant, 2002) or some components generated may not be reliable, as was originally believed (Cliff, 1998). According to Reio and Wiswell (2006), eigenvalue > 1 rule tends to be less accurate when the number of variables exceeds 30 and can often grossly overestimate the number of factors.

Cattell's scree test

This is a strongly promoted alternative rule of thumb as described by Cattell and Vogelmann in 1977 (O'Connor, 2000). This method involves eyeball searches of plots for sharp demarcations between the eigenvalues for major and trivial factors. It has been suggested that all factors above the elbow, or break in the plot should be retained as they contribute the most to the explanation of the variance in the data set (Pallant,

2002). However, in practice, existence of such demarcations is doubtful (Reio and Wiswell, 2006) or there may be more than one demarcation point. Many published studies not surprisingly, have therefore shown low reliability of scree plot interpretations (O'Connor, 2000).

Bartlett's chi –square test of sphericity

This is commonly used in the SPSS statistics package to help assess the factorability of the data (Pallant, 2002). Bartlett's test of sphericity should be statistically significant with a p-value < 0.05 for the factor analysis to be considered appropriate. However, studies have shown that this test was very inconsistent. According to Henson (2006), the utility of Bartlett's chi square test in exploratory factor analysis (EFA) studies may be very little as it is heavily influenced by sample size.

MAP (minimum average partial) test

This is a statistically based procedure that focuses on the relative amounts of systematic and unsystematic variance remaining in a correlation matrix after extractions of increasing numbers of components (O'Connor, 2000). Before this procedure is used, the researcher must determine how many components or factors to extract before they begin their factor extractions. The MAP test involves a complete principal components analysis followed by the examination of a series of matrices of partial correlations (Henson, 2006). Unfortunately, the MAP test is seldom employed in published research probably due to the fact that it is one of the two less well-known procedures (O'Connor, 2000). However, this extraction method is considered to be one of the two reliable methods in factor analysis

Parallel Analysis

This is considered to be one of the most accurate extraction procedures in factor analysis. Parallel analysis involves extraction of eigenvalues from random data sets that parallel the actual data set with regard to the number of cases and variables (O'Connor, 2000; Reio and Wiswell, 2006). O'Connor (2000) cited an example of a parallel analysis of a data set in which the original data set consists of 305 observations for each of eight variables, then a series of random data matrices of this size (305 x 8) would be generated, and eigenvalues would be computed for the original data and for each of the random data sets. The eigenvalues derived from the

actual are then compared to the eigenvalues derived from the random data. Factors or components are retained as long as the *i*th eigenvalue from the actual data is greater than the *i*th eigenvalue form the random data.

Different parallel analysis programs exist. However, all parallel analysis programs use random number generators, and different programs or even different runs of the same program may produce slight differences in the results (e.g., a 0.04 difference in the 95^{th} percentile eigenvalues from one run to another) (O'Connor, 2000). For this research, we used a program called Monte Carlo PCA for Parallel Analysis.

Factor rotation and interpretation

According to the published literature, there are numerous strategies to perform factor rotations. These are performed to facilitate interpretation of the factor results. Basically, factor rotations can be either orthogonal or oblique (Tabachnick and Fidell, 2001). According to these two authors, results from orthogonal rotations are easily interpretable and reportable; but the researcher needs to assume that the underlying constructs are not correlated and therefore independent. On the other hand, oblique approaches are more difficult to interpret and report, however, they do allow for the correlation of the factors (Tabachnick and Fidell, 2001).

In practice, both orthogonal and oblique rotations often produce similar solutions when the pattern of correlations among the variables is clear. Henson and Roberts (2006) suggested that in exploratory factor analysis, the contribution of a variable to a given factor is indicated by both factor pattern coefficients and factor structure coefficients. Thompson and Daniel, (1996) further noted that the factor structure matrix gives the correlations between all observed variables and all extracted factors. The two commonly used methods of rotations are the varimax (orthogonal) and Direct Oblimin (oblique).

Reliability

A measure is judged to be reliable when it consistently produces the same results, particularly when applied to the same subjects at different time periods when there is no evidence of change (Bowling, 2005b). The reliability of a scale can vary

depending on the sample that it is used with. In general, the acceptable minimum value for a reliability coefficient for an instrument used for group comparison is 0.70 (Pallant, 2002). Reliability may be estimated through a variety of methods which include: internal consistency (for example, split-half, item-item correlations and item-total correlations), test-retest, intra-rater, and inter-rater agreement and sensitivity to change.

Internal consistency reliability

This is the average degree of association or homogeneity between the items in the test. Each item within a test should be measuring different aspects of the same factor while consistently contributing to the total score for the test. This method of reliability test can take the form of correlations between the items in the scale, or within each scale domain, or between the two halves of the scale where the scale can be divided into two equivalent parts (split-half reliability) (Bowling, 2005b). According to Boyle (1991), the term "internal consistency" has been used extensively to refer to the reliability of a scale based on the degree of within-scale item intercorrelation measured by either the split-half method, Cronbach's alpha, as well as the Kuder-Richardson-20 and 21 (KR_{20} and KR_{21}) coefficients.

Cronbach's alpha is the most commonly reported form of reliability coefficient and its calculation is based on the average correlation among the items and the number of items in the instrument. Its value ranges from 0 to 1. According to Bowling (2005b), a low coefficient alpha (e.g. below 0.50) indicates that the item does not come from the same conceptual domain.

Test –retest reliability

This is the correlation between scores obtained by the same person on two separate occasions. It is a form of stability of the measure over time. The main problem with this is that the first administration may affect responses on the second and also there can be problems with interpretation of observed change, given the potential for observer errors with any scale, and the potential for genuine individual change between administrations which affects the estimate of reliability (Bowling, 2005b).

In addition, random fluctuations in performance give rise to variation between the two observations; therefore low test-retest reliability may not reflect the psychometric properties of the test (Walker, 2002). Researchers differ in their opinions as to the length of time period, but intervals between 2 and 14 days have been considered suitable in practice (Walker, 2002).

Inter-rater reliability

This relates to the degree of concordance shown between two or more raters in assessing the HRQOL of a common cohort of subjects using the same HRQOL instrument. It is only considered for interview and interview-administered measures and the likelihood of chance agreement between raters must be taken into account with instruments using a categorical scale (Walker, 2002). Inter-rater reliability is determined from correlations between different raters' responses and the reliability coefficients are calculated using Kendall's index of concordance (W) (Walker, 2002). The coefficient ranges from 0 to 1, with 1 indicating complete inter-rater agreement (Lua, 2002). In the case of categorical measures, the kappa coefficient is the statistic of choice. The Kappa coefficient is defined as the actual inter-rater agreement beyond chance divided by the potential inter-rater agreement beyond chance.

Mathematically, $k = O - C / 1 - C$.
O = observed agreement beyond chance
C = chance agreement
1 = maximum level of agreement that can be reached among raters.

If the kappa value falls below 0.40, the result is considered to be "poor"; kappa value above 0.40 but less than 0.60 is considered to be "fair"; also, if the value of kappa is above 0.60 but less than 0.80, this result is classified as "good"; and any value of kappa above 0.80 is classified as "excellent".

Sample size

A question a researcher is often faced with is: how large should his sample be in order to conduct an adequate survey? There is no universally accepted number of cases to be included in a particular sample. According to Bailey (1987), much depends on: 1) the nature of the population under study, 2) the purpose of the study, and 3) the

desired target difference if applicable. Sample size is governed by the power of the statistical test used. Both are critical to any study where HRQOL is an important endpoint. The power of a statistical test is determined by effect size, reliability of the measurement and the significance level (Lua, 2002; Walker, 2002). The significance level can be chosen in advance and reliability can be evaluated as necessary.

In order to increase precision, representativeness and greater reliability of the data, many authors do recommend the use of a large sample. It has been suggested that the correct sample size depends upon the purpose of the study, design of the study, data collection methods used, and the nature of the population under scrutiny (Lua, 2002). However, due to the exploratory nature of this research, sample size calculations appear irrelevant in this research study.

Responsiveness to change

This is the ability of an instrument to be responsive to actual changes that occur over time. It is a measure of the association between the change in the observed score and the change in the true value of the construct. This involves correlating the instrument's scores with other measures that reflect any anticipated changes. This is extremely important as an indicator of validity in evaluative instruments (Walker, 2002). The greater an instrument is sensitive to change, the more useful it is in a clinical trial situation, because it will be more sensitive to clinical intervention. Responsiveness can be poor due to floor and ceiling effects, which is where improvement or deterioration goes undetected in those subjects with either the best or worst HRQOL score respectively in the instrument under validation. Low responsiveness rather than small sample size may be responsible for an instrument reporting no difference when a true change has occurred leading to type 2 errors (Walker, 2002).

RESEARCH PLAN

The rationale and issues that need to be considered for the development of a new socioeconomic measure have been discussed in the previous section. The second section of this chapter focuses on the research plan for the development of the SEIP and its establishment as a novel socioeconomic assessment instrument for use in

patients with medication-related problems especially of cardiovascular drugs. Figure 2.3 shows the conceptual framework of the research.

Literature Review

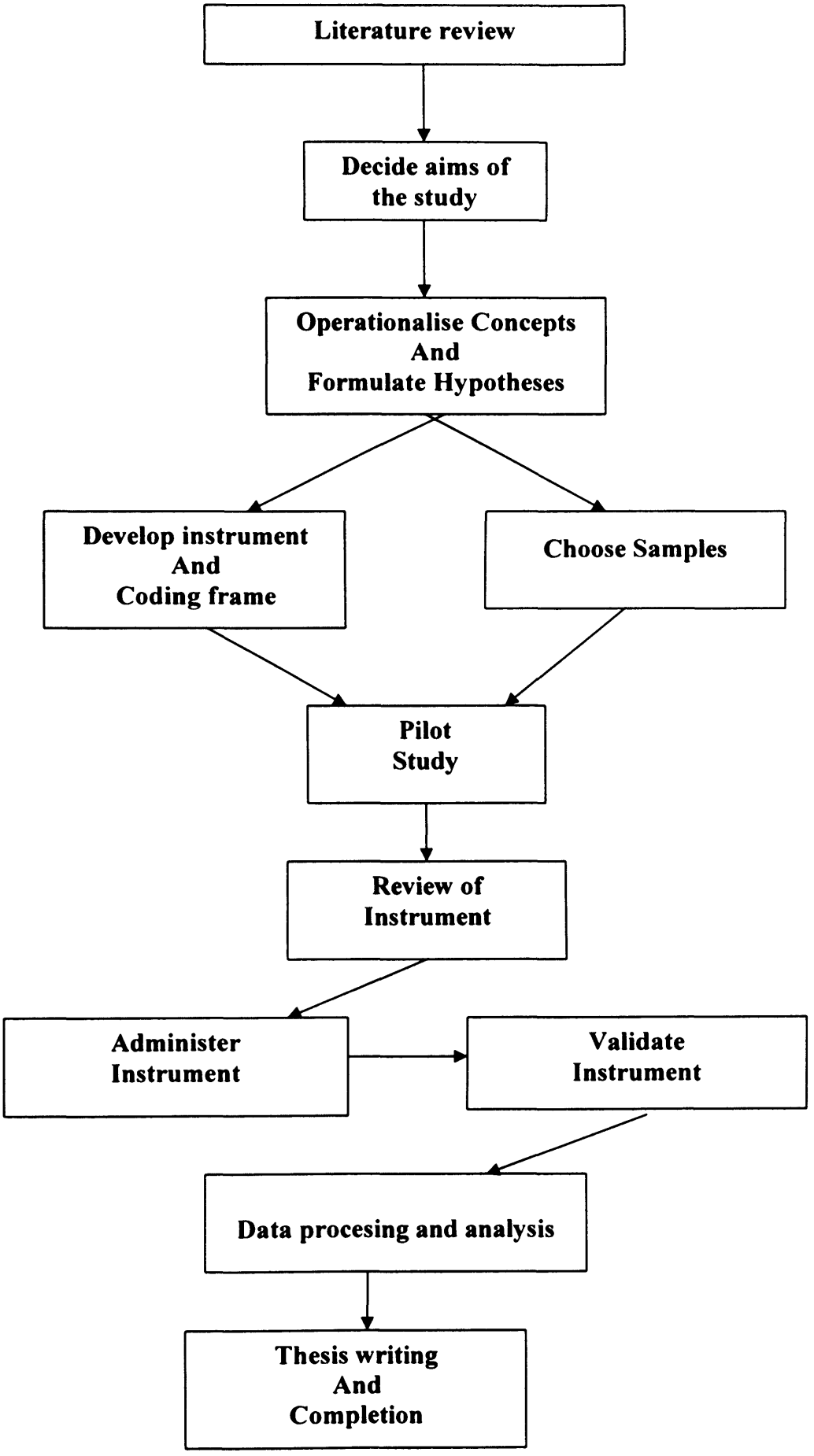
The first stage of the research was to carry out a comprehensive literature search setting the scene for this research programme. A systematic literature search for articles on the topic of medication side effects and their socioeconomic impact was conducted.

Development of the SEIP

This part of the research is divided into three stages: conceptualisation, item generation, and item reduction phase. The conceptualisation stage involved discussion of the proposed model with experts in this field and four sources of material were tapped for domain and item generation: (a) a review of the literature in the areas of medication–related problems, cardiovascular drug side-effects, and socioeconomic indicators; (b) a focus group with some health professionals with clinical experience in the area of medication reviews and counselling; (c) a series of semiformal interviews and discussions with community managed cardiovascular patients on chronic multiple drugs, most of whom were on four weekly repeat prescriptions of their medications from their local community pharmacies; and (d) internet-based first person narratives.

The Item generation stage on the other hand included generation of an initial pool of 46 items / statements as well as conduction of a rigorous literature search of reported cases of medication side effects of cardiovascular drugs. In addition, various generic and disease-specific quality of life instruments were again examined for suitability of their contents in this measure being developed.

Figure 2.3 Overview of the research programme



Item generation was followed by four stages of pre-testing to reduce the initial item pool. Some items were reworded, modified, merged or made totally redundant. In the first step, the 6 domains of SEIP as well as the initial 31 items were tested in an in-depth face-to-face interview with fifteen cardiovascular patients covering the three areas of disease groups (hypertension, angina pectoris and heart failure). Participants were asked whether the items captured their language and whether they felt it was relevant to their socioeconomic condition. The development of the SEIP is fully documented in chapter 4.

Reliability and Practicality Study

The next phase of this research comprises reliability and practicality studies that will be carried out concurrently. Two types of reliability are to be established: test-retest reliability and internal consistency reliability. Test-retest reliability will be performed by administering the questionnaires on two occasions with a seven-day interval. It is assumed that there has been no significant change in respondents' condition. Over this period, the questionnaire should not demonstrate a change and can therefore be considered to be reliable and not prone to large variation when there is no actual change to be measured. Internal consistency is also a type of reliability that needs to be established and demonstrates that the items in the questionnaire relate to each other and are as a whole measuring what the questionnaire is intending to measure.

Validity Study

Validity can be determined in a number of ways as already discussed earlier in this chapter. The SEIP will be assessed in terms of its content validity (chapter four). Attempts were focused on assessing construct validity (both convergent and discriminant). The relationships between SEIP, MIDAS and SF-12 were looked at in the validation study. MIDAS and SF-12 were preferred for the assessment of construct validity of SEIP rather than other well-known generic and cardio-specific instruments such as Minnesota Living with Heart Failure Questionnaire (MLHF) and the Quality of life after myocardial infarction (QLMI-2) for the following reasons:

1. Although, MLHF and QLMI-2 had already established psychometric properties than MIDAS, only MIDAS had a domain that focused on medication side effects of cardiovascular drugs and was therefore closely

related to SEIP. Moreover, by using MIDAS in this comparative study, it supports evolvement of its psychometric properties.

2. SF-12 in comparison with SF-36 is quicker to complete and therefore not time consuming.

Data Processing and Analysis

Data processing and analysis will be carried out using the statistical package, SPSS for Windows. The edited data will be coded appropriately for analysis. The dilemma many young researchers face is choosing the correct statistical technique to analyse their data. Researchers should ask themselves four vital and important questions in order to analyse the results of the research effectively and successfully (Borg and Gall, 1983). These are:

1. What statistical tools are available?
2. Under what condition is each tool used?
3. What the statistical results mean?
4. How the statistical calculations are made?

There are two different types of statistical techniques commonly used in research:

1. The descriptive statistical method
2. The analytical statistical method.

The descriptive statistical method can be used to summarise or describe a collection of data so as to present meaningful information. Both of these techniques will be employed in this study. Another most important issue in this study was whether to use parametric or non-parametric technique depending on the nature of the data. According to Al-Mansoori (2003), before selecting appropriate statistical technique for use (parametric or non-parametric), the following assumptions should be considered:

1. Random sampling: in the parametric technique for example, analysis of variance (ANOVA), t-tests, require random sampling of individuals. Non-randomisation of sample selection may result in a lack of independence of the items or in heterogeneity of variances or non-normal distribution (Al-Mansoori 2003).
2. Homogeneity of variances: Tabachnick and Fidell (2001) stated that for any type of analysis of variance, there is the assumption that samples are obtained from populations of equal variances. Al-Mansoori, (2003), in his thesis cited an example of this in applying a t-test for the significance of the difference between two means or groups. According to this author, the statistical test is valid only if one can assume that the variances of the two samples are equal.
3. Normality: It is assumed that the populations from which the samples are taken are normally distributed (Tabachnick and Fidell, 2001). In addition to random sampling and equality of variances of samples, the data distribution must be normal if parametric tests such as ANOVA are to be valid and justified (Al-Mansoori, 2003). However in a lot of research, scores on the dependent variable are not normally distributed. Fortunately, with large enough sample sizes (e.g. 30+), the violation of this assumption should not cause any major problems (Gravetter and Wallnau, 2000)

At this stage of development, if data generated in this present study fails to meet the fundamental assumptions required for parametric analysis, the use of non-parametric methods will be taken into consideration.

The type of non-parametric test depends on the nature of the data. In addition to this, non-parametric techniques do not have stringent requirements and do not make assumptions about the underlying population distribution. However, they do have their disadvantages. According to Tabachnick and Fidell (2001), they tend to be less sensitive than their more powerful parametric cousins, and therefore may fail to detect differences between groups that actually do exist.

The following existing parametric and non-parametric techniques will be employed in this research work. They include: analysis of variance (ANOVA), Mann-Whitney U

Test, Wilcoxon Signed Rank test, Spearman Rank Order Correlation Coefficient, Kruskal-Wallis Test.

Analysis of variance (ANOVA)

Analysis of variance is a parametric technique that is used in many research situations to compare the mean scores of more than two groups. This technique compares the variance (variability in scores) between the different groups due to the independent variable, with the variability within each of the groups believed to be due to chance (Pallant, 2002). In ANOVA results, an F ratio are calculated which represents the variance between the groups, divided by the variance within the groups. According to Pallant, (2002), a large F ratio indicates that there is more variability between the groups (caused by the independent variable), than there is within each group (referred to as the error term).

The Mann-Whitney U Test

The Mann Whitney U Test is used to test for differences between two independent groups on a continuous measure. It has been considered to be one of the most powerful of the non-parametric tests (Al-Mansoori, 2003). This test is the non-parametric alternative to the t-test for independent samples (Pallant, 2002) and has been used to compare the difference between two independent populations. Instead of comparing means of the two groups as in the case of the parametric t-test, Pallant (2002) stated that this technique actually compares medians and the scores on the continuous variable are converted to ranks across the two groups.

In any research, testing of hypotheses is very important. For example the purpose of t-tests and analysis of variance is to test hypotheses. However, with these types of analyses there is always the possibility of reaching the wrong conclusion (Pallant, 2002). The literature has shown that there are two types of errors that can be committed- Type 1 and Type 2 errors. In a Type 1 error, the null hypothesis (H_0) may be rejected when it is, in fact true. For example when a researcher hypothesises (H_1) that there is a difference in HRQOL of patients suffering from a disease, but there really is not. In a Type 2 error, the researcher fails to reject a null hypothesis when it is, in fact false (i.e. believing that the groups do not differ, when in fact they do). In order to avoid a Type 1 error, researchers always set the probability of committing

this error to 0.05 represented by P value as the "level of significance". The larger the P value, the more likely it is that H_0 will be falsely rejected (Al-Mansoori, 2003). On the other hand, a significance level of 0.05 or less indicates that H_0 does not apply and that H_1 is accepted (Al-Mansoori, 2003).

Kruskal-Wallis Test

This is the non-parametric alternative to a one-way between-groups analysis of variance that allows you to compare the scores on some continuous variable for three or more groups (Pallant, 2002). This technique is also considered by some authors to be an extension of the Wilcoxon rank sum test (Petrie and Sabin, 2005). The technique tests the null hypothesis (H_0) as to whether K Independent Samples come from the same population or from identical populations with respect to the average. The test assumes that the variable under study has an underlying continuous distribution and it requires at least ordinal measurement of that variable. According to Petrie and Sabin (2005), under the null hypothesis of no differences in the distributions between groups, the sums of the ranks in each of the K groups should be comparable after allowing for any differences in sample size.

Spearman Rank Correlation Coefficient (rho)

This coefficient is a measure of association between the scores, which require that at least one of the variables is measured on an ordinal scale and neither of the two variables is normally distributed (Petrie and Sabin, 2005) and can also be used when the sample size is small. This technique is used to calculate the strength of the relationship between two continuous variables. It is the non-parametric alternative to Pearson's product –moment correlation (Pallant, 2002).

Wilcoxon Signed Rank Test

This technique is designed for use with repeated measures when the respondents in a survey are measured on two occasions, or under two different conditions. It is the non-parametric alternative to the repeated measures t-test. Using this technique, the Wilcoxon actually converts scores to ranks instead of comparing means and also compares them at Time 1 and at Time 2 (Pallant, 2002). The Wilcoxon signed ranks test also takes account not only of the signs of the differences but also their magnitude.

Missing data

Missing data are ubiquitous in research and can seriously affect the results of the research. Carpenter and Kenward (2004) suggested that unplanned missing data inevitably introduce ambiguity into the inferences that can be drawn from a study and ignoring missing data or assuming that excluding missing data is sufficient may therefore result in reaching invalid and insignificant results. In this present study, issues that need to be considered on the types of missing data will be included where concerned since they may result in loss of power and analytical bias and ultimately influence the interpretation of results (Lua, 2002).

Types of missing data

Acock (2005) described different classifications of missing values that may influence the optimal strategy for working with missing values. This includes: 1) missing by definition of the subpopulation, 2) missing completely at random (MCAR), 3) missing at random (MAR), and 4) non-ignorable (NI) missing values. In missing by definition of the subpopulation, an investigator needs to eliminate these values from the data before describing any problems with missing values. Furthermore, the researcher as well as the number of respondents who fit the definition of the study population should note the total sample size. Acock (2005) further suggests that it is important to distinguish between observations that are deleted by the nature of the subpopulation being studied and observations that should be included but which have missing values.

Data which are missing completely at random (MCAR), are normally ignorable because they do not introduce bias into the results (Lua, 2002). However, according to Acock (2005), the only limitation to MCAR is that it introduces uncertainty by the imputation process, which may reduce statistical power compared to having complete data.

Missing at random (MAR) on the other hand has the likelihood that missing data is not related to the participant's score on the variable after controlling for other variables in the study.

Most missing data handling techniques involve either treating the data as missing or using only the available data or by mean imputation (replacing missing value with the domain mean provided more than half of the domain items have been answered). It can also be tackled by a general imputation method, which reflects the most likely value for the item. Nevertheless, imputations can also be biased and may result in strange numbers (Lua, 2002).

SUMMARY

- This chapter has described the rationale behind the development of the Socioeconomic Impact Profile (SEIP);
- It has also elaborated extensively on the general methodology and data processing and analysis techniques that will be involved in each phase of the research plan, also discussed are different types of psychometric properties that will be tested with this new measure;
- The next chapters will be focused on the followings:
    - Chapter 3 –Evaluating medication-related problems of cardiovascular drugs in community pharmacy settings
    - Chapter 4 –Development and Content Validation of the Socioeconomic Impact Profile (SEIP)
    - Chapter 5 –Content Validation of the Socioeconomic Impact Profile (SEIP)- Factor Analysis and Internal Consistency tests
    - Chapter 6 –Practicality, Test-Retest Reliability and Internal Consistency Reliability of the SEIP
    - Chapter 7 –Validity (convergent and divergent) of the SEIP
    - Chapter 8 –General Discussion
- And finally, specific details relating to methodology, data processing and analysis techniques in each phase of the research will be discussed within the relevant chapters.

CHAPTER 3

Evaluation of the Medication-Related Problems of Cardiovascular Drugs in Community Pharmacy Settings

INTRODUCTION

A person's health can be influenced not only by social circumstances, but also by the outcome of drug therapy. When people are diagnosed with heart disease for example, the treatment options may be in several different ways. The initial change they will have to make include cutting down on fat and cholesterol intake and stop smoking if they are smokers. Exercise will also become part of their lives, if possible. Drug therapy may be the next course of action. Frequent use of drugs in this modern day is due to the high prevalence of multiple morbidities and the increased availability of pharmacotherapeutic options (Vinks et al., 2006).

Vinks et al., (2006) also reported that the increasing adoption of the concept of evidence-based medicine could have contributed to polypharmacy because new drugs are usually studied as an addition to a cocktail of drugs that until then had proven to be the best treatment. In the past few decades for example, the variety and scope of cardiovascular drugs have increased tremendously and new drugs are being approved annually. However, as a result of multiple drug therapy, there is the possibility of frequent occurrence of different medication-related problems such as adverse drug reactions, drug-drug interactions, contraindications and drug underutilisation (Murray and Callahan, 2003).

In the pharmacotherapy of cardiovascular diseases for example, although people with hypertension or any other form of cardiovascular disease live longer due to lifelong medication therapy (Bardage, 2000), many still experience medication-related problems such as inappropriate dosage regimen. Part of pharmacists' training is to identify dose appropriateness for each individual patient. Furthermore, pharmacists are trained to collaborate with other healthcare professionals in policy implementation and patient monitoring in order to achieve definite outcomes and desirable quality of life for their patients. Whenever medications are administered, there are possibilities for occurrence of certain problems that may diminish a patient's quality of life.

Apart from inappropriate drug prescribing (such as inappropriate dosage form, dosage interval or duration) by the prescribers, low compliance by the patient as well as poor concordance may have negative therapeutic outcomes and hence impact on the

patient's quality of life. Pharmacists should have the skills to prevent drug-related morbidity, which is in most cases associated with any of the above-mentioned medication-related problems.

Implementation of medication-related problems assessment tools in community pharmacy practice

The clinical and humanistic outcomes of medication-related morbidity are potentially substantial. According to Morris et al (2003), reducing preventable medication-related morbidity could potentially improve the quality of life of patients and improve the safety and quality of the health care system. There is therefore a need for incorporation of some of the community-oriented risk assessment tools in community pharmacy practice. Most community pharmacists are not aware of the existence of such tools. With the introduction of medication review as part of advanced services in the new pharmacy contracts in the United Kingdom, community pharmacists are now in better position to access these tools to document medication-related side effects they identify while performing medicine use reviews for their patients.

In order for pharmacists to become better familiarised with these risk assessment tools, there is a need to develop pharmacist versions of some of the existing DRP classification schemes. Medication-related problems have been considered to have a major impact on public health. ADRs for example, are a common cause of admission to hospital and a leading cause of morbidity and death (Routledge and O'Mahony, 2003). Many patients do not know whether the side effects they experience are medication-related or due to their condition. It is therefore difficult to assess what is due to disease state and what is due to prescribed drug treatment or over the counter medicines (OTC) inclusive. Pharmacists should therefore be competent to identify, prevent and resolve any MRPs, which might occur. Furthermore, an essential element of pharmaceutical care is that pharmacists should accept responsibility for the patient's pharmacotherapeutic outcomes.

AIMS OF THE PRESENT STUDY

One of the main priorities of drug therapy management is to ensure that the prescribed treatment is well tolerated and the patient feels better and satisfied. Naturally, once a

drug is prescribed, the patient has the utmost responsibility to use the drugs for his or her own benefit. However, non-adherence to medications due to side-effects is common. Documenting drug–related problems frequently associated with multiple drug use in chronic conditions can improve the quality of pharmaceutical care hence ensuring continuity of positive outcomes of drug therapy. However, documenting medication-related issues identified by community pharmacists during pharmaceutical care processes in daily pharmacy practice has not been easy due to certain limitations. Buerger (1999) noted that developing, refining and validating medication-related problems risk assessment tools is one thing; their implementation in the real–world clinical situations to drive better prescribing and improved outcomes is another thing. Schaefer et al., (2002) suggested that a suitable coding system for drug-related problems must be user friendly in its applicability in the provision of pharmaceutical care on a daily basis and also has to fulfil certain criteria in order to render it to wider acceptability.

In 1999, a consensus was reached by expert panels in the area of pharmaceutical care to create a medication-related problem classification scheme with wider usability and acceptability. This led to the creation of an instrument called the Pharmaceutical Care Network Europe Drug-Related Problem System (PCNE_DRP). Although the system has undergone several validation processes since the development of its first version in 1999 up to the latest version 5.00, its validity is still questionable. It is therefore hoped in this chapter to identify and document frequency and type of patient-reported medication-related problems of cardiovascular drugs using the PCNE-DRP V5.00.

METHODS

This was a prospective multicentre study of patients with cardiovascular conditions attending five community pharmacies in South Wales, UK during July and August 2005. During this period, medication records of cardiovascular patients on repeat prescriptions were reviewed. Patients on cardiovascular drugs were identified using the patient medication records system from the participating pharmacies and were subsequently invited for medication review. Dosage appropriateness, side effects, relevant drug interactions and compliance with drug therapy were checked among

others. The identified medication-related problems were documented on the PCNE-DRP V5.00 classification scheme.

Patient inclusion criteria

The patients on repeat prescriptions with four or more cardiovascular drugs were recruited from five community pharmacies in South Wales UK. As criteria for recruitment, patients should:

- Have been on repeat prescription of cardiovascular drugs for three months minimum;
- Be non- institutionalized;
- Be aged 20 and above;
- Belong to any of the cardiovascular diseases groups (hypertension, angina, and post MI)
- Agree to sign informed consent-forms at the intake.

Pharmacy inclusion criteria

Community pharmacists with active interest in the project and who are actively involved in medication surveillance were recruited. Criteria for their inclusion were:

- Pharmacists should keep patient medication record electronically;
- Offer a repeat prescription service particularly to the patient groups of interest mentioned above and;
- Should have a private consultation area in the pharmacy.

Data collection

Participating pharmacists were given copies of the PCNE-DRP V5.00 reporting forms to document any medication-related issues they encountered during their daily pharmaceutical care activities with patients on cardiovascular drugs. The researcher (a UK registered pharmacist) visited the pharmacies two days per week to assess the Patient Medication Records of cardiovascular patients in order to identify any drug related issues. At each visit, the researcher also performed face–to-face medication reviews with cardiac patients on repeat prescriptions who visited the pharmacies for

their medications. For each patient, a drug use profile from their PMR was printed listing all prescribed drugs dispensed 3 months to the date of inclusion. Dosage appropriateness, potential drug interactions (such as drug-drug, drug-disease, drug-age and drug duplications) and compliance with drug therapy were checked and documented on the PCNE_DRP report form. Any health or other medication issues were also addressed.

Classification of Medication-Related Problems

Medication- related problems were defined in accordance with the definition of the Pharmaceutical Care Network Europe- Drug Related Problems classification scheme: *a drug-related problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes* (Van Mil, 1999). Operational classification of MRPs was therefore performed based on the fifth version of PCNE_DRP classification scheme (Appendix 1). This classification had already been used and validated for some years as a routine classification by a network of researchers in an attempt to standardize the classification procedure (Ellison, 2003; Alvarez-de-Toledo, 2004). The fifth version of this documentation tool has both problems and causes codes separated as well as separate intervention and outcomes sections (see appendix 1). The problems domain was categorized into seven sections, which were hierarchically structured. The main categorizations used include:

1. Adverse reactions
2. Drug choice problem
3. Dosing problem
4. Drug use problem
5. Interactions
6. Adverse events
7. Patient related problems.

According to Blix et al. (2006), "*one medication may introduce more than one MRP, some of them depend on each other. For example, a given drug may have caused an interaction; a dose reduction may be needed, and monitoring of the drug by laboratory tests may also be required. Thus, three MRPs could be related to the drug. However, the patient might perceive only one MRP- the actual drug itself*".

In this present study, the reported frequencies of MRPs were based on the counting of all recorded MRPs.

DATA PROCESSING AND ANALYSIS

The data was processed and analysed using SPSS 12.0 for Windows. Descriptive statistics are shown as means with range or standard errors. The patients' medication-related problems were categorised on the PCNE_DRP V5.00 report forms into seven hierarchically structured groups. Potential interactions identified were classified using the *British National Formulary*. Relationships between some sociodemographic characteristics such as gender, age and number of drugs taken and medical condition were examined using Spearman's rank order correlation with significance level set at 5%. In addition two-way between-groups analysis of variance (ANOVA) was carried out to test the difference between two groups namely (male and female).

RESULTS

Patient demographic characteristics

A total of 120 patients were recruited into the study of whom 58 (48.3%) were female, with a mean and median age of 63.2 and 65.0 (range 22-85) respectively. Seventy-eight (65.0%) of the study participants were hypertensive, twenty-two (18.3%) were taking medications for angina pectoris while the remaining twenty (16.7%) were community-managed post myocardial infarction patients. Forty-eight (40.0%) patients suffered from one or more co-morbidity (Table 3.1). Apart from suffering from a cardiovascular disease, 11(9.2%) patients were taking medications for asthma, 3 (2.5%) were on antidepressants, 12 (10%) were diabetic and 14 (11.5%) suffered from arthritis-related illness. The mean number of medications taken by the study participants was 5.80 ± 1.9 SD. A total of 157 (52.3%) of all medication-related problems were discovered by pharmacists during routine pharmaceutical care services they provided to their patients while 32 (10.7%) cases of MRPs were self-reported by the patients

Medication-Related Problems

Table 3.2 below shows that the number of MRPs detected was positively correlated with the number of medications taken by the participating patients (r_s = 0.16, P = 0.005) but no correlation was found between the MRPs detected and their medical condition (r_s = 0.02, P = 0.775) suggesting that the predominant factor in determining medication-related problem is polypharmacy and not the disease itself.

Table 3.1 Demographic characteristics of the study participants (n=120)

Characteristics	Number (%)
Age (years)	
Mean	63.2
Median	65.0
Range	22-85
Sex	
Male	62 (51.7)
Female	58 (48.3)
No of drugs taken	
Mean	5.80 ±1.9
Median	5.00
Problem discovered	
By patient	32 (10.7)
By pharmacy	157 (52.3)
Medical condition	
Hypertension	78 (65.0)
Angina	22 (18.3)
Post MI	20 (16.7)
Co morbidity	
Respiratory	11 (9.2)
Gastrointestinal	1 (0.83)
Depression	3 (2.5)
Sleeping problems	6 (5.0)
Diabetes	12 (10.0)
Arthritis	14 (11.5)
Genitor-urinary problem	1 (0.3)
No co-morbidity	**72 (60.0)**

Furthermore, the mean number of drugs taken by the 120 patients was significantly positively correlated with their age (r_s = 0.268, P < 0.005) (Figure 3.1) but not related to their medical condition (r_s = -0.03, P = 0.593). This was supported by the results from two-way analysis of variance (ANOVA) conducted to explore the impact of gender and age on the number of drugs taken by the patients. For this purpose, patients were divided into three groups according to their age (Group 1: 22-60 years; Group 2: 61-70 years; Group 3: 71 years and above). There was a statistically significant main effect for age [F (2, 118) = 11.01, p=0.001] and gender [F (1, 118) = 6.39, p=0.012] as well as the interaction effect [F (2, 118) =6.31, p=0.002] meaning that male and female patients in the study differed in terms of the number of drugs they were taking. Furthermore, there was a difference in the number of drugs taken among the three age groups of the study participants (Table 3.3). Older patients received a greater number of medications and older females' a greater number of medication than their male counterparts (Figure 3.1).

Table 3.2 Correlation between MRPs, No of drugs taken, age and medical condition

Variables	Medication-Related Problem	Medical Condition	Age in years	No of drugs taken
Medication Related Problem	1.00			
Medical Condition	0.02	1.00		
Age in years	0.33**	-0.01	1.000	
No of drugs taken	0.16**	-0.03	0.27**	1.000

** Spearman's Correlation is significant at the 0.01 level (2-tailed).

Positive significant correlation shown between age and MRPs (Table 3.2) could be explained by older patients being prescribed a greater number of drugs.

Table 3.3 Comparisons† of the impact of gender and age on the number of drugs taken by the study participants

Age group	Gender	Mean (SD)	*Levene's Test of Equality of error Variances				Tests of Between-Subjects Effects			
22-60	Males	5.55 (1.43)	**F**	**Df1**	**Df2**	**Sig**	**Source**	**df**	**F**	**Sig**
	Females	5.08 (1.52)	2.19	5	118	0.056	**Gender**	1	6.39	0.012
	Total	5.32 (1.48)								
61-70	Males	5.31 (1.89)					**Age group 3**	2	11.01	0.000
	Females	6.13 (2.21)								
	Total	5.72 (2.05)								
71+	Males	5.89 (1.78)					**Gender *age group 3**	2	6.31	0.002
	Females	7.13 (1.95)								
	Total	6.51 (1.87)								
							Error	118		

*Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

†Analysis of Variance.

Figure 3.1 Comparison of the number of drugs taken by males and females in different age groups.

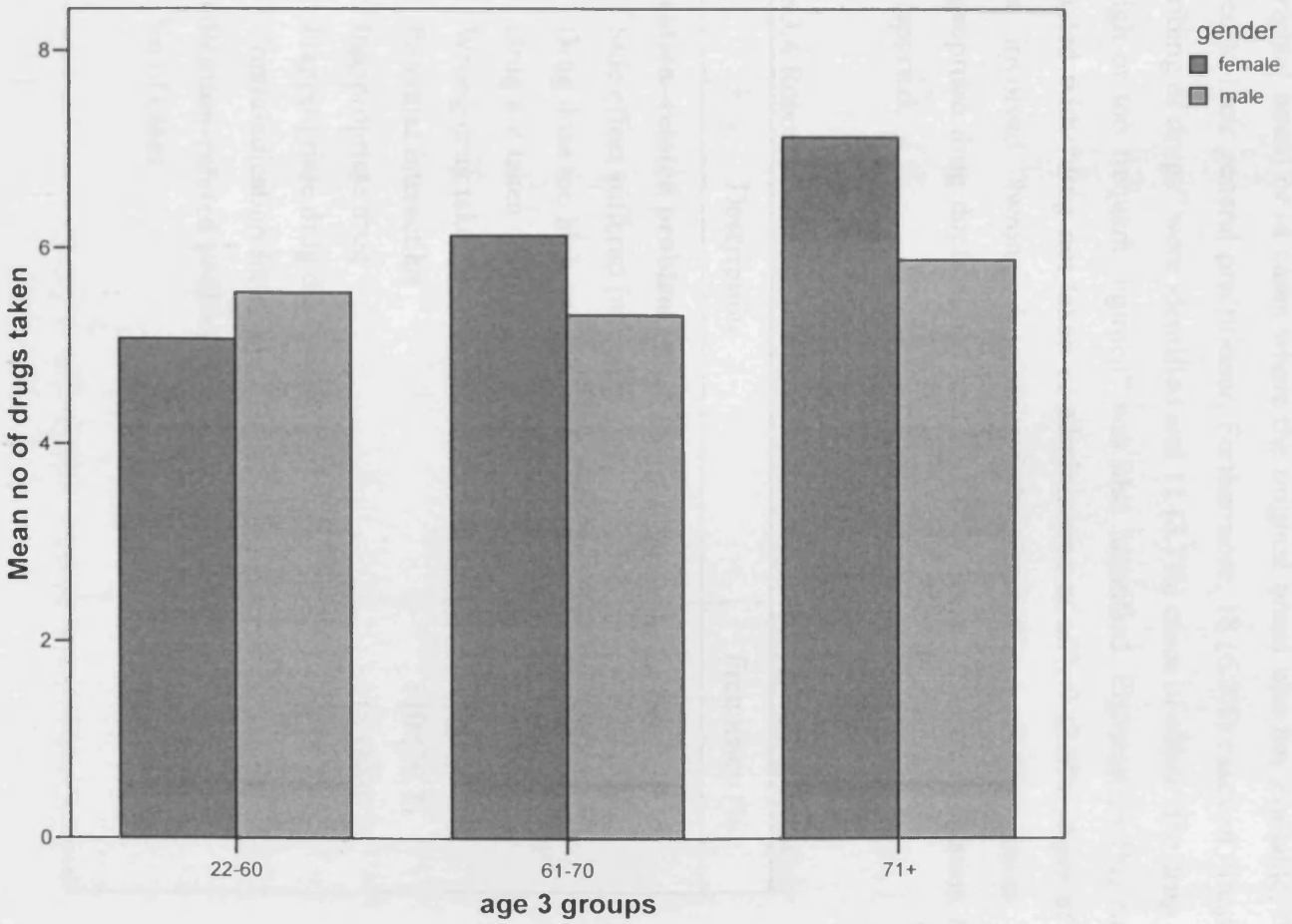
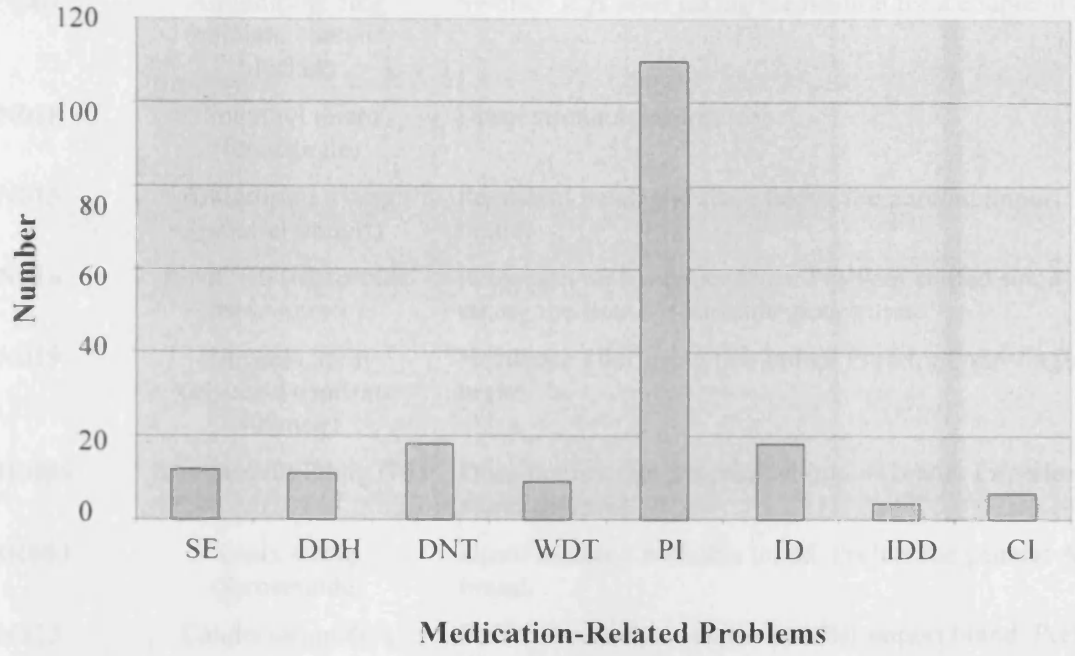


Table 3.4 shows the frequencies of categories of MRPs. Out of the total of 300 PCNE_DRP report forms completed with the patients, MRPs were identified in 187 (62.7%) cases and the remaining 112 (37.3%) cases showed that patients did not have problems with the use of their medications (Figure 3.2). Overall, "Potential drug interactions" accounted for 110 (36.7%) of the most frequently occurring medication–related problems. Twelve (4.0%) cases of the reported MRPs showed that some patients suffered from side effects of a non allergic nature to their medications, in particular patients on a parallel import (PI) of felodipine 5mg tablets (istin ^{R}) complained of a rash they had never had before and this drug had to be substituted for the original brand or in cases where the original brand was not available, they were referred to their general practitioner. Furthermore, 18 (6.0%) cases of "inappropriate prescribing of drugs" were identified and 11 (3.7%) cases of either "the drug dose was too high or too frequent regimen" was also identified. Eighteen (6.0%) cases were associated with "drug not taken or administered at all", 9 (3.0%) cases of reported MRPs involved "wrong drug taken/administered", 4 (1.3%) cases involved "inappropriate drug duplication" and 6 (2.0%) cases of "contraindication for drug" were reported.

Table 3.4 Reported cases of Medication-Related Problems during the study

Description	Frequency (%)
Medication–related problem (n=187)	
Side effect suffered (non allergic)	12 (4.0)
Drug dose too high or regimen too frequent	11 (3.7)
Drug not taken /administered at all	18 (6.0)
Wrong drug taken/ administered	9 (3.0)
Potential interaction	110 (36.7)
Inappropriate drug	18 (6.0)
Inappropriate drug duplication	4 (1.3)
Contraindication for drug	6 (2.0)
No medication-related problems	
No of cases	112 (37.3)

Figure 3.2 Categories of reported Medication-Related Problems



SE= Side effect suffered (non allergic); DDH= Drug dose too high or regimen too frequent
DNT= Drug not taken / administered at all; WDT= Wrong drug taken/administered
PI= Potential interaction; ID= Inappropriate drug; IDD= Inappropriate drug duplication
CI= Contraindication for drug.

Medications involved

Table 3.5 shows examples of reported cases of "non-allergic side effects" in this study. For example a situation where a patient who was initiated on candersartan 4mg (angiotensin-II receptor antagonists) experienced headache, flushing and swollen gums, or a patient who was prescribed a parallel import version of amlodipine 5mg for blood pressure experienced swollen leg and rashes on his upper arms, were referred to their GP. Another patient on parallel import (PI) of candersartan suffered headache as a result of intolerance to the brand and was later stabilised on the original brand.

Table 3.5 Examples of reported cases of "non-allergic side effects"

Reported case no	Medication involved	Type of side effect suffered by patient
N007	Amlodipine 5mg (calcium channel blocker)	Swollen legs after taking medication for a couple of days.
N010	Lipanthyl micro (fenofibrate)	Upset stomach (diarrhoea)
N015	Amlodipine 10mg (parallel import)	Persistent headache since taking the parallel import brand.
N016	ISMO 40 (isosorbide mononitrate)	Itchy rash on his upper arms. Problem started since taking the brand isosorbide mononitrate.
N019	Nitromin spray (glyceryl trinitrate 400mcg)	Headache after using this brand. Preferred nitrolingual brand.
BR006	Atorvastatin 20mg (PI)	Does not tolerate the parallel import brand. Experience stomach upset.
BR003	Lasix 40mg (furosemide)	Upset stomach with this brand. Prefers the generic APS brand.
N023	Candersartan 8mg	Suffers headache with the parallel import brand. Prefers the original Amias brand.
N037	Felogen XL 10mg (felodipine)	Suffers headache with the brand. Prefers plendil brand
N008	Candersantan 4mg	Headache, flushing, swollen gums and red eyes after taking medication.
BR008	Ramipril 10mg	Fatigue and occasional dry cough
N009	Losartan 100mg	Headache after initiation with medication

Furthermore, Table 3.6 shows examples of cases involving inappropriate drug use. Two patients were prescribed furosemide- a loop diuretic to lower blood pressure. However, they were initiated on 40mg to be taken at 6pm in the evening. This dosage regimen may affect patients' quality of life by interfering in their sleep. The patient's GPs were contacted and changes in the dosage regimen were suggested and corrected by their GP. The drug groups mostly associated with potential drug interactions in this study included prescriptions of anticoagulants such as warfarin and aspirin and combination therapy of statins and fibrates in patients with hyperlipidaemia (Tables 3.7.1 to 3.7.13). Other reported cases of MRPs included potential interaction between ramipril (ACE-inhibitor) and diclofenac (anti-inflammatory drug), amiodarone (anti-arrhythmics) and warfarin (anticoagulant), amiodarone and flecainide (anti-arrhythmics).

Table 3.6 Examples of reported cases of inappropriate drug use by observed patients

Case no	Medication involved	Type of inappropriate drug use
BR002	Furosemide 40mg (diuretic)	Patient takes one tablet at 6pm
N001	Furosemide 40mg	69 year old female patient takes furosemide tablets at 6pm in the evening
N006	Nifedipine (Adalat LA) 20mg	Patient was prescribed twice daily dose of adalat LA brand instead of adalat retard brand.
N021	Simvastatin 10mg	Patient was taken the tablets in the morning instead of at night.
BR004	Felodipine MR 10mg	Patient was prescribed twice daily dose of the modified release brand instead of once daily dose usually in the morning.

Table 3.7.1 Examples of identified cases of potential drug interactions

Patient no: BR016 Age: 58yr Gender: male

PMR: Warfarin 5mg as directed Epanutin (Phenytoin) 100mg capsules, 2 daily
Warfarin 3mg as directed Omeprazole 20mg, one daily
Warfarin 1mg as directed Simvastatin 40mg one daily
Epilim Chrono (sodium valproate M/R) 300mg 2 BD
Tramacet (paracetamol and tramadol) tablets as directed

Drugs involved	Potential drug interactions
Warfarin + Tramacet (tramadol and paracetamol)	Anticoagulant effect of warfarin is increased and may increase risk of bleeding
Warfarin +Epanutin (phenytoin)	Anticoagulant effect may be increased.
Warfarin + Omeprazole	Anticoagulant effect may be increased.
Warfarin + Simvastatin	Anticoagulant effect may be increased.
Warfarin + Clopidogrel	Increased risk of bleeding
Epilim + Tramacet	Anticonvulsant effect antagonised.

Table 3.7.2 Examples of identified cases of potential drug interactions

Patient no: NP064 **Age: 70yrs,** **Gender: female**	**PMR: Furosemide 40mg one each morning** **Simvastatin 40mg one at night** **Stemetil (prochlorperazine) 5mg three times daily** **Clarithromycin 500mg twice daily**
Furosemide + Stemetil	Increase risk of arrhythmias due to hypokalaemia
Simvastatin + clarithromycin	Risk of myopathy due to increase plasma level of statin

Table 3.7.3 Examples of identified cases of potential rug interactions

Patient no: BR082 **Age: 49 years** **Gender: Male**	**PMR:** **Amlodipine 10mg one each morning** **Aspirin 75mg one daily** **Atorvastatin 20mg one daily** **Bendroflumethiazide 2.5mg one daily** **Doxazosin 4mg two daily** **Levothyroxine 100mcg one daily** **Levothyroxine 50mcg one daily** **Levothyroxine 25mcg one daily** **Ramipril 10mg capsules one daily** **Avandamet† 2mg/500mg two twice daily**
3* bendroflumethiazide 2.5mg + Doxazosin 4mg	Increased postural hypotensive effect of **FIRST DOSE** of alpha blocker
3* bendroflumethiazide 2.5mg + Avandamet 2mg/500mg	Bendroflumethiazide 2.5mg reduces hypoglycaemic effect of avandamet

†Avandamet = rosiglitazone 2mg and metformin 500mg; **3*=** interaction level warning signal

Table 3.7.4 Examples of identified cases of potential drug interactions

Patient no:BR002 **Age: 69 years** **Gender: female**	**PMR** **Atenolol 100mg one each morning** **Bendroflumethiazide 2.5mg one each morning** **Lansoprazole 15mg capsules one daily** **Warfarin 1mg as directed** **Warfarin 3mg as directed** **Warfarin 5mg as directed**
3*Zoton (lansoprazole) + warfarin	Zoton may increase anticoagulant effect of warfarin

Table 3.7.5 Examples of identified cases of potential drug interactions

Patient no: BR015 **Age: 66 years** **Gender: female**	**PMR** **Aspirin dispersible 75mg one daily** **Bendroflumethiazide 2.5mg one each morning** **Diclofenac sodium EC 50mg one three times daily** **Losartan 50mg one daily** **Simvastatin 40mg one at night** **Movicol sachets one daily**
3* Aspirin + Diclofenac	Increased risk of bleeding

Table 3.7.6 Examples of identified cases of potential drug interactions

Patient no: BR010 **Age: 68 years** **Gender: female**	**PMR** **Ferrous sulphate 200mg three times daily** **Ascorbic 50mg tablets one daily** **Citalopram 10mg one at night** **Gliclazide 80mg half a day** **Doxazosin 4mg one daily** **Losartan 100mg one daily** **Aspirin 75mg one a day** **Atorvastatin 20mg one daily** **Bendroflumethiazide 2.5mg one each morning** **Avandamet 4/1000mg one twice a day**
Aspirin + citalopram	Increase risk of bleeding **3***
Bendroflumethiazide + doxazosin	Increased postural hypotensive effect **3***
Bendroflumethiazide + avandamet	Reduced hypoglycaemic effect of avandamet **3***

Table 3.7.7 Examples of identified cases of potential drug interactions

Patient no: BR080 **Age: 80 years** **Gender: female**	**PMR** **Furosemide 40mg one each morning** **Digoxin 125 mcg one daily** **Warfarin 1mg one daily as directed** **Perindopril 2mg one daily** **Simvastatin 40mg one at night** **Gabapentin 300mg one twice a day** **Co-codamol 30mg/500mg one four times a day**
Warfarin + simvastatin	Simvastatin increases anticoagulant effect **3***
Digoxin + furosemide	Digitalis toxicity increased by hypokalaemic effect of furosemide **3***

Table 3.7.8 Examples of identified cases of potential drug interactions

Patient no: BR176 **Age: 86 years** **Gender: female**	**PMR** **Tildiem (diltiazem) MR 60mg one twice a day** **Omeprazole GR 10MG one daily** **Simvastatin 20mg one at night** **Levothyroxine 50mcg one daily** **Candesartan 8mg one daily**
Tildiem + simvastatin **3***	Increased plasma level of statin/risk of myopathy

Table 3.7.9 Examples of identified cases of potential drug interactions

Patient no: NP 058 **Age: 40 years** **Gender: male**	**PMR** **Aspirin dispersible 75mg one daily** **Clopidogrel 75mg one daily** **Gabapentin 300mg two each morning, two at night and one midday** **Lisinopril 2.5mg one daily** **Rosuvastatin 10mg one daily** **Tramadol capsules 50mg one four times a day**
Aspirin + Clopidogrel Gabapentin + tramadol	Increased risk of bleeding **3*** Anticonvulsant effect antagonised **3***

Table 3.7.10 Examples of identified cases of potential drug interactions

Patient no: NP 079 **Age: 46 years** **Gender: male**	**PMR** **Aspirin dispersible 75mg one daily** **Ramipril 10mg one each morning** **Doxazosin 2mg one twice a day** **Atenolol 100mg one each morning** **Bendroflumethiazide 2.5mg one each morning**
Doxazosin + Atenolol	Increased postural hypotensive effect of first dose of alpha blocker **3***
Doxazosin + Bendroflumethiazide	Increased hypotensive effect of first dose of alpha blocker **3***
Ramipril + Atenolol	Enhanced hypotensive effect **1* - 2***
Bendroflumethiazide + Ramipril	Enhanced hypotensive effect **1* - 2***

Table 3.7.11 Examples of identified cases of potential drug interactions

Patient no: NP 005 **Age: 77 years** **Gender: male**	**PMR** **Atenolol 50mg one a day; Atenolol 25mg one a day** **Simvastatin 25mg one at night; Perindopril 4mg one each morning; Glucosamine 1500 one daily;** **Paracetamol 500mg capsules two four times a day;** **Amlodipine 5mg one a day** **Senna 7.5mg one to two at night** **Aspirin 75mg two each morning** **Diclofenac EC 50mg one three times a day**
Aspirin + diclofenac	Increased risk of bleeding **3***
Atenolol + Perindopril	Enhanced hypotensive effect **2***
Atenolol + Amlodipine	Enhanced hypotensive effect **2***
Perindopril + Amlodipine	Enhanced hypotensive effect **2***

Table 3.7.12 Examples of identified cases of potential drug interactions

Patient no: NP 063 **Age: 60 years** **Gender: female**	**PMR** **Beclomethasone aqueous nasal spray** **Half-Inderal (propranolol) LA 80mg one each morning** **Co-codamol 30/500 one four times a day** **Metformin 500mg one four times a day** **Atorvastatin 20mg one a day**
Half – Inderal (Propranolol) + Metformin	Beta blockers increase hypoglycaemic effect- mask warning signs **3***

Table 3.7.13 Examples of identified cases of potential drug interactions

Patient no: NP 085 **Age: 56 years** **Gender: female**	**PMR** Novomix 30 flexipen inj as directed Aspirin 75mg one each morning Atenolol 50mg one each morning Rosuvastatin 10mg one daily Bendroflumethiazide 2.5mg one each morning Valsartan 160mg one each day Glimepiride 2mg one daily Rosiglitazone 8mg one each day
Rosiglitazone + Novomix	Manufacturer of rosiglitazone advises **AVOID 4***
Atenolol + bendroflumethiazide	Enhanced hypotensive effect **2***
Atenolol + Valsartan	Enhanced hypotensive effect **2***
Valsartan + bendroflumethiazide	Enhanced hypotensive effect **2***

Causes of medication-related problems

A total of 187 causes of medication-related problems were identified (Table 3.8). The most common causes identified (118; 63.1%) included pharmacokinetic problems. 16 cases (8.6%) of MRPs were as a result of "Inappropriate drug selections" and 18 cases (9.6%) were due to "inappropriate dosage selection". Furthermore, Pharmacists revealed that in 23 cases (12.3%) "Patient had concerns with drugs" led to the identified MRPs. Dispensing errors such as wrong drug or dose dispensed were also responsible for 9 (4.8%) of the MRPs reported (Figure 3.3).

Table 3.8 Causes of Medication-Related Problems identified during the study (n=187)

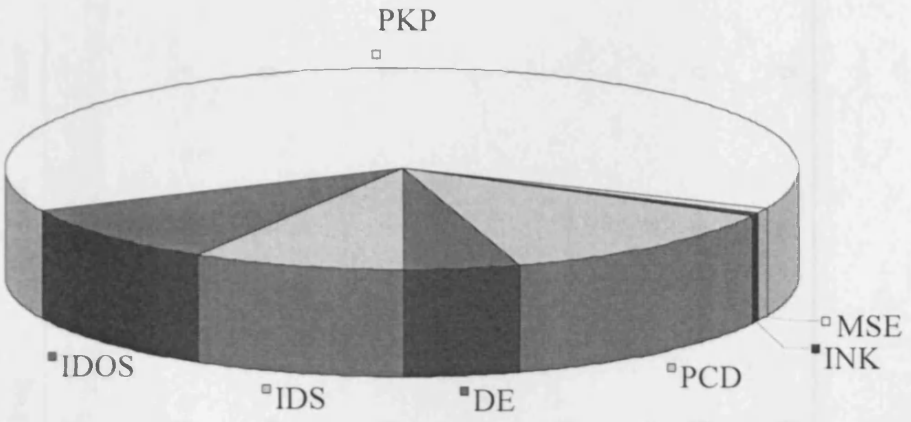
MRP causes	Frequency (Percentage)
Inappropriate drug selection	16 (8.6)
Inappropriate dosage selection	18 (9.6)
Pharmacokinetic problems	118 (63.1)
Manifest side effect, no other cause	2 (1.1)
Instructions for use /taking not known	1 (0.5)
Patient has concerns with drugs	23 (12.3)
Dispensing error (wrong drug or dose dispensed)	9 (4.8)
Total	187

Pharmacist interventions to solve reported MRPs

There was no intervention in 28 cases (9.3%) out of the 300 cases (Table 3.9). Pharmacists recorded 272 interventions in 112 patients (Figure 3.4). Of these 272 interventions made, 138 (50.7%) were made at patient/carer level. Fifty- one of the 138 (36.9%) recommendations at patient/carer level involved medication counselling and 87 of the remaining 138 (63.1%) interventions at patient/carer level were directed towards the prescriber (referral to prescriber). Of the total 112 interventions made at the prescriber level, the pharmacists proposed 53 interventions to the prescriber or physician and all were approved (Table 3.10). However, only one intervention proposed by the pharmacist was not approved by the prescriber and the outcomes of other 32 interventions proposed were not known during the period of the study. At the

drug level, for 15 cases the pharmacists' intervention involved a switch of drug to another dosage or formulation. Other interventions proposed included brand switching especially with parallel import drugs.

Figure 3.3 Causes of MRPs



PKP= Pharmacokinetic problem; IDOS= Inappropriate dosage selection
IDS= Inappropriate drug selection; DE= Dispensing error; PCD= Patient has concerns with drug
INK= Instruction for use not known; MSE= Manifest side effect, no other cause

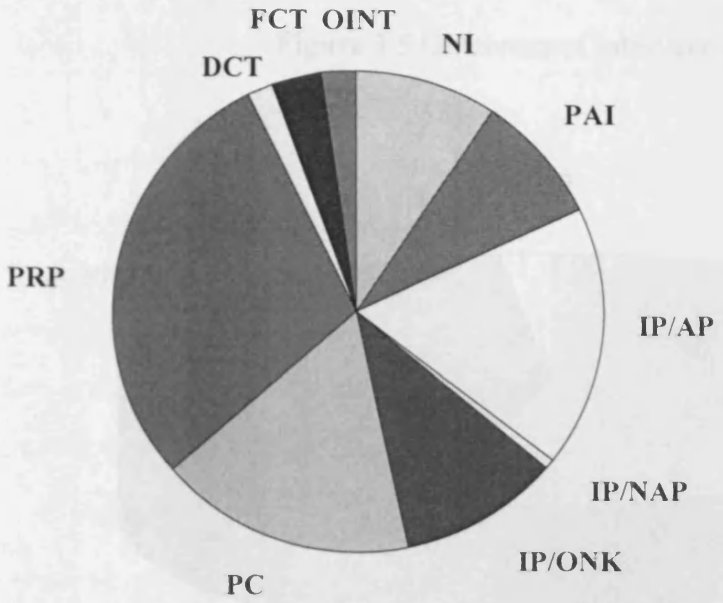
Table 3.9 Interventions to MRPs identified in the study

Interventions	Number (percentage)
No intervention	28 (9.3)
Prescriber asked for information	26 (8.7)
Intervention proposed, approved by prescriber	53 (17.7)
Intervention proposed, not approved by prescriber	1 (0.3)
Intervention proposed, outcome unknown	32 (10.7)
Patient (medication) counselling	51 (17.0)
Patient referred to prescriber	87 (29.0)
Dosage changed to.....	5 (1.7)
Formulation changed to.....	10 (3.3)
Other intervention	7 (2.3)

Table 3.10 Medication-related problems and the pharmacist's interventions

	Medication-related problems							
Interventions	Side effect suffered (non allergic)	Inappropriate drug	Inappropriate drug duplication	Contra-indication for drug	Drug dose too high	Drug not taken	Wrong drug taken	Potential interaction
Prescriber asked for information	8	3	3	2	0	2	0	8
Intervention proposed, approved by prescriber	11	8	0	4	6	3	2	19
Intervention proposed, not approved by prescriber	0	0	0	0	0	0	0	1
Intervention proposed, outcome unknown	1	4	1	5	1	2	2	16
Patient (medication counselling)	23	2	7	1	12	0	0	6
Patient referred to prescriber	16	15	3	2	2	7	2	40
Dosage changed to....	0	1	0	1	0	1	1	1
Formulation changed to.....	0	1	0	0	1	0	7	1
Other interventions	1	0	0	0	1	0	2	3

Figure 3.4 MRPs interventions



PRP= Patient referred to prescriber **PC**= Patient counselling **NI**= No intervention
DCT= Dosage changed to... **FCT**= Formulation changed to... **OINT**= Other interventions
PAI= Prescriber asked for information; **IP/AP**= Intervention proposed, approved
IP/NAP= Intervention proposed, not approved; **IP/ONK**= Intervention proposed, outcome unknown

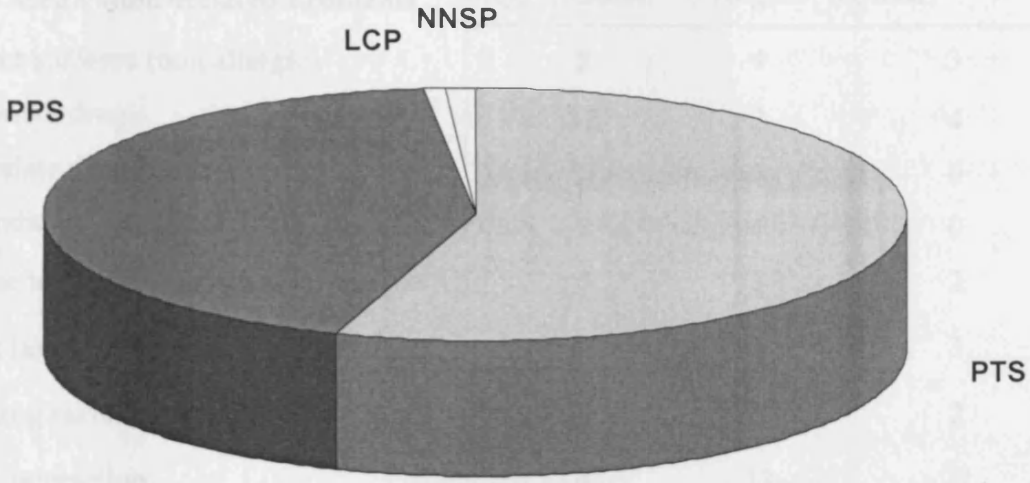
Outcomes of intervention

Out of the total of 272 interventions proposed by the pharmacists who participated either at patient/carer level, prescriber's level or drug level based on the PCNE_DRP V5.00 classification scheme, over half (150; 55.1%) of them resulted in satisfactory outcome (Table 3.11). In addition, 117 (43.0%) interventions were partially solved and 5 interventions remained unsolved partly due to lack of cooperation of the respective prescriber or no need or possibility of solving the problem (Figure 3.5).

Table 3.11 Outcomes of intervention

Outcomes	Number (percentage)
Problem totally solved	150 (55.1)
Problem partially solved	117 (43.0)
Lack of cooperation of physician	2 (0.7)
No need or possibility to solve problem	3 (1.1)

Figure 3.5 Outcomes of intervention



PPS= Problem partially solved **LCP**= Lack of cooperation of physician

PTS= Problem totally solved **NNSP**= No need or possibility to solve problem

MRPs reported by the three patient groups

Out of the total of 187 cases of medication-related problems discovered in the patients, 70 (37.2%) cases of potential drug interactions occurred among the hypertensive patient group, 18 (9.5%) among the anginal group and 22 (11.7%) among the post MI group (Table 3.12). Table 3.12 further revealed that a total of 20 cases of drug choice problem (such as "inappropriate drug", "inappropriate drug duplication", and "contra-indication for drug") were identified among hypertensive patients, 4 cases in angina patients and 4 in post MI patients. Also, a total of 21 cases of drug use problem ("drug not taken/administered at all", "wrong drug taken/administered") were detected in hypertension patient group. In addition, 1 case of "drug use problem" in anginal patient and 5 cases in post MI patients were also detected.

Table 3.12 MRPs identified in the three patient groups

Type of Medication-Related Problems	No of cases of MRPs in three patient groups		
	Hypertension	Angina	Post MI
Side effect suffered (non allergic)	5	4	3
Inappropriate drug	12	2	4
Inappropriate drug duplication	3	1	0
Contra-indication for drug	5	1	0
Drug dose too high or regimen too frequent	6	3	2
Drug not taken/administered at all	14	1	3
Wrong drug taken/administered	7	0	2
Potential interaction	70	18	22
No medication-related problem present	73	23	16

Causes of reported MRPs in the three patient groups

Table 3.13 summarises the distribution of Cause of MRPs identified among the three observed patient groups while Table 3.14 shows in details what cause of MRPs was responsible for what type of medication-related problem.

Table 3.13 Causes of MRPs identified in three patient groups

	Condition		
	Hypertension	Angina	Post MI
Inappropriate drug selection	12	1	3
Inappropriate dosage selection	10	4	4
Pharmacokinetic problems	75	21	22
Manifest side effect, no other cause	1	1	0
Instructions for use /taking not known	0	1	0
Patient has concerns with drugs	16	2	5
Dispensing error (wrong drug or dose dispensed)	7	0	2

Apart from "pharmacokinetic problems", other common predictors of medication-related problems identified in this study included "inappropriate drug selections", "inappropriate dosage selection", "dispensing error" and "patient has concerns with drugs". For example, inappropriate drug selection (15 cases) and "patient has concerns with drugs" (3 cases) were the two predictors of 18 cases of inappropriate drugs identified during the study (Table 3.14). An example of this involved a 75 year old female patient who found it difficult to swallow verapamil 80mg tablets prescribed by her general practitioner. After consultation with her prescriber, it was resolved to switch her medication from a tablet formulation to a liquid preparation.

Furthermore, 12 reported cases of "non allergic side effects" in the study were as a result of 1) inappropriate dosage selection (7 cases); 2) pharmacokinetic problem (2 cases); 3) instruction for use/taken not known (1 case); and 4) patient has concerns with drugs (2 cases). All the 11 cases of "drug dose too high" were classified as a result of inappropriate dosage selection. Also, cases where the patients had concerns with drugs such as direction for use, drug formulation issues contributed to some of the 18 reported cases of the "drugs were not taken/administered" (Table 3.14).

DISCUSSION

The characteristics of the study participants showed several differences such as large variation in the type of medical conditions these participants suffered from, co-morbidity and how the problems were discovered. Perhaps not surprising, the number of patients who were on different medications was quite high. This is probably due to the fact that hypertension is the most common chronic health problem especially in Western society (Graham-Clarke and Hebron, 1999). According to the Blood Pressure Association (2007), hypertension affects 16 million adults in the United Kingdom and about 4 million people are on drug therapy for this condition on a daily basis (Blood Pressure Association, 2007). In addition a number of studies have identified and documented medication-related problems in patient groups similar to those included in this study (Westerlund et al. 1999a; Westerlund, et al. 1999b; Paulino et al., 2004; Blix et al., 2006).

Table 3.14 Relationship between Medication-related problems and their causes

Cause of MRPs	Medication-related problems							
	Side effect suffered (non allergic)	Inappropriate drug	Inappropriate drug duplication	Contra-indication for drug	Drug dose too high	Drug not taken	Wrong drug taken	Potential interaction
Inappropriate drug selection	0	15	0	1	0	0	0	0
Inappropriate dosage selection	7	0	0	0	11	0	0	0
Pharmacokinetic problem	2	0	1	5	0	0	0	110
Manifest side effect, no other cause	0	0	2	0	0	0	0	0
Instruction for use / taken not known	1	0	0	0	0	0	0	0
Patient has concerns with drugs	2	3	0	0	0	18	0	0
Dispensing error (wrong drug or dose dispensed)	0	0	0	0	0	0	9	0

For example, a study published by Titley-Lake and Barber (2000) showed that 63.7% of patients who participated in the study had suffered one or more drug–related problem and four years later, a similar study by Paulino et al (2004) showed that an average of 5.9 potential drug-related problems per patient was identified.

Medication-Related Problems

Although, according to some authors, most of the medication-related problems may seem not to have direct clinical consequences, they could be associated with compliance problem hence a decrease in therapeutic benefits in the long run (Paulino et al., 2004). Westerlund et al (1999a) found that 2.5% of the observed population suffered a drug-related problem. The fact that in this present study the proportion of hypertensive patients with MRPs is much higher indicates that this patient group is at increased risk of experiencing medication-related problems especially in the community setting probably as a result of multiple antihypertensive drug therapy involved. This study also confirms that hypertensive patients are an important target group for pharmacy intervention such as medicine use review (part of an enhanced pharmacy contract recently introduced in the United Kingdom).

The proportion of potential drug interaction in this study was higher than other identified MRPs. The cause of this is probably due to pharmacokinetic problems. These occur when one of the prescribed drugs alters the absorption, distribution, metabolism, or excretion of another, thus increasing or reducing the amount of the first drug available to produce its pharmacological effects. Many of these drug interactions are harmless and many of those which are potentially harmful only occur in a small proportion of patients. Moreover, the severity of an interaction varies from one patient to another and often involves drugs with a small therapeutic index and those which require careful control of dosage. In this study, all the five pharmacies where data were collected had in place a sound system of identifying potential drug interactions whereby the pharmacist is alerted of any drug interactions involved in the patient's prescribed medicines. For example, the warning signals were divided into 1* (one star), 2** (two stars), 3*** (three stars), and 4**** (four stars).

These stars warning signals indicate the level of seriousness of the potential drug interactions involved. The four stars (4****) warning signals were considered to be potentially very serious and always received the pharmacist's immediate attention. In such situations, the pharmacist exercised caution in interpreting the suspected drug interaction in order to avoid undue panic, in particular for patients who were stabilised on a specific drug for a considerable period of time.

Pharmacist intervention

In this study, pharmacists evaluated the likelihood that medications were causing drug-related problems and intervened with the GP and patient, where appropriate. Most of these interventions involved advice on drug dosage adjustment, brand switching where necessary, verbal instructions about their medical condition, drug therapy, diet and exercise. On patient/carer level for example, "patient (medication) counselling" and "patient referred to prescriber" were the most common pharmacy interventions. This can be explained by the nature of the MRPs identified, and hence the associations found between MRPs and the subsequent interventions. In most of the cases where patients experienced upset stomach or rash as a result of brand switching (for example, parallel import of amlodipine tablet vs original brand), patients were reassured of the fact that the main active ingredient in both drugs were the same, however they were advised to stop taking the medication and referred to the prescriber for an alternative medicine or change in their prescribed medication. Furthermore on the prescriber level, it is important to highlight the fact that when an intervention was proposed by the pharmacist, in most cases, it received the prescriber's approval. Similar studies have also supported this notion of pharmacists proposing an intervention and getting positive response from the prescriber (Schumock et al., 1994; Granas and Bates 1999; Westerlund et al., 1999a).

The fact that pharmacists did not intervene in 28 cases may be explained by the association between the lack of intervention and having a side effect as the identified MRPs. A previous study has reported that in 32% of cases when an adverse drug event occurs and is reported to a health care provider, the drug is continued as before,

with no further intervention from the healthcare provider (Gray et al., 2001; Lassetter and Warnick, 2003; Paulino et al., 2004).

SUMMARY

- This study has shown that a systematic intervention by community pharmacists would result in detection of a high number of medication-related problems relevant for patient health outcomes.

- This study has highlighted that patients with more changes in their drug regimens (such as new drugs added, use of parallel imports medications, changes in dosage) and patients on multiple drug therapy are more likely to experience MRPs.

- This study has demonstrated that the use of a drug-related validation tool in community pharmacy practice would help to prevent MRPs, in particular in areas such as cardiovascular disease where patients are normally prescribed multiple drug therapy.

CHAPTER 4

Development and Content Validation of the Socioeconomic Impact Profile (SEIP)

INTRODUCTION

The study presented in chapter three has revealed that patients on multiple drug therapy especially in cardiovascular diseases are prone to medication-related problems (MRPs) such as medication side effects. These MRPs could dramatically affect a patient's health-related quality of life (HRQOL) leading to social and emotional distress. The question that needs to be asked is: do these medication-related problems have any socio-emotional or socio-economic consequences? In order to answer this question, a literature search was performed to look for any reported cases that might have focused on such issues.

Over the past three decades, a number of instruments have been developed to measure the impact of a disease state on social, economic and total wellbeing of patients (Scott et al., 1999; Yu et al., 2004), however, little or no published work has been carried out on the social and economic impact of medication-related problems. An instrument is therefore needed to document medication side effects in chronic conditions, such as cardiovascular diseases, and its social and economic impacts on patients. To date, many studies have shown that depression, fatigue and sexual dysfunctions are indicators of social well being and emotional status of human beings (Bardage, 2000). As such, some of these studies have strongly associated these indices to common side effects of beta blockers therapy though with limited evidence (Ko et al., 2002). Measuring the social and economic impacts of medication–related problems will therefore be helpful in guiding policymakers, health service researchers and clinician interested in this area to determine which area of drug therapy need more focus and attention. In addition, patients are likely to benefit if the information obtained through the use of such an instrument is accessible to clinician as this will ensure that those questions which contribute to a person's HRQOL can be monitored and considered when treatment protocols are drafted, thereby enabling comprehensive and holistic treatment decision taking.

Antihypertensive drugs and patients' health-related quality of life (HRQOL)

The effect of antihypertensive treatments on patients' HRQOL have been described to be complex in various published studies with persistence in negative perception of

drug treatment due to their side effects (Bremner, 2003). For example, calcium channel blockers such as felodipine or isradipine can cause severe ankle swelling as a late–onset side effect (Douglas and McLay, 1996) resulting in poor HRQOL of patient (Testa et al., 1998). Dry, persistent cough commonly associated with ACE inhibitors such as enalapril has been demonstrated to have negative influence on sleep patterns and in many cases has lead to either low concordance among patients or discontinuation from ACE inhibitor therapy (Israili and Hall, 1992; Fletcher et al., 1994). Studies have also shown that beta-blockers have an immediate negative impact on patients' well being and therefore need to be carefully titrated with low doses when initiating treatment (Tregaskis and McDevitt, 1990).

In the United Kingdom in 2006, use of beta–blockers came under scrutiny following a publication on the re-evaluation of the benefits of beta-blockers (Carlberg et al., 2004). As a result of this, the British National Formulary (BNF) 51 suggested reconsideration of use of this class of antihypertensive drugs as a first choice in routine initial therapy for hypertension. In addition, studies have associated beta blockers with side effects such as impotence (Ostergren et al., 1996), depression and decreased life satisfaction (Breckenridge, 1991), and an assessment of the impact of these side effects on such areas as emotional well being, performance at work and overall perception of well being needs a constant focus and attention.

Cardiovascular drugs and compliance

Studies have shown that drug therapy for cardiovascular disease is lifesaving and necessary to limit the complications of the disease. However, distressing side effects from drug treatment as mentioned above often contribute to withdrawing from medication or low compliance (Bardage, 2000). In the treatment of hypertension for example, several side effects and symptoms such as tiredness, mood changes, and sleep disturbances, blurred vision, dry cough and impotence associated with these medications are also indicators of socio-economic and emotional status which can adversely affect the HRQOL of patients. All these attributes were therefore taken into consideration at this stage of development of the new measurement instrument, the Socioeconomic Impact Profile (SEIP).

Clearly, in order to minimise medication–related problems among cardiovascular patients and improve adherence with antihypertensive medications, certain interventions are needed. However, if such interventions are to be successfully designed, targeted and cost–effective, it is critical to understand the social and economic consequences of these medication–related problems and identify ways for their modification. One way of doing this is to develop a standardised instrument that is aimed at systematically measuring these social and economic impacts.

METHODS

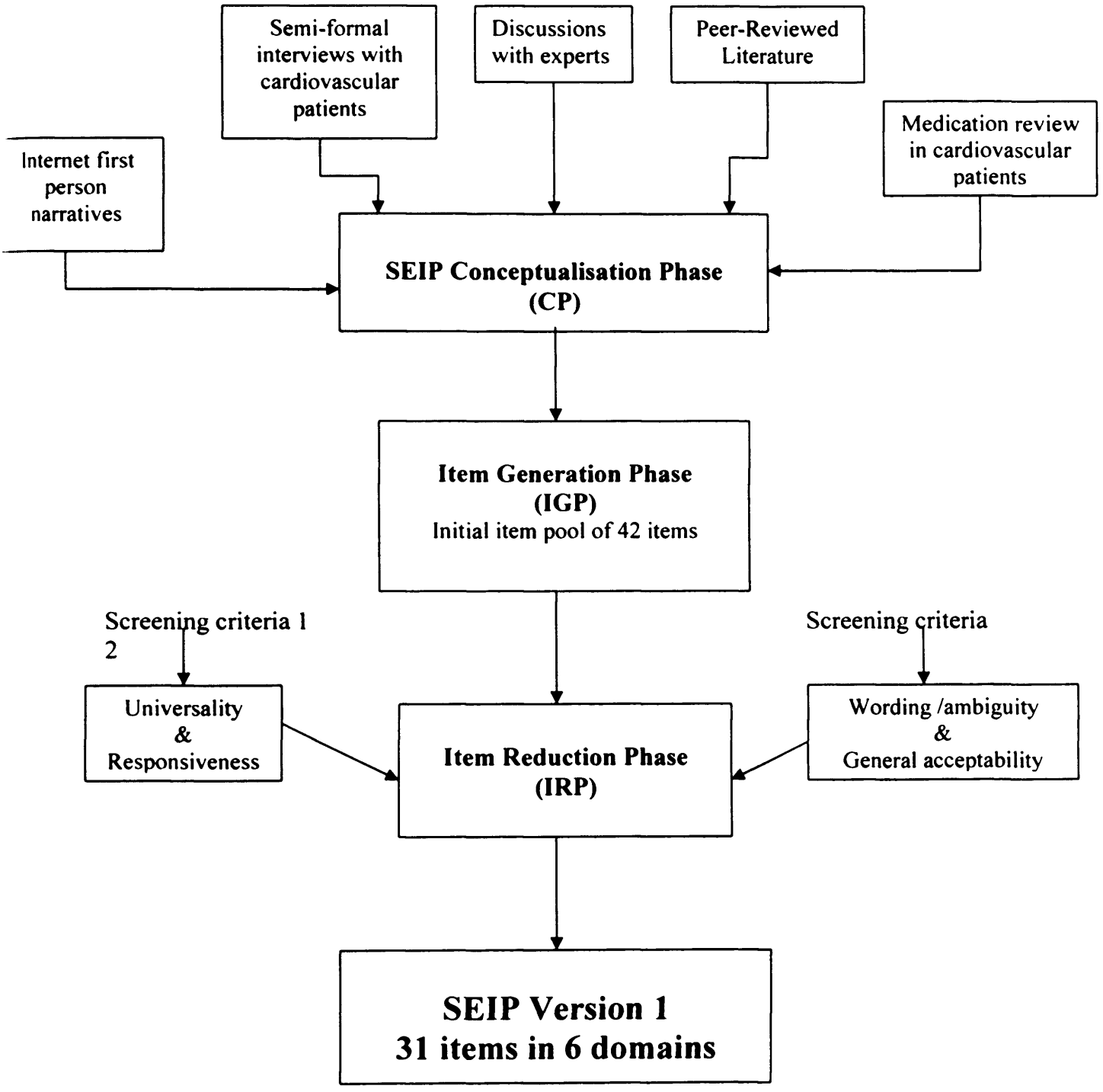
Development of the instrument

The Socioeconomic Impact Profile (SEIP) was designed to investigate the social and economic consequences of medication-related problems especially in patients on long-term use of cardiovascular drugs. A multi-source and multi-stage process (Figure 4.1) was used to develop and finalise the draft instrument. Given that the primary goal of developing a new instrument is to create a valid measure of an underlying construct (Clark and Watson, 1995), a critical first step in scale development is to develop a precise and detailed conception of the target construct and its theoretical context. With this in mind, the Version 1(pilot version) of the questionnaire was developed after undergoing three developmental stages: conceptualisation phase; item generation phase; and item reduction phase.

Phase 1: Conceptualisation

In this phase of development, the proposed model was discussed with some community pharmacists with clinical practice experience. The information from the discussion with these experts was used to elaborate a survey for identifying medication-related problems of cardiovascular drugs they encounter during pharmaceutical care process in their pharmacies. This was followed by a bibliography review in the areas of medication–related problems and cardiovascular drugs side effects in order to identify the most relevant aspects describing the impact of cardiovascular drugs side effects on the patients' social and economic wellbeing. The MEDLINE database and Google scholar search engine generated samples of items describing symptoms and side effects of antihypertensive drugs.

Figure 4.1: Developmental stages of SEIP version 1



Some of these symptoms such as depression, fatigue and sexual dysfunction were attributable to beta blockers. Each symptom was further assessed in terms of its importance for the patient and the frequency with which it is reported in the community pharmacy during the pharmaceutical care process. Furthermore, ideas about this concept were also sought from research pharmacists and a heart failure specialist nurse. Comments were sought on any medication-related issues that these community pharmacists might have come across during pharmaceutical care processes in their pharmacies.

In addition, in depth semi-structured interviews were held with fifteen community managed cardiovascular patients (hypertensive, angina and heart failure patients). The questions used to elicit thoughts on medication side-effects and their impact on social, emotional and economic life in patients interviewed targeted phrases or ideas that addressed the areas of life most affected by medication side effects. The interviews lasted between 15 and 20 minutes. After transcribing the interviews, relevant phrases/expressions were obtained. Finally, first person narratives posted by individuals with side effects to some cardiovascular drugs such as statins–anticholesterol agents on the internet and reporting on impact of these medication-related side effects on their quality of life were systematically sampled and analysed.

Phase 2: Item Generation

It has been suggested that the content of an initial item pool during an item generation stage should be over inclusive and item wording should be carefully studied before testing the item pool along with variables that assess closely related constructs (Clark and Watson, 1995). The conceptualisation procedure of the Socioeconomic Impact Profile (SEIP) was followed by generation of an initial pool of 42 items / statements. Many of these included verbatim quotations as described above. Others included rigorous literature search of reported cases of medication side effects of cardiovascular drugs. In addition, various generic and disease-specific quality of life instruments were examined for suitability and relevance of their contents to the measure being developed. Some of the generated items consisted of statements

written in the first person, for example, "I have lost interest in things I usually enjoy", and the way patients described themselves.

After eliminating redundancies, the concepts were grouped using a card-sort approach and consensus discussion with experts resulting in six SEIP domains: (A) patient's perception of treatment (e.g., "I have felt like all energy drained out of me" or "I have lost interest in sexual activity"), (B) impact on sexual functioning and physical activity (e.g., "my sexual desire has decreased" or "I feel calm and peaceful after walking a mile or doing some exercise"), (C) accessibility to health services (e.g., "I have been admitted to hospital " or "I have stayed in hospital for a couple of days"), (D) work-related limitations (e.g., "I have cut down on the amount of my working time" or "I have taken some days off sick"), (E) impact on social activities (e.g., "I prefer to stay at home than visiting friends and family"), and (F) brand switching (e.g., "I have had allergic reactions such as hives, rash etc.").

Some of the items referred to medication side effects and emotional distress were experienced by patients (e.g. beta blockers and insomnia, impotence; antihypertensive drugs and tiredness, depression). Other items made reference to the use of healthcare services as a result of medication-related problems. Items were included that reflected the impact on patient's productivity as a result of adverse drug reactions or any medication–related problems encountered in the course of drug therapy.

Phase 3: Item Reduction

An initial qualitative reduction of the identified items/statements was carried out, in which statements considered inappropriate, ambiguous or redundant were excluded. Some of the remaining items were slightly rephrased, merged or modified to fit the intended purpose. The decision to retain or remove an item was also based on the following four principles:

- Responsiveness: the item is expected to be sensitive to change over time.
- Universality: the item should capture behaviours/feelings of individuals across the observed groups and a broad age range;

- Wording/ambiguity: the item should be clearly worded and understood and is unlikely to evoke a variety of interpretations.
- General Acceptability: the item should resonate with focus group participants and should be felt appropriate for the target population.

Finally, the identified items were edited to create a self-administered preliminary questionnaire for a sample of 15 cardiovascular patients covering the three areas of disease groups (hypertension, angina pectoris and heart failure). Participants were asked whether the items captured the way they would describe themselves and whether they felt it was relevant to their social and economic condition. Suggestions were made for additions and revisions of items and only those items relating to the concept being measured were retained.

This finally led to the construction of an initial 31- item instrument covering six socio-economic related domains: 1) social interaction and emotional behaviour (10 items); 2) reactions to cholesterol lowering agents (5 items); 3) use of health services (5 items); 4) work (4 items); 5) change of medication (4 items); and 6) satisfaction with medication treatment (3 items). In addition, each domain of the SEIP version 1 (pilot version) included response scaling with either a 5-point or 4-point scale. For example, a 5-point frequency type response anchors was used in domain 1(i.e. "never", "a little of the time", "some of the time", "most of the time" and "all of the time".). On the other hand, another form of 4-point frequency type response anchors was used in domain 2 (i.e. "never", "seldom", "frequently", and "more frequently"). As with domain 1, a 5-point frequency type response option was adapted for domain 3 ("no, not at all", "seldom", "sometimes", "a little", and "a lot").

The 31-item instrument was then subjected to assessment of validity by some experts in order to create a version of the questionnaire that would provide a valid representation of the criterion to be measured. To allow for a more individualized assessment, participants in the validity assessment were required to rate their agreement or disagreement with each statement using a 4-point Likert-type scale ranging from 1 (strongly agree) to 4 (strongly disagree). This agree-disagree response

format was chosen over possible alternatives (never-always) as being the most appropriate for the types of items used.

Validation of SEIP - Content Validity

Content validity of health measurement scales has been described as how adequately the items sampled represent the range of each domain assessed by the instrument. Yaghmaie (2003) referred to content validity of an instrument as the degree that the instrument covers the content that it is supposed to measure. Barker et al (2002) pointed out that validity is a fundamental component of any research initiative and without conducting a validity assessment of any instruments; many researchers believe you do not have anything.

The content validation procedure in this study should raise two major questions: 1) is the instrument really measuring the kind of behaviour that is assumed by the investigator? 2) Does it provide an adequate sample of that behaviour? Ozsogut (2001) suggests that content validity is best assessed with a definitional or semantic judgement by a group of panel members. The key issue to bear in mind is, whether the instrument has the right focus and emphasis for the construct being measured for the intended population.

To assess the content validity of SEIP, both qualitative and quantitative study design were used. Pharmacists of various professional backgrounds and one cardiac nurse and a language expert were recruited to form an "expert panel" for the validity assessment. Their composition was: twelve community pharmacists, four research pharmacists, one cardiovascular specialist nurse, one linguistic expert and two cardiac patients. Validation instruments included the Version 1 (pilot version) of the SEIP and the content validation rating forms.

Quantitative assessment of SEIP by the expert panel

For the quantitative assessment study, the version 1 of the SEIP and the content validity rating forms were sent out to the expert panel for completion prior to a panel meeting. The panel was asked to assess the questionnaire on a 4-point scale (1 =

strongly agree, 2 = agree, 3 = disagree and 4 = strongly disagree) using the following five criteria:

- Clarity – the item must be clear, unambiguous and straightforward in its intentions;
- Completeness – the item must show a degree of relevance, and fully reflect the intended meaning, focus and emphasis;
- Linguistic clarity – the item / statement should be straightforward and easily understood by anyone with a minimum knowledge of reading and writing and should be jargon - free;
- Relevance – reflect the target population and their condition that is being measured;
- Scaling – fitting with the way items / statements are structured.

They were also told to make any written comments about any ambiguities in the questionnaire and suggestions concerning rewording, rephrasing or redundancy of any item.

Qualitative assessment of SEIP by the expert panel

The qualitative assessment method involved an expert panel meeting conducted after the quantitative analysis of the questionnaire. All the participants in the quantitative part of the study were asked whether they would be willing to take part in a round table discussion. Only two community pharmacists and one research pharmacist were able to attend the expert panel meeting. This session was held at the Welsh School of Pharmacy, lasted for 90 minutes and the members of the expert panel gave consent for being audio taped. In addition, face-to-face interviews with two cardiovascular patients and a specialist heart failure nurse were conducted to broaden the acceptability of the outcomes. The results of the quantitative assessment of the questionnaire by the expert panel were discussed during the meeting.

Following the meeting, further adjustments were made to the question structure to remove the ambiguities. Those experts who participated in the meeting were again sent another validity assessment form to re-evaluate the new version of the questionnaire. The questionnaire was then pilot tested among patients on repeat

prescriptions of cardiovascular drugs in five community pharmacies to further assess psychometric properties of the instrument such as factor analysis and internal consistency reliability test (chapter five).

Data Processing and Analysis

The expert panel meeting and the interviews were recorded and transcribed verbatim. Descriptive statistics were used to express the demographic characteristics of the expert panel members. The information was analysed by assessing the degree of concordance among experts for each of the five criteria response scale (clarity, completeness, language clarity, relevance, and scaling) by calculating the mean and standard deviation. Level of agreements among the panel members was further assessed by determining the Cohen kappa coefficient value. Under normal circumstances, Cohen kappa is used to determine the level of agreement between two raters. But in cases where the numbers of raters are greater than two, Cohen kappa macro syntax is computed. Kappa coefficient is defined as the actual inter-rater agreement beyond chance divided by the potential inter-rater agreement beyond chance.

Mathematically, $k = O - C / 1 - C$.

O = observed agreement beyond chance

C = chance agreement

1 = maximum level of agreement that can be reached among raters.

If the kappa value falls below 0.40, the result is considered to be "poor"; kappa value above 0.40 but less than 0.60 is considered to be "fair"; also, if the value of kappa is above 0.60 but less than 0.80, this result is classified as "good"; and any value of kappa above 0.80 is classified as "excellent".

RESULTS

Development of the SEIP

Item generation and reduction phase

Based on literature reviews and interviews with community pharmacists during the item generation phase, 42 items were identified (Table 4.1). During the item reduction

phase, 17 of these items were reworded (e.g. the title of domain A–"patient perception of treatment" became "social interaction and emotional behaviour", and domain D–"work–related limitation" was shortened to "work" etc.). Four other items were modified (e.g. item A2–"I have lost interest in things I usually cared about or enjoyed", or item A8–"I had constant headache after I started to take my medicine"), four items were merged into two (e.g. all items on domain B-"Impact on sexual functioning and physical activity" were moved to domain A since these items were examples of medication side effects which domain A actually captured.). Six items remained unchanged (e.g. items A1, A4, A6, C1, C2, and D2.) while nine items were made redundant (Table 4.2).

The title of domain 1 (patient perception of treatment) was reworded to "social interaction and emotional behaviour" as the contents indicated patients' emotional reactions to the side effects of their medicines. The SEIP Version 1 therefore comprised a total of thirty one items covering six socioeconomic-related domains: 1) social interaction and emotional behaviour, 2) reactions to cholesterol lowering agents, 3) use of health services, 4) work, 5) change of medication, and 6) satisfaction with medication treatment.

Content Validity

Socio-demographic characteristics of the expert panel members

Twenty individuals of different professional background were contacted to form the members of an expert panel for the content validation process. Eight were male and 12 were female. Their professional backgrounds were as follows: twelve community pharmacists, four research pharmacists, one cardiovascular specialist nurse, one linguistic expert and two cardiac patients.

Quantitative assessment results

Eighteen content validity rating forms were returned from the panel with comments and suggestions (Table 4.3). Two pharmacists did not complete but returned the forms.

Table 4.1 Statements compiled during Item generation Phase of the SEIP

As a result of medication side effects.....

1. I feel anxious and tense inside for no obvious reason.	2. I have difficulty swallowing the pills
3. I have lost interest in things I usually care about or enjoyed	4. I have problems opening or closing the containers.
5. I feel like all the energy has drained out of me.	6. I have problems getting the medication out of the containers
7. I have horrible nightmares and night terrors.	8. I have problems reading the labels on the containers.
9. I feel constipated for 4 or 5 days with no pain	10. I have stopped taking my medications.
11. I feel unpleasantly cold in my hands and feet.	12. I have been admitted to hospital
13. I have a troublesome cough that will not go away.	14. I have stayed in hospital for a couple of days.
15. I have a constant headache after taking my medicine.	16. I have called the NHS Direct number for an emergency.
17. I have swollen legs for a couple of days.	18. I have made an urgent appointment with my local surgery.
19. My sexual desire has decreased.	20. I have made an urgent appointment with my pharmacist.
21. I have lost interest in sexual activity.	22. I have made an urgent appointment to see my general practitioner.
23. I get tired during sexual activity.	24. I prefer to stay at home than visiting friends and family.
25. I have erection problems.	26. I am afraid of going to the cinema, leisure centres, church etc.
27. I have had allergic reactions such as rash , hive etc.	28. I think about myself being an embarrassment to people around me.
29. I have had an upset stomach.	30. I feel I am a nuisance to my friends.
31. I wake up at night to urinate more.	32. I have cut down on the amount of my working time.
33. I feel dryness in my mouth and the need to drink more water.	34. I have taken some days off sick.
35. I have gained some weight.	36. I am limited in the kind of work/activities I can do.
37. I have lost weight.	38. I have taken longer to do the work/activities I used to do.
39. I cannot see properly with my eyes.	40. I have no memory of events I did on the previous day.
41. I have suffered hair loss.	42. My speech is slurred.

Table 4.2: SEIP items following Item Reduction Phase (sample items to illustrate the process)

Domains and items	Outcome of Item Reduction Phase
A. Patient perception of treatment	**Reworded**
A1. I have felt anxious and tense inside for no obvious reason.	Unchanged
A2. I have lost interest in things I usually cared about or enjoyed.	Modified
A3. I have felt like all energy drained out of me	Modified
A4. I have had horrible nightmares and night terrors.	Unchanged
A5. I have felt constipated 4 or 5 days with no pain.	Discarded
A6. I have felt unpleasantly cold in my hands and feet.	Unchanged
A7. I have had troublesome cough that would not go away.	Modified
A8. I have had constant headache after I started to take my medicine.	Modified
A9. My legs got swollen for a couple of days.	Discarded
B. Impact on sexual functioning and physical activity	**Discarded**
B1. My sexual desire has decreased.	Merge with A
B2. I have lost interest in sexual activity.	Merge with A
B3. I have had erection problems.	Merge with A
B4. I feel calm and peaceful after walking a mile or doing some exercise.	Discarded
C. Accessibility to health services	**Modified**
C1. I have been admitted to hospital	Unchanged
C2. I have stayed in hospital for a couple of days.	Unchanged
C3. I feel embarrassed to talk about the side effect with my doctor.	Discarded
C4. I feel embarrassed to talk about the side effect with my local pharmacist.	Discarded
D. Work-related limitations	**Reworded**
D1. I have cut down on the amount of my working time.	Reworded
D2. I have taken some days off sick.	Unchanged
D3. I am limited in the kind of work /activities I can do.	Modified
D4. I have taken longer to do the work /activities I used to do.	Discarded
E. Impact on Social activities	**Merge with D**
E1. I prefer to stay at home than visiting friends and family.	Discarded
E2. I am afraid of going to cinema, leisure centres, church etc.	Discarded
F. Brand switching	**Reworded**
F1. I have had allergic reactions such as rash, hive etc.	Discarded
F2. I have had stomach upset diarrhoea and felt sick.	Discarded
F3. I have had problem swallowing the pills.	Discarded
F4. I have stopped taking my medications.	Discarded

Table 4.3: Expert panel members' response rate

Participants	Quantitative data N=18	Qualitative data N=6
Research pharmacists	4 (20%)	1 (16.6%)
Community pharmacists	10 (50%)	2 (33.3%)
Cardiac nurse	1 (5%)	1 (16.6%)
English language expert	1 (5%)	0
Cardiac patients	2 (10%)	2 (33.3%)

Table 4.4 shows the mean scores of the five criteria used by the expert panel members to rate all the items in the questionnaire. The analysis of each item's rating score generated by eighteen experts showed good expert consistency as regards the items' level of clarity and relevance. Table 4.5 describes the panel responses to the five criteria response scale of the SEIP. When they were asked whether the title of the questionnaire was clear, unambiguous and straightforward, three panel members (16.7%) strongly agreed, nine (50.0%) agreed and three (16.7%) disagreed. Three of the respondents did not complete this area of their rating.

On the issue of completeness of sentence, the experts were asked to take into consideration whether the questionnaire included complete and meaningful sentences which were easy to understand without requiring extra time to complete by patients, two panel members (11.1%) strongly agreed, eleven (61.1%) agreed and two (11.1%) disagreed. Three (16.7%) were not sure how to answer this question and therefore did not complete this aspect of the question.

The experts could not agree on the issue of linguistic clarity of the questionnaire. When they were asked whether the instrument is understandable, simple and clear language that is jargon–free, one (5.6%) of them strongly agreed, six (33.3%) agreed with this view while eight (44.4%) disagreed and one (5.6%) strongly disagreed. Two (11.1%) did not complete this section. In this scenario, half of the expert panel (most of them were practising community pharmacists) thought the title of the questionnaire

was too scientific for a lay patient to understand. Suggestions were made for improvement and to make the questionnaire simpler.

Table 4.4 The mean scores of the five criteria used in the validity process of SEIP 31 items by the expert panel (n=18)

Variables	Mean (SD)				
	Clarity	**Completeness**	**Linguistic clarity**	**Relevance**	**Scaling**
Q1	1.80 (0.41)	1.85 (0.37)	2.10 (0.31)	2.00 (0.00)	2.00 (0.00)
Q2	1.55 (0.51)	1.65 (0.49)	2.20 (0.52)	2.00 (0.00)	1.95 (0.22)
Q3	1.80 (0.52)	1.90 (0.31)	2.10 (0.45)	1.95 (0.22)	1.95 (0.22)
Q4	1.90 (0.31)	1.90 (0.31)	2.00 (0.32)	1.95 (0.22)	1.95 (0.22)
Q5	1.85 (0.49)	1.70 (0.57)	2.15 (0.59)	1.90 (0.31)	1.90 (0.31)
Q6	1.95 (0.39)	1.90 (0.31)	2.35 (0.49)	1.90 (0.31)	2.00 (0.00)
Q7	1.75 (0.55)	1.75 (0.55)	2.15 (0.59)	1.80 (0.41)	1.90 (0.31)
Q8	1.80 (0.41)	1.85 (0.49)	2.30 (0.57)	1.40 (0.50)	1.95 (0.22)
Q9	1.80 (0.41)	1.85 (0.49)	1.90 (0.45)	1.95 (0.22)	1.85 (0.37)
Q10	1.75 (0.44)	1.60 (0.50)	2.10 (0.64)	1.85 (0.37	1.85 (0.37)
Q11	1.90 (0.31)	1.90 (0.31)	2.00 (0.46)	1.85 (0.37	1.90 (0.31)
Q12	1.75 (0.44)	1.75 (0.55)	2.10 (0.55)	1.90 (0.31)	1.90 (0.31)
Q13	1.95 (0.22)	1.85 (0.37)	2.25 (0.55)	1.90 (0.31)	2.00 (0.00)
Q14	2.05 (0.22)	2.00 (0.32)	2.05 (0.39)	2.00 (0.00)	1.95 (0.22)
Q15	1.95 (0.22)	1.90 (0.31)	2.00 (0.32)	1.95 (0.22)	1.95 (0.22)
Q16	1.80 (0.410	1.75 (0.44)	1.75 (0.44)	1.95 (0.22)	1.75 90.44)
Q17	1.95 (0.22)	1.90 (0.31)	1.95 (0.39)	1.75 (0.45	1.90 (0.31)
Q18	1.75 (0.44)	1.75 (0.44)	1.80 (0.52)	1.90 (0.31)	1.75 (0.44)
Q19	1.95 (0.39)	2.05 (0.22)	2.20 (0.41)	1.75 (0.45)	2.00 (0.00)
Q20	2.00 (0.00)	1.80 (0.52)	2.05 (0.51)	2.00 (0.00)	1.85 (0.37)
Q21	1.95 (0.22)	1.95 (0.22)	1.95 (0.39)	1.85 (0.37	1.95 (0.22)
Q22	1.95 (0.22)	1.95 (0.22)	2.00 (0.00)	1.95 (0.22)	2.00 (0.00)
Q23	1.90 (0.31)	1.90 (0.31)	2.00 (0.32)	2.00 (0.00)	1.90 (0.31)
Q24	1.75 (0.44)	1.75 (0.44)	2.20 (0.41)	1.90 (0.31)	2.05 (0.39)
Q25	1.95(0.22)	1.95 (0.22)	2.10 (0.31)	2.05 (0.39)	1.95 (0.22)
Q26	1.95 (0.22)	1.95 (0.22)	2.10 (0.31)	1.95 (0.22)	1.95 (0.22)
Q27	2.05 (0.22)	2.00 (0.32)	2.15 (0.37)	1.95 (0.22)	1.90 (0.31)
Q28	2.00 (0.00)	1.55 (0.51)	2.15 (0.59)	1.90 (0.31)	1.70 (0.47)
Q29	1.95)0.22)	1.80 (0.52)	2.00 (0.46)	1.70 (0.47	1.85 (0.37)
Q30	2.00 (0.00)	1.90 (0.31)	2.05 (0.39)	1.85 (0.37	1.90 (0.31)
Q31	2.00 (0.00)	1.70 (0.57)	2.25 (0.55)	1.90 (0.31)	1.90 (0.48)

The level of agreement also varied on whether the included items showed a degree of relevance and reflected sample areas of interest to the observed patient population .The response rates were as follows: three (16.7%) strongly agreed, thirteen (72.2%) agreed and one (5.5%) disagreed.

Table 4.5 Agreement level of the expert panel to five criteria response scale

Response option	Number (%)				
	Clarity	**Completeness**	**Language Clarity**	**Relevance**	**Scaling**
Strongly agree	3 (16.7)	2 (11.1)	1 (5.6)	3 (16.7)	2 (11.1)
Agree	9 (50.0)	11 (61.1)	6 (33.3)	13 (72.2)	14 (77.8)
Disagree	3 (16.7)	2 (11.1)	8 (44.4)	1 (5.5)	1(5.5)
Strongly disagree	0	0	1 (5.6)	0	0
Missing value	3 (16.7)	3 (16.7)	2 (11.1)	1 (5.5)	1(5.5)
Total			**18 (100)**		

Qualitative assessment results

An expert panel meeting was organised after the results of the quantitative assessments had been analysed. Only three out of the eighteen expert panels were able to attend this meeting. Those present were shown the results from the quantitative assessments including comments and suggestions that were proposed for further deliberations (Table 4.6). The results of the quantitative assessment were further discussed among the expert panel members who participated in the discussion meeting until consensus was reached and all members agreed on the contents of the final version of the SEIP. During the discussion meeting, it was suggested that a broader, more generic title was needed for the instrument if it were to be administered to lay patients in general. As it is impossible to assess whether side effects suffered by cardiac patients are due to their medication or their medical condition, suggestions

were made to add a column to ask patients about their thought on the cause of the side effects they experience. Several amendments were further made to the questionnaire to reflect suggestions made by some expert panels during the panel discussion. Some questions were further removed in order to reduce the length of the questionnaire and some questions had extra options added or removed from them.

Table 4.6 Comments and suggestions about the questionnaire from some of the expert panel

Expert panel	Comments and suggestions
CP 1	The title – "I feel would put a lot of people off. It is too complicated.
CP 2	"Although the title of the questionnaire is relevant to the person conducting the survey, a member of the general public may not understand the term - socioeconomic impact profile. A broader, more general title is needed".
CP 2	"The instructions are fine, as it is clear, concise and to the point"
	"Title is unlikely to be understood by the less educated"
RP 1	"Good title for professionals to understand"
CP 3	"Not too sure if the title (SEIP) will confuse people – what does it mean? Could put people off showing interest in the survey"
NURSE	"I feel the title is a bit off-putting for the lay person. Why do they need to know the title, it is just a questionnaire as far as they are concerned"
	"It is not made clear in the paragraph if this is a one-off survey or if there is a time scale for repeating it".
	"I feel the scale for income does not go down far enough-what if they earn less than £5000 per annum?"
	"In the section "use of health services" our patients would probably ring us not NHS direct"
	"Where it says "what is your condition"- patients may have multiple pathology so perhaps it should have been what your cardiac/heart condition is?
	"Marital status-many people live together so I do not know what they would put there".

CP- community pharmacist, RP – research pharmacist

The new version of the SEIP now consisted of 24 items (Table 4.7). These items were grouped into 5 domains: 1) medicated-related problems and socio-emotional distress (13 items); 2) impact on healthcare services utility (6); 3) work and

productivity impacts (3); 4) change in medication (1); and 5) satisfaction with change in medication treatment (1).

Table 4.7: Structure of the new version of SEIP

SEIP domain	No of items
1. Medication-related problems and socio-emotional distress	13
2. Impacts on healthcare services utility	6
3. Work and productivity impacts	3
4. Change in medication	1
5. Satisfaction with change in medication treatment	1

Kappa coefficient

In order to determine the level of agreements among all the participants in the expert panel meeting, data obtained from the completed validity rating forms by the panel members were coded and analysed using the Statistical Package for the Social Sciences (SPSS) version 12. The level of agreement among the six members of the panel as determined by Cohen kappa coefficient value was excellent ($k = 0.85$; $P < 0.0001$), supporting the content validity of the instrument (Table 4. 8).

Table 4.8: Level of agreement among the experts using kappa statistics

No of raters	No of items	Percent of raters	Kappa Value	Standard Error	P	Lower 95% Confidence Limit	Upper 95% Confidence limit
6	24	0.93	**0.85**	0.69	0.0001	0.72	0.98

DISCUSSION

The present study deals with the development of a specific questionnaire designed to assess the impact of medication-related problems on social and economic wellbeing of chronically ill patients on cardiovascular drugs. Badia et al. (2007) suggested that

the main advantage of a specific questionnaire with respect to a generic instrument is that the former allows one to assess domains relevant to the impact of medication side effects on patients' social and economic wellbeing.

In the developmental phase of the questionnaire, a methodology based on a literature review and round table discussion with experts in this area was used, thus yielding complementary results that reinforce the robustness of the data in this study. Other authors have used these methodologies as well in the development of questionnaires, with equally positive results (Priesto et al., 2005; Badia et al., 2005).

There was a varying level of agreement among the expert panel who completed and returned the questionnaire. During a panel discussion meeting, the results of the quantitative assessment by all of the eighteen expert panel members were discussed and comments were made. From the point of view of research pharmacists, the title of the questionnaire needed to be more scientific whereas community pharmacists thought that the title should be simple for a lay person to understand. According to a comment from one of the community pharmacists, "although the title of the questionnaire is relevant to the person conducting the survey, a member of the general public may not understand the term socioeconomic impact profile. A broader, more general title is needed". Another community pharmacist commented on the title - "I feel the title would put a lot of people off – it's too complicated".

According to some of the community pharmacists who completed the assessment form, items included in section A (social interaction & emotional behaviours) of the questionnaire captured common side effects of most cardiovascular drugs and therefore were appropriate to be included. However, it was agreed to merge section B (reactions to cholesterol lowering agents) with section A (social interaction & emotional behaviour). The reason for this was that items on cholesterol lowering agents related to side effects of statins, which are also cardiovascular drugs. Moreover, section A (social interaction & emotional behaviours) de facto focuses on side effects of most cardiovascular drugs.

In erms of the psychological effects of medication, a patient on a new cardiovascular drug for example, a beta blocker, may be told by his general practitioner of possible

side-effects of such a medicine before it is prescribed, thus a suggestion was made to add an additional column to section A (social interaction & emotional behaviour) to ask patients whether they think the side-effects they experience are due to their current medication, or their medical condition. Regarding the content validity, there was a varying level of agreement among the experts and the patients who rated each item and the questionnaire in total. The majority of the experts agreed that the content of the questionnaire was clear and straightforward, relevant and reflected sampled areas of interest to the observed population. However, strong objections were made to the linguistic clarity. Improvements were therefore made on this area, although the majority of those objections on linguistic clarity came from community pharmacists, thus there could be some professional bias in their comments. However, the statistical analysis of the content validity results demonstrated that the questionnaire was in concordance with its task to measure what it was actually designed to do, having the required focus and emphasis for what was being measured.

Summary

- The SEIP is the first instrument to be used to evaluate the socioeconomic impact of medication-related problems among cardiovascular patients
- Both the results of its qualitative and quantitative assessments by the expert panel have demonstrated that the instrument possesses favourable measurement properties by supporting its content validity.
- Therefore, to enhance wider acceptability of the instrument, further psychometric tests will be carried out among cardiovascular patients in community pharmacies to further establish its validity (factor analysis), reliability and applicability.

CHAPTER 5

Construct Validation of the Socioeconomic Impact Profile (SEIP) -Factor Analysis and Internal Consistency

INTRODUCTION

A measuring instrument is usually designed with certain underlying constructs in mind. If it were thought for example, that patients may be anxious and depressed about their condition after drug treatment, and that this would affect their social and economic wellbeing, one might wish to include an assessment of anxiety or depression (Karimova and Martin, 2003). However, it is generally accepted that concepts such as anxiety or depression cannot be measured in any direct, simple and objective manner using a single question (Zigmond and Snaith, 1983). Instead, one or more questions must be composed with a view to tapping into the presumed underlying concept of anxiety, which is regarded as a "latent construct" that can only be indirectly measured.

In order to measure the social and economic wellbeing of patients and its correlation with medication-related side effects, an instrument is needed with sufficient measurement properties. It is hoped that this chapter will examine the most important property, factor analysis of the SEIP.

Factor analysis

Factor analysis is a multivariate analysis method which aims to explain the correlation between a large set of variables in terms of a small number of underlying independent factors. It is used to explore the relationships between items of a new questionnaire and to assess the degree to which items measure the same concept. It is assumed that each of the variables measured depends upon the underlying factors but is also subject to random errors. As a wider component of construct validity, factor analytic technique has been well documented in chapter two of this thesis. In research, factor analysis is primarily engaged to reduce a large number of variables to a smaller number of clusters while retaining maximum spread among experimental units (Pallant, 2002). Many researchers have shown that this method can be used to provide an operational definition for an unobserved, hypothetical construct by using observed variables, or to test a theory about the nature of underlying variables (Ang and Huan, 2006).

Exploratory factor analysis (EFA)

Factor analysis can be either exploratory or confirmatory. Exploratory factor analysis (EFA) groups together variables that are intercorrelated. According to Finch (2006), EFA is used when the researcher is primarily interested in trying to identify potential factors underlying a set of items, but may not have a strong *a priori model* that he or she would like to test. Tabachnick and Fidell (2001) pointed out that this kind of factor analysis is usually used in the early stages of research when hypothesis about relationships in a reduced data set can be generated.

On the other hand, Fayers and Hand (1997) explained that the fundamental objective of exploratory factor analysis (EFA) is to group together those variables which are highly correlated with each other but are also relatively uncorrelated with other variables; these groups are then regarded as potential evidence of an underlying structure. Fayers and Hand (1997) also stated that EFA has been widely used as a form of construct validation. That it to say, if an instrument is believed to be measuring several different underlying constructs (such as anxiety, depression, or emotional distress) then one would expect it to be possible to group the questionnaire items into the corresponding clusters, solely on the basis of the item-to-item correlations. Factor analysis should therefore produce evidence of the "factor structure" of the items. If the expected factors are produced, "construct validity" is claimed for the instrument (Fayers and Hand, 1997).

Confirmatory factor analysis (CFA)

Confirmatory factor analysis (CFA) tests the goodness-of-fit of a pre-specified factor model (Fayers and Hand, 1997). It is considered by many proponents of Structural Equation Modelling (SEM) to be a far more appropriate method for construct validation (MacCallum et al., 1993; Fayers and Hand, 1997; Kline, 2005). These authors further stated that CFA enables testing of adequacy of fit of the data to the postulated underlying construct. Confirmatory factor analysis (CFA) is a more complex set of techniques used later in the research processes to confirm hypothesis about the structure of underlying set of variables. In this case, variables are specifically chosen to reveal underlying structural processes. CFA can also be applied

in a situation where specific model linking items to factors is to be tested (Finch, 2006).

In this present study, EFA will be applied as a means of exploring the structure of the SEIP. EFA will also be used to confirm that the instrument appears to possess an appropriate structure (construct validity), and to help further develop the instrument by revealing items that may be dropped from the questionnaire because they contribute little to the presumed underlying factors.

METHODS

The socioeconomic Impact profile (SEIP) was pilot tested among 175 cardiovascular patients on repeat prescriptions from five community pharmacies across England and Wales. Patients' consent was sought while waiting for their repeat medications in these pharmacies. Those who agreed to take part were given the questionnaire to complete and some who could not wait to fill in the questionnaire in the pharmacy agreed to return the completed questionnaire to the pharmacy either by post or in person.

Exploratory factor analysis

The returned questionnaires were coded and exploratory factor analysis was performed on the 24 –item SEIP using SPSS 12.0 statistical software. Since all SEIP questions are worded positively, there was no need to invert any negatively worded questions before carrying out the factor analysis. Therefore a high score for any item represents an excellent health state (improvement with increasing score). All items were subjected to Principal Components Analysis (PCA) for item reduction. The criteria chosen to determine that an extracted factor accounted for a reasonably large proportion of the total variance was based on an eigenvalue greater than 1. The factor analytic techniques used in this chapter have been described extensively in chapter two.

A maximum likelihood factor extraction procedure was chosen since this method of factor condensation is the most widely used approach in published studies (Martin and Thompson, 2000). Orthogonal (Varimax) rotation was performed initially to aid the

interpretation of the components and the results were compared to an oblimin non-orthogonal factor rotation procedure due to the possibility that extracted factors are likely to be correlated (West, 1991). Determination of a significant item-factor loading was set at a coefficient level of 0.30 or greater, this level based on a rationale of generating a more complete interpretation of the data set, this being a level consistent with the published work in this area (Martin and Thompson, 2000; Karimova and Martin, 2003; Mccue et al., 2003). Extracted factors were tested for internal reliability. The significance of the association between the factors themselves and between the factors and responses to certain questions of the questionnaire was assessed using the non-parametric test bivariate correlations (Spearman's rho), where appropriate.

Factor extraction

The pilot version of the socioeconomic impact profile (SEIP) contained following content validity, five sections totalling to 24 items. All the 24 items were subjected to factor extraction using SPSS 12.0 for windows. Data generated were assessed to ensure that they were suitable for factor analysis. The correlation matrix generated was inspected for coefficients of 0.30 and above, the value of the Bartlett's test of sphericity (Bartlett, 1954) and the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy (Kaiser, 1970; Kaiser, 1974) calculated were checked for their level of significance.

Three statistical rules were taken into consideration to determine the number of factors to extract: 1) Kaiser's criterion, 2) scree test and, 3) parallel analysis. Kaiser's criterions should display components with Eigen values of 1 or more in order to be considered. In the Scree plot generated by SPSS, sharp demarcations in the shape of a plot were looked for and only components above these points were retained for further exploration (Catell, 1966). Parallel analysis was performed by using Monte Carlo PCA for parallel analysis. With this technique, a list of Eigen values generated in Total Variance Explained table were used along with the number of variables analysed (in this case 24) and the number of subjects in the sample data (in this case 160). Also the number of replications was specified at 100 as a default. The programme further generated 100 sets of random data of the same size as the original

real data file (24 variables x 160 cases). The average Eigen values for these 100 randomly generated samples were calculated. The first Eigen value obtained in SPSS with the corresponding first value from the random results generated by parallel analysis was systematically compared. SPSS factor values larger than the criterion values from parallel analysis were retained, while the least values were rejected.

Factor rotation

Rotation of the data was performed after the numbers of factors had been determined. This was done by "rotating" the factors in order to present the pattern of loadings in a manner that would be easier to interpret. The varimax rotation technique was initially used and the results were then compared to oblique (Direct Oblimin) rotation. The outputs generated were checked for interpretation.

Internal consistency reliability test of the extracted factors

The internal consistency of items within a factor was estimated using the reliability coefficient (Cronbach's coefficient alpha). This is to indicate the strength of the relationship of each item within the factor. Ideally, the Cronbach alpha coefficient should be above 0.7 which would imply that 70% of the measured variance is reliable and 30% is owing to random error. In some cases however, due to the sensitivity of the values to the number of items in a scale, the Cronbach coefficient values may be lower than expected (Pallant, 2002). In this case, it may be more appropriate to report the mean inter-item correlation for the items. An optimal range for the inter-item correlation of 0.2 to 0.4 is commonly recommended.

RESULTS

Socio - demographic characteristics

A total number of 160 / 175 (91.4%) patients from five community pharmacies completed and returned the questionnaire. The age range was 37 to 81 with a mean of 55.6. Table 5.1 shows the socio-demographic characteristics of those who participated in the pilot study. Seventy-six (47.5%) were male, 90 (56%) were mainly on antihypertensive drugs and the mean duration of their medical condition was 64.7 months. 122 (76.3%) were employed and over 53% were earning between £20,000 and £30,000 annually.

Table 5.1 Socio-demographic characteristic of the study participants

Variables	Frequency (n)	Percentage (%)
Sex		
Male	76	47.5
Female	84	52.5
Medical condition		
Hypertension	90	56.3
Heart failure	5	3.1
High cholesterol	9	5.6
Angina	14	8.8
Heart attack	11	6.9
Diabetes	5	3.1
Hypertension and diabetes	18	11.3
Hypertension and others	8	5.0
Education		
Primary school	1	0.6
High school	99	61.9
University degree	60	37.5
Marital status		
Single	3	1.9
Married	136	85.0
Living with a partner	5	3.1
Separated	4	2.5
Divorced	5	3.1
Widowed	7	4.4
Employment status		
Employed	122	76.3
Retired due to health	1	0.6
Retired not due to health	33	20.6
Employed and receive income support benefit	3	1.9
Employed and receive other social support	1	0.6
Annual income		
£10,000 < E < £20,000	8	5.0
£20,000 < E <£30,000	86	53.8
£30,000 < E < £40,000	40	25.0
E > £40,000	26	16.3

Correlation and Component Matrix results

Generation of the correlation matrix for the 24 items of the SEIP was followed by a check for evidence of coefficients greater than 0.30. Tabachnick and Fidell (2001) suggested that if few correlations above this level were found, then factor analysis may not be appropriate. SPSS also generated two statistical measures to help assess the factorability of the data: Bartlett's test of sphericity and the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy. According to Tabachnick and Fidell (2001), the Bartlett's test of sphericity should be significant ($P< 0.05$) for the factor analysis to be considered appropriate, and the KMO index should range from 0 to 1, with 0.6 suggested as the minimum value for a good factor analysis.

In this study, the Kaiser–Meyer-Olkin measure of adequacy value was 0.82 (Table 5.2), exceeding the recommended value of 0.60 and the Bartlett's Test of sphericity reached statistical significance ($P < 0.001$). The correlation matrix result for the 160 completed questionnaires of the Socioeconomic Impact Profile (SEIP) revealed the presence of some coefficients of 0.3 and above (Table 5.3) thereby fulfilling one of the criteria for suitability of factor analysis. Variables that do not have a correlation of greater than 0.30 should be considered for removal from subsequent factor analysis. Although values greater than 0.3 in the component matrix were accepted as significant, in this factor analysis, 19 out of 24 of the questions produced values > 0.40 indicating the robustness of the solution.

Table 5.2 Assessment of the suitability of items in the SEIP for factor analysis

Kaiser-Meyer-Olkin Measure of Sampling Adequacy.		0.82
Bartlett's Test of Sphericity	Approx. Chi-Square	1070.87
	Df	276
	P value	0.0001

Table 5.3 Correlation matrix* between the 24- items of the initial version of the SEIP

	A1	A2	A3	A4	A5	A6	A7	A8	A9	A10	A11	A12	A13	B1	B2	B3	B4	B5	B6	C1	C2	C3	D	E
A1	1.00																							
A2	0.41	1.00																						
A3	0.42	0.45	1.00																					
A4	0.73	0.55	0.72	1.00																				
A5	0.70	0.31	0.32	0 26	1.00																			
A6	0.81	0.48	0.72	0 77	0 44	1.00																		
A7	0.63	0.50	0.99	0 41	0 43	0.98	1.00																	
A8	0.52	0.45	0.52	0 39	0 40	0.65	-0 08	1.00																
A9	0 25	-0 13	-0 02	0 31	0 29	0 14	0 27	-0 10	1.00															
A10	0.40	0.50	0.36	0.36	0.71	0 18	-0.38	0.77	0 06	1.00														
A11	0 29	0.57	0.56	0.39	-0.81	0.74	-0 20	0 04	0 11	0.72	1.00													
A12	0 28	-0 04	0 26	0 18	-0 24	0.31	-0.33	0 25	0 27	-0 29	0 27	1.00												
A13	0.89	0.81	0.37	0.57	0.39	0.36	-0.38	0 11	0 24	0.50	0.70	0 15	1.00											
B1	0.41	0.45	0.35	0.41	0.42	0 10	0.70	0.58	-0 06	0.44	-0.35	-0 27	0.71	1.00										
B2	0.86	0.64	0.42	-0.77	0.48	0 18	0.31	0.87	-0.32	-0.30	-0.94	-0 25	0.67	0.33	1.00									
B3	0.75	0.91	0.76	0.36	-0.33	0.48	0.38	-0.49	0.35	-0 15	-0.47	-0.35	0 15	0 18	0 13	1.00								
B4	0.71	0.44	0.33	0.72	-0.60	0.56	-0 94	0.69	0 25	0.89	0.32	0 29	0.30	0.90	0..45	0.49	1.00							
B5	0.53	0.88	0.43	0.89	-0.39	0.88	-0 32	0.72	0 22	0.99	0 25	0 29	0 29	0.76	0 14	0.84	0.67	1.00						
B6	0 29	-0 23	-0 22	-0.30	0 20	-0 19	-0 13	-0 27	0 31	-0 27	0 12	0.38	0 20	0 27	0 13	0.37	0 08	0.63	1.00					
C1	0 19	0.32	0.39	-0.37	0.70	0 09	0.90	-0.68	0 22	-0.48	-0.51	-0 25	0.71	0.32	0.86	0.31	0.54	0.52	0 27	1.00				
C2	-0.68	0.78	0.31	-0.71	0.71	0.36	0 16	0 06	-0 39	-0.46	-0.43	-0 12	0 13	0..31	0.52	0 19	0.68	0.42	0.38	0.82	1.00			
C3	0 29	0.83	0.35	-0.60	0 26	0.86	0.39	0.38	-0 25	-0 28	-0.89	-0 15	0.49	0.43	0.63	0.71	0 23	0.73	0.30	0.44	0.57	1.00		
D	-0 12	-0 24	0 25	-0.39	0 29	0 21	-0 11	-0 17	0 28	-0 22	-0 15	0 12	0..38	0 22	0.37	0.30	0 26	0 21	0 17	0.30	0 13	0 25	1.00	
E	0 28	0 25	0 18	0 20	-0 12	-0.33	0 12	0 23	-0.30	-0 16	-0 19	-0 26	0 14	0 23	0 23	0 22	0 24	0 05	0 11	0 28	0.45	0 27	0.38	1.00

*Spearman rank correlation coefficient, r_s

The matrix produced by factor analysis is rotated to give the maximum number of items loading on the minimum number of factors. Furthermore, the results of the initial extraction with Principal Components Analysis (PCAs) revealed nine components with Eigen values greater than 1 with percentage of variance 14.69, 12.82, 8.04, 6.46, 6.19, 5.74, 4.87, 4.48 and 4.24 respectively (Table 5.4). These nine components explain a total of 67.52 percent of the variance (see Cumulative % column). The eigen values determine which components remain in the analyses because those factors with an eigen value of less than one are excluded.

Table 5.4 Principal Component Analysis describing the Total Variance Explained

Component	Initial Eigen values			Extraction Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	**3.53**	14.69	14.69	**3.53**	14.69	14.69
2	**3.08**	12.82	27.51	**3.08**	12.82	27.51
3	**1.93**	8.04	35.55	**1.93**	8.04	35.55
4	**1.55**	6.46	42.01	**1.55**	6.46	42.01
5	**1.48**	6.19	48.19	**1.48**	6.19	48.19
6	**1.38**	5.74	53.93	**1.38**	5.74	53.93
7	**1.17**	4.87	58.80	**1.17**	4.87	58.80
8	**1.07**	4.48	63.28	**1.07**	4.48	63.28
9	**1.02**	4.24	67.52	**1.02**	4.24	67.52
10	0.96	3.98	71.49			
11	0.84	3.51	75.00			
12	0.79	3.27	78.28			
13	0.70	2.93	81.21			
14	0.68	2.84	84.04			
15	0.61	2.54	86.58			
16	0.56	2.34	88.92			
17	0.52	2.16	91.08			
18	0.48	1.98	93.06			
19	0.38	1.57	94.63			
20	0.33	1.38	96.00			
21	0.31	1.29	97.29			
22	0.26	1.10	98.39			
23	0.22	0.92	99.31			
24	0.17	0.69	100.00			

Extraction Method: Principal Component Analysis.

Table 5.5 below shows component matrix with loadings of each of the items on nine components. The factors extracted account for a certain proportion of the total test variance, i.e. the combined variance demonstrated by all the items in the questionnaire. It is visible from this table that most of the items loaded quite strongly (above 0.30) on the first six components. SPSS suggested that any loadings above this value should therefore be considered for further exploration

Table 5.5 Component Matrix (nine components extracted*) of SEIP

	Component								
	1	2	3	4	5	6	7	8	9
C3. Work limitation	**0.72**	0.09	0.02	0.12	-0.15	0.28	-0.07	-0.03	-0.12
A3. Feel of energy loss	**0.67**	0.27	0.05	-0.09	0.11	**-0.35**	-0.02	0.18	0.00
A2. Loss of interest	**0.62**	-0.01	**0.38**	-0.12	0.17	-0.16	-0.17	0.03	0.10
C2. Day off due to sickness	**0.60**	-0.16	0.18	**0.42**	**0.42**	0.05	0.26	-0.06	0.11
C1. Reduce workload due to fatigue	**0.56**	-0.13	**0.32**	0.24	0.06	0.05	0.42	-0.06	**0.36**
B4. Appointment with GP	-0.24	**0.79**	0.22	0.17	0.17	0.01	0.11	-0.06	0.07
B5. Appointment with practice nurse	-0.09	**0.72**	0.26	0.06	0.10	-0.15	-0.18	0.03	-0.04
A12. Fatigue	**-0.33**	**0.49**	**0.33**	**0.39**	0.19	0.24	0.00	-0.03	0.07
A4 Nightmares and terror	0.03	**0.48**	-0.13	**-0.40**	0.00	0.26	0.17	-0.09	0.18
A6. Cough	0.23	**0.47**	0.15	0.01	-0.12	-0.18	-0.04	-0.01	**-0.31**
A13. Memory loss	-0.03	**0.46**	-0.10	0.03	-0.17	-0.01	-0.13	**-0.40**	**0.33**
E. Satisfaction	**0.31**	**-0.37**	0.20	**-0.35**	**0.32**	**0.31**	-0.07	-0.19	0.03
B1. Hospital admission	**0.38**	**0.35**	**-0.64**	0.18	0.07	-0.19	0.05	-0.03	-0.04
A5. Cold in hands and feet	**0.33**	0.21	**-0.54**	0.20	-0.17	**0.36**	-0.02	0.20	0.19
D. Medication change	-0.05	-0.03	0.16	**0.49**	**-0.42**	-0.15	**-0.43**	0.06	0.26
A1. Anxious and tense	**0.39**	**0.33**	**0.35**	**-0.40**	-0.04	-0.03	**-0.31**	0.21	-0.04
B3. NHS Direct call	**0.35**	0.16	**0.33**	-0.23	**-0.53**	-0.00	0.15	-0.13	0.04
A7. Headache	**0.47**	-0.09	-0.02	-0.06	**-0.50**	0.14	0.23	-0.02	-0.21
A8. Loss of sexual drive	**0.30**	**0.31**	**-0.34**	-0.18	0.17	**0.51**	**-0.37**	-0.02	0.14
A10. Slurred speech	0.12	**0.39**	**-0.42**	-0.27	0.24	**-0.48**	0.29	-0.01	0.05
A9. Erection problem	-0.12	**0.33**	0.05	0.06	**-0.35**	0.15	**0.39**	**0.38**	-0.02
B6 Enquiry with pharmacist	-0.12	-0.04	0.08	-0.09	0.19	0.12	0.00	**0.75**	0.16
B2. Hospital stay	**0.45**	0.03	-0.14	**0.40**	0.17	0.07	-0.15	0.02	**-0.52**
A11. Pain in calf	**-0.33**	**0.33**	0.22	-0.06	0.13	**0.38**	0.21	-0.09	**-0.38**

*Extraction Method: Principal Component Analysis.

Scree test

Many studies have shown that too many components (factors) are often extracted using the Kaiser criterion (Tabachnick and Fidell, 2001), it is therefore recommended to also look at the Scree plot generated by SPSS. As described in chapter two, scree test was another approach that was used in deciding the number of factors to retain. According to Taberchnick and Fidell (2001), this method involved plotting each of the eigen values of the extracted factors and inspecting the plot to find a point at which the shape of the curve changes direction and becomes horizontal. Cattel (1966) recommended retaining all factors above the elbow, or break in the plot, as these factors contribute the most to the explanation of the variance in the data set.

In this result, a study of the scree plot showed breaks after the third, the fourth and seventh components (Figure 5.1). The demarcation after the fourth component was sharper than the demarcation at the seventh component. An evaluation of scree plot results therefore suggested that either three or six factors could be retained for further exploration.

Parallel analysis

Parallel analysis of the results was also performed and the initial results (Table 5.6) supported the decision from the screeplot to retain six components; the first six factors were the only ones with Eigen values exceeding the corresponding criteria values for a randomly generated data matrix of the same size (24 variables x 160 respondents). Guided by the scree plot, and parallel analysis results, six factors initially extracted yielded Eigen values of 3.53 (14.7%), 3.08 (12.8%), 1.93 (8.0%), 1.55 (6.5%), 1.48 (6.2%), and 1.38 (5.7%), explaining 53.9% of the total variance. Comparing the eigen values from the parallel analysis results with the eigen values from the PCA, the first six eigen values from the PCA were higher than from the parallel analysis. These six components were therefore retained for further explorations (Table 5.7).

Figure 5.1 Scree Plot for the Socioeconomic Impact Profile

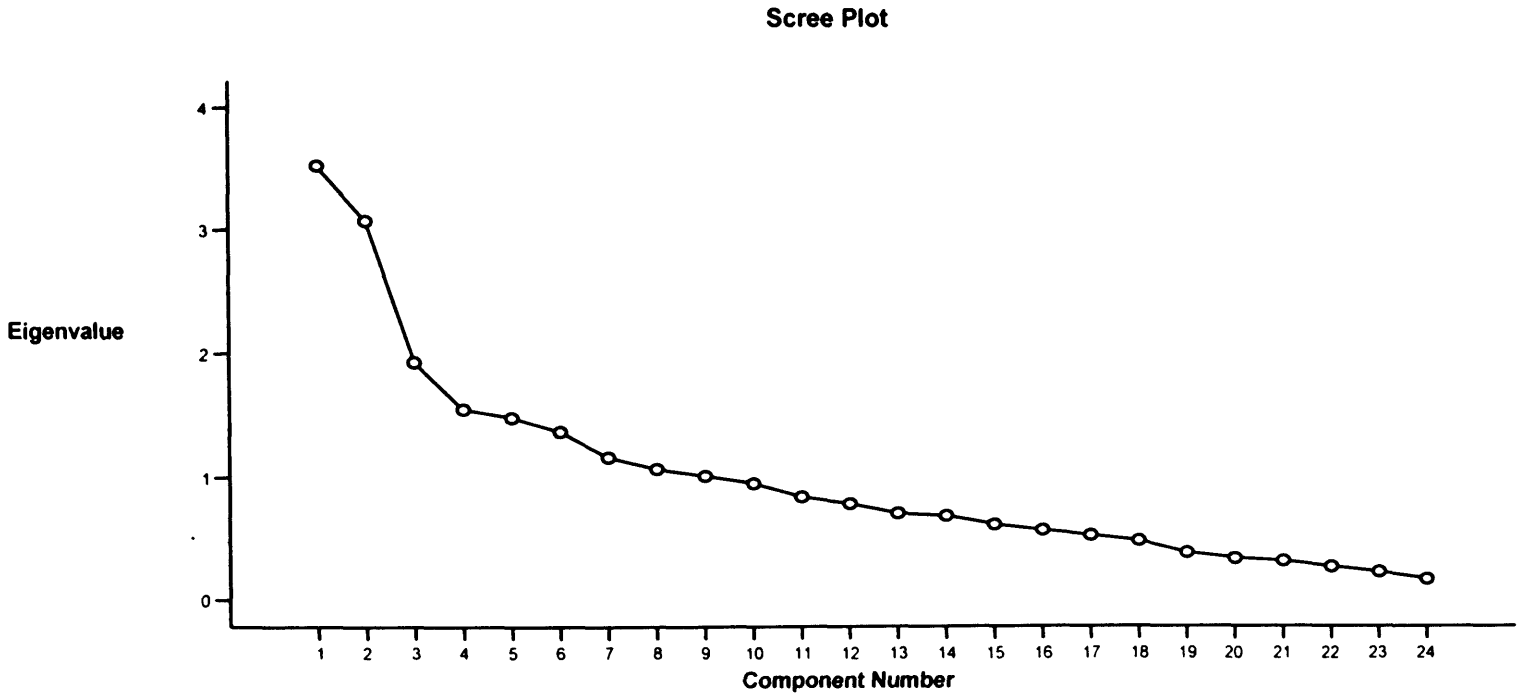


Table 5.6 Parallel analysis of the SEIP using Monte Carlo PCA method

Eigenvalue	Random Eigenvalue	Standard Dev
1	1.78	0.07
2	1.65	0.06
3	1.55	0.05
4	1.46	0.04
5	1.39	0.03
6	1.32	0.04
7	1.26	0.03
8	1.20	0.03
9	1.14	0.03
10	1.09	0.03
11	1.04	0.03
12	0.98	0.03
13	0.93	0.03
14	0.88	0.03
15	0.83	0.02
16	0.79	0.02
17	0.75	0.03
18	0.71	0.03
19	0.66	0.03
20	0.62	0.03
21	0.57	0.03
22	0.53	0.03
23	0.48	0.03
24	0.41	0.03

Factor rotation and its interpretation

Following determination of the number of factors, the next step was an attempt to interpret them. In this case, Varimax and Direct Oblimin rotation methods were used. Initially, six factors were identified from the rotated factor. These factors accounted for 53.9% of the total variance and are shown in Table 5.8 along with the percentages of total variance explained. The first factor accounted for the highest proportion of variance (11.7%) of any of the factors and this is because this type of analysis often produces a general factor which in this case includes two subgroups (statins and its impact on healthcare service utilization). Factor two accounted for 10.7% of the total variance explained. Factor three accounted for 9.2% of the Total Variance Explained, factor four = 8.3%, factor five = 7.8% and factor six accounted for 6.3%. It is

important to note that the cumulative total variance explained (53.9%) does not change after rotation, just the pattern of distribution among the six factors in comparison with Table 5.4 described earlier.

Table 5.7 Comparison of Eigen values from principal components analysis (PCA) and the corresponding criterion values obtained from parallel analysis.

Component number	Actual Eigen value from PCA	Criterion value From parallel Analysis	Decision
1	**3.53**	**1.78**	**Accept**
2	**3.08**	**1.65**	**Accept**
3	**1.93**	**1.55**	**Accept**
4	**1.55**	**1.46**	**Accept**
5	**1.48**	**1.39**	**Accept**
6	**1.38**	**1.32**	**Accept**
7	1.17	1.26	Reject
8	1.07	1.19	Reject
9	1.02	1.14	Reject

Table 5.8 Total variance explained for each factor based on 24 item SEIP

Factor	Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %
1	2.81	11.69	11.69
2	2.56	10.66	22.34
3	2.21	9.22	31.56
4	1.99	8.28	39.84
5	1.88	7.83	47.67
6	1.50	6.26	53.93

Extraction Method: Principal Component Analysis.

Varimax rotation of the six-factor solution of the SEIP

In the Rotated Component Matrix table (Table 5.9), there were factors with a number of strong loadings above 0.40 and most variables loaded substantially on component 1 to 4 with fewer cross loadings on some components.

Table 5.9 Varimax Rotated Component Matrix (a) for SEIP (Pairwise method)

	Component					
	1	2	3	4	5	6
Appointment with GP	**0.87**					
Fatigue	**0.77**					
Appointment with practice nurse	**0.74**					
Pain in calf	**0.49**					
Memory loss	0.33					
Erection problem						
Day off due to sickness		**0.87**				
Reduce workload due to fatigue		**0.64**				
Loss of interest		**0.55**	**0.45**			
Hospital stay		**0.54**		0.30		
Work limitation		**0.49**	**0.41**	**0.46**		
NHS Direct call			**0.75**			
Anxious and tense			**0.64**			
Headache			**0.50**	0.30		
Cough	0.35		0.36			
Cold in hands and feet				**0.79**		
Loss of sexual drive				**0.66**		**0.40**
Slurred speech					**0.81**	
Hospital admission				**0.53**	**0.63**	
Feel of energy loss		**0.44**	**0.43**		**0.53**	
Medication change						**-0.64**
Satisfaction	-0.31					**0.59**
Nightmares and terror				0.34		0.35
Enquiry with pharmacist						

Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization.

To allow the six components to be correlated with one another, it was decided to perform Oblimin rotation-another rotation technique frequently used. Generally, it is very vital to consider three tables from the Oblimin rotation output: Pattern Matrix, Structure Matrix and Component Correlation Matrix (Pallant, 2001). However, in this study, the Direct Oblimin rotation did not support the expected six dimensions since it failed to generate any values. Therefore Three-factor solution as another option was considered for exploration.

The Rotated Component Matrix and the Total Variance Explained of the three components are presented in Tables 5.10 and 5.11, respectively. Table 5.10 shows that factor 1 is accounted for 13.2% of the total variance explained while factor 2 and 3 explain 12.5% and 9.9% respectively of the total variance. The factor pattern / structure coefficients for the three components are shown in table 5.12 and 5.13 respectively while table 5.14 shows its Component Correlation Matrix. The Total Variance Explained describes how the deviation from the mean responses can be explained in terms of each of the components defined in the Pattern Matrix. Thus, 13.17% of the total variance (deviation from the mean) of correlations between items can be explained by Component 1, 12.52% of the total variance can be explained by Component 2, and 9.86% of the total variance can be explained by Component 3.

Table 5.10 Three factors of the SEIP with its total variance explained

Factor	**Rotation Sums of Squared Loadings**		
	Total	% of Variance	Cumulative %
1	3.16	13.17	13.17
2	3.01	12.52	25.69
3	2.37	9.86	35.55

Extraction Method: Principal Component Analysis.

The interpretation of the rotated component matrixes of the three factors by varimax method in Table 5.11 is similar to the six extracted factor solutions on Table 5.9. There are strong loadings on the three components with very few cross loadings. The first seven items, under Component 1 indicate medication side effects and impacts on productivity. The issue of productivity loss is significant in this component, possibly

because many cardiovascular patients with medication-related side effects may be prone to taking time off work as a result.

Table 5.11 Rotated Component Matrix (a) of the three extracted components

	Component		
	1	2	3
Loss of interest	**0.73**		
Work limitation	**0.64**		0.32
Feel of energy loss	**0.63**		0.34
Reduce workload due to fatigue	**0.63**		
Day off due to sickness	**0.60**		
Anxious and tense	**0.53**	0.32	
NHS Direct call	**0.48**		
Headache	0.39		
Hospital stay	0.33		0.31
Appointment with GP		**0.85**	
Appointment with practice nurse		**0.77**	
Fatigue		**0.63**	
Pain in calf		**0.45**	
Cough	0.31	**0.43**	
Memory loss		**0.40**	
Nightmares and terror		0.40	
Satisfaction	0.34	-0.36	
Erection problem		0.35	
Hospital admission			**0.82**
Cold in hands and feet			**0.67**
Slurred speech			**0.54**
Loss of sexual drive			**0.52**
Medication change			
Enquiry with pharmacist			

Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization.
a = Rotation converged in 5 iterations.

The second component may be considered as impact of medication side effects on healthcare service utilization while the third component may relate to side effects to antihypertensive drugs and its impact on hospital admission. It is also visible that two items did not load on any of the components (medication change, and enquiry with pharmacist). The reasons for these are unclear. Further exploration is therefore required to confirm their removal from the questionnaire.

The Pattern Matrix (Table 5.12) showed similarity to the Rotated Component Matrix (Table 5.11) provided in the Varimax rotation solution. The value of a pattern matrix is that it allows grouping of variables into like elements to compare with each other. The factor loadings of each of the items were comparable to the Varimax rotation solution and could be interpreted in the same way. This standardized correlation matrix shows three main clusters of factors, grouping together factors that show common correlations to each other and to other factors. To further examine the Pattern coefficients of the three components extracted, seven out of eleven items on factor 1 possessed high factor loadings (above .40). Factor loadings < 0.40 were suppressed to build a tighter set of fewer variables. Likewise, half of the items loaded strongly on factor 2 while all items on factor 3 yielded negative factor pattern coefficients. It should also be noted that the sign of the loading indicates the direction of the relationship between the factor and the variable.

Overall, 35.6% of the expressed variance was contained in these three components. The results of the Pattern matrix further confirmed the assumption that the two items that did not load on any of the factors should be removed. ("Medication change" and "Enquiry with pharmacist"). The Structure Matrix (Table 5.13) was slightly similar in the sense that eighty percent of all items on factor 1 were strongly loaded, likewise with factor 2 where seven out of nine items possessed factors above 0.40. Half of all items on factor 3 were strongly loaded

Table 5.12 Pattern Matrix (a) of the three extracted components

	Component		
	1	2	3
Loss of interest	**0.74**		
Reduce workload due to fatigue	**0.63**		
Work limitation	**0.62**		
Feel of energy loss	**0.62**		
Day off due to sickness	**0.60**		
Anxious and tense	**0.55**	0.34	
NHS Direct call	**0.50**		
Headache	0.38		
Satisfaction	0.34	-0.34	
Hospital stay	0.30		
Appointment with GP		**0.85**	
Appointment with practice nurse		**0.77**	
Fatigue		**0.64**	
Pain in calf		**0.46**	
Cough	0.32	**0.44**	
Memory loss		0.39	
Nightmares and terror		0.39	
Erection problem		0.35	
Hospital admission			**-0.82**
Cold in hands and feet			**-0.67**
Slurred speech			**-0.54**
Loss of sexual drive			**-0.51**
Medication change			
Enquiry with pharmacist			

Extraction Method: Principal Component Analysis. Rotation Method: Oblimin with Kaiser Normalization.
a Rotation converged in 8 iterations.

What is unique about this analysis is that from the Component Correlation Matrix (Table 5.14), the values generated showed that the correlation between the three components was quite low (-0.08, -0.14 and -0.06), confirming the assumption that the three components were not related (it should be noted that for the components to be strongly correlated, the values would have to be above 0.30).

Table 5.13 Structure Matrix of the extracted three components

	Component		
	1	2	3
Loss of interest	**0.72**		
Work limitation	**0.66**		-0.36
Feel of energy loss	**0.65**		-0.39
Reduce workload due to fatigue	**0.63**		
Day off due to sickness	**0.61**		
Anxious and tense	**0.52**		
NHS Direct call	**0.47**		
Headache	**0.41**		
Hospital stay	0.35		-0.33
Appointment with GP		**0.85**	
Appointment with practice nurse		**0.76**	
Fatigue		**0.63**	
Pain in calf		**0.45**	
Cough		**0.42**	
Memory loss		**0.41**	
Nightmares and terror		**0.41**	-0.31
Satisfaction	0.34	-0.38	
Erection problem		0.35	
Hospital admission			**-0.82**
Cold in hands and feet			**-0.67**
Slurred speech			**-0.54**
Loss of sexual drive			**-0.53**
Medication change			
Enquiry with pharmacist			

Extraction Method: Principal Component Analysis. Rotation Method: Oblimin with Kaiser Normalization.

Table 5.14 Component Correlation Matrix of oblimin rotation for the three components

Component	1	2	3
1	1.00	-0.08	-0.14
2	-0.08	1.00	-0.06
3	-0.14	-0.06	1.00

With regards to this three-factor solution, items from "domain one" of the instrument, for instance, had factor Pattern / Structure coefficients associated equally with Factors 1, 2 and 3. Domain two items Pattern / Structure coefficients were also associated with Factors 1, 2 and 3; whereas domain three items factor Pattern / Structure coefficients were linked with only Factor 1. These results therefore suggested that no clear domain emerged from the factors due to the large number of factor Pattern / Structure coefficients (>0.40) being associated simultaneously with more than one factor. Items which did not load significantly on any factor (i.e. F >0.40) were assessed further using the internal consistency of the extracted factors.

The internal consistency of the extracted factors

After thorough consideration, it was decided to further explore the three factor solutions previously extracted because of strong loadings of items on them. Internal consistency of the extracted factors was also examined. Items "appointment with GP", "fatigue", appointment with practice nurse" and "pain in calf" were strongly associated with factor 1 (Table 5.15).

The statements with low values (less than 0.30) of item-total correlation were considered for deletion from the scale because this may be an indication that the item is measuring something different to the scale as a whole and as such can reduce the value of alpha coefficient. Consequently, it was decided to remove the item "pain in the calf" and to explore its impact on the Cronbach alpha value for this factor. This produced a better cronbach alpha value (0.77) (Table 5.15).

Table 5.15: Item-Total Statistics for factor 1 before items deletion

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Appointment with GP	12.62	1.57	0.71	0.57
Fatigue	11.56	1.57	0.57	0.65
Appointment with practice nurse	12.42	1.88	0.53	0.68
Pain in calf	11.29	2.03	0.34	0.77

The result shown in Table 5.16 demonstrates similarity to factor 1. The values for the corrected item-total correlation suggested that removal of item "hospital stay" was justified due to its low value (0.26). This removal led to increase in the value of Cronbach alpha coefficient from 0.69 to 0.71.

Table 5.16: Item-Total Statistics for factor 2 before item deletion

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Day off due to sickness	18.76	0.51	0.69	0.53
Reduce workload due to fatigue	18.77	0.57	0.50	0.62
Work limitation	18.72	0.71	0.45	0.65
Loss of interest	18.79	0.53	0.43	0.68
Hospital stay	19.71	0.81	0.26	0.71

The reliability scores for factor 3 suggested that seven items with low values (less than 0.30) of corrected items-total correlation should be removed in order to increase the alpha coefficient value of the factor (Table 5.17). However, there was a dramatic reduction in the value of Cronbach alpha from 0.62 to 0.55 following items deletion. This therefore explained a weak to moderate association between factor 3 and its

items. It was therefore decided not to remove any items from this component. The overall cronbach alpha values for the three factors are therefore 0.77, 0.71 and 0.62.

Table 5.17: Item-Total Statistics for factor 3 before item deletion

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Loss of sexual drive	49.65	4.67	0.35	0.58
Cough	50.08	4.88	0.28	0.60
Anxious and tense	49.48	5.06	0.32	0.59
Feel of energy loss	49.69	4.32	0.42	0.56
Hospital admission	50.30	5.55	0.45	0.59
Cold in hands and feet	49.48	4.96	0.31	0.59
NHS Direct call	50.26	5.97	0.20	0.62
Hospital stay	50.28	5.89	0.18	0.61
Memory loss	49.48	5.30	0.19	0.62
Nightmares and terror	49.47	5.22	0.30	0.59
Slurred speech	49.31	5.56	0.28	0.60
Headache	49.30	5.78	0.18	0.61

Correlation between factors

Figure 5.2 shows the final outcome of the exploratory factor analysis of the three factor structures of the SEIP. The relationship between factor 1 and factor 2 was investigated using Spearman's rho – a non parametric correlation technique. The results showed weak association between these two factors (Table 5.18). Similarly, there was a weak correlation between factor 1 and factor 3, and between factors 2 and 3 (Tables 5.19 and 5.20, respectively). However, further exploration of the factor scores indicated that there were strong correlations between an individual factor and items they contained (i.e. within factor correlation). For example, a large correlation was found between "appointments with GP and fatigue" and "appointments with nurse and fatigue" in factor 1. This therefore suggested a strong relationship between them (Table 5.21). There were also strong relationships between factor 2 and its items (Table 5.22) and between factor 3 and its items (Table 5.24).

Table 5.18 Correlations between factor 1 and 2 (n= 160)

Variables	Factor 2			
Factor 1	**Day off due to sickness**	**Reduce workload due to fatigue**	**Work limitation**	**Loss of interest**
Appointment with GP	-0.10	-0.13	-0.14	-0.18*
Fatigue	-0.01	-0.09	-0.09	-0.20*
Appointment with practice nurse	-0.13	-0.15	0.01	0.01

*P<0.05

Table 5.19 Correlations between factor 1 and factor 3 (n= 160)

Variables	Factor 1		
Factor 3	**Fatigue**	**Appointment with GP**	**Appointment with practice nurse**
Anxious and tense	0.09	0.15	0.26*
Feel of energy loss	-0.08	0.05	0.16*
Nightmares and terror	0.16*	0.30**	0.20*
Cold in hands and feet	-0.04	0.05	0.02
Cough	0.16*	0.33**	0.33**
Headache	-0.21**	-0.20*	-0.13
Loss of sexual drive	0.09	0.15	0.13
Slurred speech	-0.05	0.21**	0.22**
Memory loss	0.19*	0.29**	0.25**
Hospital admission	-0.13	0.10	0.08
Hospital stay	-0.05	-0.04	0.02
NHS Direct call	-0.08	0.05	0.09

**P<0.01; *P<0.05

Table 5.20 Correlations between factor 3 and factor 2 (n= 160)

Variables	Factor 3											
Factor 2	**Anxious and tense**	**Feel of energy loss**	**Headache**	**Loss of sexual drive**	**Cold in hands and feet**	**Cough**	**Nightmares and terror**	**Slurred speech**	**Memory loss**	**Hospital admission**	**Hospital stay**	**NHS Direct call**
Loss of interest	0.28**	0.43**	0.28**	0.12	-0.06	0.24**	-0.03	-0.06	-0.07	0.04	0.10	0.27**
Reduce workload due to fatigue	0.09	0.26**	0.30**	-0.08	0.03	0.02	-0.02	-0.05	-0.06	0.05	0.11	0.29**
Day off due to sickness	-0.06	0.23**	0.08	-0.06	-0.03	-0.06	-0.13	-0.05	-0.12	0.07	0.30**	-0.02
Work limitation	0.26**	0.26**	0.36**	0.19*	0.05	0.15	0.02	-0.03	0.13	0.15	0.24**	0.49**

**P<0.01; *P<0.05

Table 5.21 Spearman's rho correlations between factor 1 and its items (n=160)

	Appointment with GP	Fatigue	Appointment with practice nurse
Appointment with GP	1.00		
Fatigue	0.65(**)	1.00	
Appointment with practice nurse	0.65(**)	0.40(**)	1.00

** P<0.01

Table 5.22 Spearman's rho correlations between factor 2 and its items

	Day off due to sickness	Reduce workload due to fatigue	Work limitation	Loss of interest
Day off due to sickness	1.00			
Reduce workload due to fatigue	0.65(**)	1.00		
Work limitation	0.14	0.43(**)	1.00	
Loss of interest	0.43(**)	0.47(**)	0.40(**)	1.00

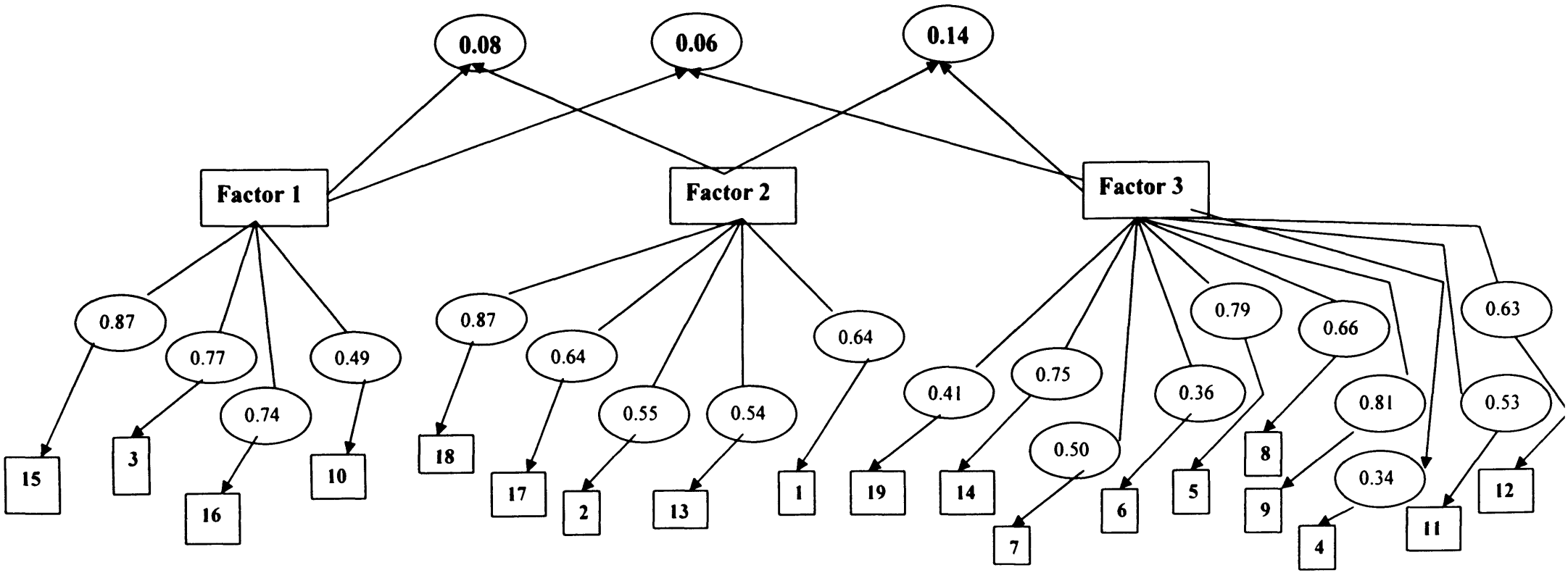
** P<0.01

Table 5.23 Spearman's rho correlations between factor 3 and its items (n= 160)

	Anxious & tense	Feel of Energy loss	Nightmares & terror	Cold in hands & feet	Cough	Headache	Loss of sexual drive	Slurred speech	Memory loss	Hospital admission	Hospital stay	NHS Direct call
Anxious & tense	1.00											
Feel of energy loss	0.37**	1.00										
Nightmares & terror	0.20*	0.08	1.00									
Cold in hands & feet	0.04	0.15	0.14	1.00								
Cough	0.17*	0.24**	0.20*	0.05	1.00							
Headache	0.08	0.17*	0.04	0.09	0.09	1.00						
Loss of sexual drive	0.17*	0.11	0.41**	0.36**	0.14	-0.01	1.00					
Slurred speech	0.07	0.31**	0.17*	0.09	0.09	-0.04	-0.08	1.00				
Memory loss	0.19*	0.09	0.18*	0.23**	0.13	-0.02	0.12	0.09	1.00			
Hospital admission	-0.02	0.20*	0.06	0.31**	0.10	0.09	0.20*	0.41**	0.20*	1.00		
Hospital stay	0.04	0.11	-0.08	0.05	0.10	0.16*	0.08	-0.03	-0.07	0.33**	1.00	
NHS Direct call	0.20*	0.15	0.16	-0.04	0.14	0.37**	-0.06	-0.02	0.16*	-0.02	-0.01	1.00

**P<0.01 *P<0.05

Figure 5.2 Exploratory factor analysis of adjusted three factor structure underlying the SEIP



Note: **14** = NHS Direct number; **3**= Loss of energy; **15**=Appointment with GP; **10**=Pain in calf; **17**=Work schedule & fatigue

16=Appointment with nurse; **2**=Loss of interest; **12**=Hospital admission; **1**=Anxious; **18**=Day off sick; **13**=Hospital stay

7=Headache; **6**=Cough; **5**=Cold hand & feet; **8**=Loss of sexual activity; **9**=Slurred speech; **4**=Nightmares & terror

11=Memory loss; **19**=Work limitation

DISCUSSION

Factor analysis is an appropriate method for scale development when analysing a set of interval-level, non-dichotomous variables. It is a mathematically complex method of reducing a large set of variables to a smaller set of underlying variables referred to as factors (De Vaus, 2002). The basic aim of factor analysis is to examine whether, on the basis of people's answers to questions, a smaller number of more general factors that underlie answers to individual questions can be identified. Using factor analysis in research is therefore aimed at reducing data to make analysis simpler, to be able to identify which variables belong together and to have a method of combining these variables into scales. In this study, two important methods involved in factor analysis were used: factor extraction, and factor rotation.

Suitability of factor analysis

When selecting variables to be factor analysed, De Vaus (2002) suggested that these variables should have at least reasonable correlations with some other variables in the analysis. This author suggested further that at the variable selection stage, a correlation matrix of potential variables should be obtained, inspected and those variables that do not correlate with any others in the analysis should be excluded. In this study, correlation matrix results demonstrated intercorrelations of items within the questionnaire and therefore fulfilling one of the conditions for factor analysis. Tabachnick and Fidell (2001) suggested that the use of factor analysis in psychometric evaluation of a new scale should be reconsidered if there were no correlation coefficient of 0.30 and above in the correlation matrix. In this case, many of the values generated were above 0.30 and therefore it was considered appropriate to use factor analysis in establishing the robustness of the new measure.

There are other ways of assessing whether a set of variables in a correlation matrix is suitable for factor analysis (Tabachnick and Fidell, 2001). Among these is a statistic called Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy. This statistic has been well documented in chapter two of this thesis. The value of KMO ranges from 0 to 1. If this statistic yields high values above 0.70, then the correlations, on the whole, are sufficiently high to make factor analysis suitable. On the other hand, the KMO values below 0.50 mean that factor analysis would be inappropriate for that set of

variables. KMO value in this study was 0.82, therefore confirming the suitability of factor analysis in this study.

Initial factor extraction

The main aim of exploratory factor analysis is to see whether a smaller number of common factors can account for the pattern of correlation between a large numbers of variables. The question that comes to the mind of a researcher is: do the individual variables co-vary because they have underlying factors in common? De Vaus (2002) suggested that before extracting factors, it is advisable to work out how many factors to extract. Since the aim of factor analysis is to represent a set of variables as simply as possible, the best factor analysis will have as few factors as necessary (De Vaus, 2002). One common way of determining which factors to keep is to use a statistic called Principal Component Analysis (PCA) and Eigenvalue. The eigenvalue is a measure that attaches to factors and indicates the amount of variance in the pool of original variables that the factor explains. The higher this value, the more variance the factor explains (De Vaus, 2002). To be retained, factors must have an eigenvalue greater than 1. Generally in factor extraction, "eigenvalue greater than 1" criteria is the most commonly used extraction technique (Henson and Roberts, 2006) and therefore it was decided to engage this method in this study.

The use of Principal Component Analysis (PCA) in factor extraction in this study revealed nine components with eigenvalues > 1. The eigenvalue of a factor is the amount of variance in all the variables that is explained by that factor. This figure is obtained by squaring the correlations in the factor matrix and then adding each of these squared figures in the column. Sometimes a large number of factors with eigenvalues greater than 1 may be generated, but for the sake of simplicity, not all the factors may be retained. How do we decide which of the factors with eigenvalues greater than 1 to retain? Considering suggestions of Reio and wiswell (2006) that eigenvalue > 1 criteria sometimes overestimate the number of factors to be retained especially when the number of variables being examined exceeds 30, two ways as described in chapter two are to perform a scree test and a parallel analysis. Scree test results in this study suggested that six out of the nine extracted components would be suitable to keep for factor rotation in order to ensure their easy interpretations. Parallel

analysis results also showed that the initial decision to consider these six extracted factors for further exploration was appropriate.

Extracting the final factors (factor rotation)

Rotation of factors is performed to clarify which variables most 'belong' to each other once the decision on how many factors to retain has been made in order to make the factors more interpretable. The initial extraction of factors did not make it clear which variables belong most clearly to which factors as many variables loaded on several factors and some factors had almost every variable loading on them. There are a number of methods of "rotating" variables; these have been described extensively in chapter two. One of the most widely used methods of rotation is varimax rotation. Although, opinion varies on how high a coefficient should be before a variable is said to load on a factor, De Vaus (2002) suggested that it would be unusual to use variables with coefficients below 0.30.

Varimax rotation results of the six-factor solution revealed strong loadings especially on factors 1 to 5. Basically if, in data analysis, there is no possibility to assume the independence of the underlying factors, the use of Oblique rotation is suggested (Tabachnick and Fidell, 2001). For example direct oblimin method. This study however, showed that direct oblimin rotational method of the six factors could not confirm that the six factors were not related. On the other hand, three factor solutions were considered for exploration and these yielded high loadings and the results of the component correlation matrix of the three factors using oblimin rotation revealed very low correlation between them.

Further psychometric evaluation of SEIP through the examination of internal consistency showed the independence of the three–factor solutions with strong relationships ($r \geq 0.40$) between individual items and their respective domains. The reliability coefficients tests of the extracted factors both before and after item deletions showed varying Cronbach alpha values. It was therefore decided to consider factors with higher Cronbach alpha coefficients. Low correlation coefficients between factor 1 and factor 2 and between factor 1 and factor 3 showed that the two factors were measuring a distantly–related concept and therefore independent of one another.

On the other hand, there were some high correlations of items between factor 2 and 3, the reason may lie in the fact that these items were measuring similar concepts. For example, items "anxious and tense" in factor 3 and "loss of interest" in factor 2 with correlation coefficient of 0.28. Despite this, majority of items in both factors showed lower correlation values, therefore indicating their degree of independence. In addition to these, majority of items in all the three factors showed high correlations within their domains. This outcome therefore provided enhanced confidence in the psychometric properties of SEIP.

Factor analysis of SEIP therefore produced three underlying components representing: 1) the impacts of statins on healthcare services use; 2) emotional distress and impacts on productivity; and 3) socio-emotional symptoms and use of healthcare services. The factor rotation results suggested the removal of two items from the questionnaire: "medication change" and "enquiry with pharmacist". This was quite surprising especially when taking into consideration that most of patients with medication-related problems consider pharmacists as their first place to seek advice about their medication use and side effects to them. One explanation for this could be because of lack of time for consultation and counselling as many pharmacists in the UK are now involved with enhanced services in order to increase their earnings.

As with other studies, there are limitations to this study. For example, the sample size used which could be considered as borderline for factor analysis (n = 160) may have affected the results produced. In order to achieve high loading marker variables such as 0.80 and above, many researchers suggested that the sample size should be 300 or more (Gorsuch, 1983; Tabachnick and Fidell, 2001; Hogarty et al., 2005).

Overall, the results of factor analysis have provided support for the psychometric properties of the SEIP as a promising socioeconomic related tool especially in cardiovascular patients with medication-related problems. The results also suggested the reduction of the 24–items questionnaire to 19 (this include item "enquiry with pharmacist"). The final version of SEIP therefore consists of 19 items with three domains (Figure 5.3).

Future work should focus on: 1) its test – retest reliability; 2) demonstrate criterion, convergent / divergent validity with other available instruments; 3) its applicability and responsiveness.

Summary

- The factor analysis of SEIP was carried out on a sample of 160 cardiovascular patients from five community pharmacies in England and Wales.
- Principal component analysis suggested consideration of nine factors for factor extractions;
- Three statistical rules: eigenvalue > 1, scree test and parallel analysis suggested six factors should be considered for factor rotation for easy interpretations;
- Rotation of six factors (varimax and oblimin methods) produced three-factor solutions with many high loading items (>0.40);
- Internal consistency reliability tests of the three factor solutions produced Cronbach alpha values of 0.74, 0.71 and 0.62 respectively therefore supporting psychometric property of SEIP;
- Spearman rho correlation coefficient results indicated low relationships between factor 1 and factor 2, factor 1 and 3 but low- moderate relationships between factor 2 and 3; however, high correlation values were indicated among items within each of the three domains, therefore supporting the notion that each factor measures similar concept and are independent of one another.

Figure 5.3 -

Final version of the Socioeconomic Impact Profile (SEIP

Confidential

To be completed on.....

Patient Identification number.....

Socio-Economic Impact Profile (SEIP)

INSTRUCTIONS

This survey asks for your views about your medications and any side effects that you may experience and in what ways are these side effects affecting your quality of life in general.

The information you provide will help your pharmacist keep track of how you feel and how well they can help to minimise the impact of medication side effects on your life, hence improve the quality of care they offer you. All responses will be treated ***in the strictest confidence.***

Answer every question by ticking the appropriate box, if you are unsure about how to answer a question, please give the best answer you can and feel free to make comments as you wish.

About Yourself

Age..... ☐ **Years.....Sex...**☐ Male.....☐ Female

What is your medical condition?.....Duration: Year..... Months.....

Education..... ☐ None ☐ Primary school ☐ High school ☐ University degree

Marital Status...☐ Single ☐ Divorced ☐ Married ☐ Widowed ☐ Living with a partner

Employment Status....☐ Employed...☐ Unemployed. **➔Due to your health?** ☐Yes ☐ No
☐ Self-employed
☐ Retired **➔ is this due to your health?** ☐Yes ☐ No
☐ Receive Income Support Benefit
☐ Receive other social support, please state.

What is your annual income...☐ Less than £10,000?
☐ More than £10,000 but less than £20,000
☐ More than £20,000 but less than £30,000
☐ More than £30,000 but less than 40,000
☐ More than £40,000

About your medication: Do you take any prescription medicine(s) regularly?
☐Yes ☐ No.

If yes, what are the medicines you are taking for?.....

A Social interaction and emotional behaviour

*The following statements are about side effects you might experience if you take some medicines for **blood pressure, high blood cholesterol** and **heart**. If so, tick the appropriate box below.*

How often have you experienced any of the following problems? **Do you think it is due to a side effect of your medicine?**

						Do you think it is due to a side effect of your medicine?		
	Never	**A little of the time**	**Some of the time**	**Most of the time**	**All of the time**	**Yes**	**No**	**Not sure**
	5	4	3	2	1			
1. I have felt anxious and tense inside for no obvious reason...	☐	☐	☐	☐	☐	☐	☐	☐
2. I have lost interest in things I usually enjoy.....	☐	☐	☐	☐	☐	☐	☐	☐
3. I have felt like all of the energy drained out of me.....	☐	☐	☐	☐	☐	☐	☐	☐
4. I have had horrible nightmares and night terrors..	☐	☐	☐	☐	☐	☐	☐	☐
5. I have felt unpleasantly cold in my hands and feet.....	☐	☐	☐	☐	☐	☐	☐	☐
6. I have had a troublesome cough that won't go away.....	☐	☐	☐	☐	☐	☐	☐	☐
7. I have had a constant headache after my medicine..	☐	☐	☐	☐	☐	☐	☐	☐
8. I have lost interest in sexual activity.....	☐	☐	☐	☐	☐	☐	☐	☐
9. My speech is slurred.....	☐	☐	☐	☐	☐	☐	☐	☐
10. I have severe pain in my calf I could hardly walk.....	☐	☐	☐	☐	☐	☐	☐	☐
11. I have no memory of events or things I did on the previous day.....	☐	☐	☐	☐	☐	☐	☐	☐

B Use of health services

*How often have you **made use** of any of the following services as a result **of side effect of your medication?***

	Never	Seldom	Frequently	More frequently
	4	3	2	1
12. I have been admitted to hospital.....	☐	☐	☐	☐
13. I have stayed in hospital for some days.....	☐	☐	☐	☐
14. I was so worried about the side effect I suffered after taking my medicine that I had to call the NHS Direct number for advice.....	☐	☐	☐	☐
15. I was so worried about the side effect I suffered after taking my medicine that I had to make an urgent appointment with my local general practitioner (GP).....	☐	☐	☐	☐
16. I was so worried about the side effect I suffered after taking my medicine that I had to make an urgent appointment with the practice nurse in my local surgery.....	☐	☐	☐	☐

C Work

The following questions are about how much your working life has been affected ***as a result of medication side effects.***

	No, not at all	**Seldom**	**Sometimes**	**A little**	**A lot**
	5	4	3	2	1
17. I have cut down my work schedule because of fatigue.....	☐	☐	☐	☐	☐
18. I have taken some days off sick.....	☐	☐	☐	☐	☐
19. I am limited in the kind of work I can do.....	☐	☐	☐	☐	☐

Date: **thank you for your time and help.**

CHAPTER 6

Evaluation of Practicality and Reliability of the Socioeconomic Impact Profile (SEIP)

INTRODUCTION

In the development of new measures such as the SEIP, testing of their applicability and practicality in the target population is of paramount importance. Similarly, establishment of the degree of measurement error (reliability) of the new measure is of equal importance. Reliability is the extent to which a test is repeatable and yields consistent scores. In the context of this research, measures of reliability are considered as an indication of what extent an instrument truly captures the attributes of health status rather than an existing measurement. However, according to some authors, the size of random measurement error should be taken into consideration while assessing the reliability of the new measure (Walker, 2002). All measurement procedures have the potential for error, so the aim is to minimise it. In general, an observed test score is made up of the true score plus measurement error. The goal of estimating reliability is therefore to determine how much of the variability in test scores is due to measurement error and how much is due to variability in true scores (http://wilderdom.com, 2004).

What is acceptable reliability for a measurement instrument?

A measure is judged to be reliable when it consistently produces the same results, particularly when applied to the same subjects at different time periods when there is no evidence of change (Bowling, 2005b). A reliability score (coefficient) of one indicates that no measurement error is present (McHorney et al., 1994). The following reliability coefficients have been published as guidelines in determining reliability (http://wilderdom.com, 2004):

0.90 = high reliability
0.80 = moderate reliability
0.70 = low reliability.

High reliability is required when: 1) tests are used to make important decisions; 2) individuals are sorted into many different categories based upon relatively small individual differences. On the other hand, lower reliability is acceptable when: 1) tests are used for preliminary rather than final decisions; 2) tests are used to sort people into small number of groups based on gross individual differences. Reliability

estimates of 0.80 or higher are typically regarded as moderate to high. Reliability estimates below 0.60 are usually regarded as unacceptably low. According to McHorney et al (1994), a reliability coefficient of 0.70 implies that 30% of the score for health status is made up of measurement error.

Types of reliability

There are a number of ways to ensure that a newly developed measure is reliable. The different modes of assessing reliability of the instrument have been described extensively in chapter two of this study. However in this chapter, two of these tests will be revisited: 1) test-retest reliability and; 2) internal consistency reliability.

Test-retest reliability

Test-retest reliability measures the stability of a score derived from serial administration of a measure by the same rater (Kulich et al, 2008). This type of reliability test is estimated when the same test is administered to the same sample on two different occasions (usually referred to as test 1 and test 2). This approach assumes that there is no substantial change in the construct being measured between the two occasions. However, the amount of time allowed between tests 1 and 2 is critical. For example, if the same thing is measured twice, the correlation between the two observations will depend partly on how much time elapses between the two measurement occasions. The shorter the time interval between T1 & T2, the higher the correlation; the longer the interval, the lower the correlation.

Internal consistency reliability

This is the most frequently used statistical test for assessing reliability of an instrument. This is normally established through a single administration of the instrument to a sample from the intended population. In effect, the reliability of the instrument is judged by estimating how well the items that reflect the same construct yield similar results. This method also looks at how consistent the results are for different items for the same construct within the measure. There are a wide variety of internal consistency tests that can be used for measurement instruments. These will be described below.

Average Inter-Item Correlation

The average inter-item correlation uses all of the items on an instrument that are designed to measure the same construct. It indicates the extent to which the items in a scale are inter-related and that the items in each subscale seem to be measuring the same dimension (McHorney et al., 1994). For example, in a computation of correlation between each pair of items in a six item instrument, 15 different item pairings can be generated (i.e. 15 correlations) (Table 6.1). The average inter-item correlation is simply the average or mean of all these correlations.

Table 6.1 An example of an Average Inter-Item Correlation of a 6-item measure

Measure items	**Average Inter-Item Correlation**						
		I_1	I_2	I_3	I_4	I_5	I_6
Item 1	I_1	1.00					
Item 2	I_2	0.89	1.00				
Item 3	I_3	0.91	0.92	1.00			
Item 4	I_4	0.88	0.93	0.95	1.00		
Item 5	I_5	0.84	0.86	0.92	0.85	1.00	
Item 6	I_6	0.88	0.91	0.95	0.87	0.85	1.00

Average Item-Total Correlation

This approach also uses the inter-item correlation. In addition to the example in Table 6.1, a total score for the six items is computed and that is used as a seventh variable in the analysis. These figures give an indication of the degree to which each item correlates with the total score. Low values (less than 0.30) indicate that the item is measuring something different to the scale as a whole (Pallant, 2002)

Cronbach's Alpha

Internal consistency commonly measured as Cronbach's Alpha (based on inter-item correlations) is often described as being mathematically equivalent to the average of all possible split-half estimates (Pallant, 2002). The greater the number of similar items are, the greater the internal consistency and hence, the higher the Cronbach's value. Generally, alpha of 0.80 is considered as a reasonable benchmark. As Pallant (2002) noted, in order to be valid, a test must be reliable; but reliability does not guarantee validity. In this chapter, it is hoped to establish practicality, test-retest and internal consistency reliability of the SEIP.

The concepts examined were:

- The completion time of the SEIP should not be more than 10 minutes;
- The questions and instructions should be clear, easy to understand and comprehensive enough to the respondents;
- The SEIP should not be difficult, unsuitable or distressing to complete for patients and be able to respond to the items with a reasonable degree of spontaneity.
- The SEIP should demonstrate high internal consistency and high test-retest reliability values.

METHODS

Study design and selection of patients

This was a prospective study to examine the practicality and reliability properties of the SEIP. Patients were recruited in 2007 over a 3 month period (March-June). Patients suffering from three cardiovascular disease states (hypertension, myocardial infarction and angina pectoris) were recruited from five community pharmacies in South West England and Wales. Those patients who met the following inclusion criteria were enrolled in the study: community managed cardiovascular patient from one of the above-mentioned patient groups; receiving three or more repeat prescriptions from the participating pharmacies for at least three months prior to the study; and be able to complete the questionnaire.

Study procedure

Practicality of the SEIP

A newly developed measure is expected to have the right emphasis for the purpose being developed and should be acceptable to the target population. For these reasons, it was decided to seek patients' views, perceptions and comments about the SEIP questionnaire. Patients on repeat prescriptions were approached by the research pharmacist while waiting to collect their repeat medications from the participating pharmacies. These patients were invited to participate in the study and the protocol of the research study was explained to them in order to seek their consent. Patients who agreed to take part were given a pre-paid envelope containing a yellow form with six practicality questions (see Appendix 7); two SEIP questionnaires for the test-retest reliability study and a Patient Information Sheet. They were advised to complete the first SEIP questionnaire on the day of recruitments and the second SEIP questionnaire seven days apart. They were also advised to fill in the details on the yellow form and make any additional comments that they wished in the space provided on the sheet. Patients were asked to return the completed questionnaires and the yellow form in the pre-paid envelope provided. Finally, they were thanked for their co-operation and participation.

Test-retest reliability of the SEIP

Patients for this study were the same group of patients recruited for the practicality study as outlined above. During their recruitment, emphasis was placed on the need to complete the first SEIP questionnaire (Test 1) on the day of recruitment and the second questionnaire (Test 2) seven days after the first questionnaire. All SEIP item scores were tested together and each domain of the SEIP was also assessed separately for its internal consistency reliability.

Data Processing and Analysis

Statistical analyses were performed with SPSS 12 for Windows. Descriptive statistics were used to present demographic characteristics of the study participants as well as most of the results for the practicality study. The internal consistency reliability of the SEIP and its sub domains were determined by calculation of Cronbach's alpha (α). In order to determine whether the mean scores of items measured on the two occasions

of the test-retest reliability were statistically significant, non-parametric Wilcoxon Signed Rank Test was engaged. Spearman rank correlation coefficient was employed to examine the relationship between Test 1 and Test 2. The probability of committing type 1 error was set at $p<0.05$.

RESULTS

Demographic characteristics of the study participants

A total of 150 patients were administered the SEIP and the yellow form with practicality questions. Ninety-three (62.0%) patients returned the questionnaires in pre-paid envelopes provided of which 92 pairs of the SEIP were evaluable for test-retest reliability analysis. One patient was excluded because her returned SEIP questionnaires were incomplete. A follow up contact was made by the research pharmacist to those who did not return the questionnaires through the participating pharmacies.

Table 6.2 shows the demographic characteristics of the study participants of whom fifty (54.3%) were male. The age of participants ranged from 39 to 78 years with a mean age of 57.7 years. Sixty-three patients (67.7%) were married, 46 (48.9%) had a high school education, 37 (40.2%) had a university degree and 10 (10.9%) had a primary education. Sixty-five (69.9%) were employed and over one-third of the participants earned between £10,000 and £20,000 annually. Fifty-nine (63.4%) were hypertensive while 23 (24.7) suffered from another concomitant medical condition. These included diabetes (typel or type II), asthma, COPD, arthritis and depression.

Practicality of the SEIP

The mean time taken to complete the SEIP was 5.7 minutes (SD=2.8). Twenty-eight (30.4%) patients completed the SEIP in 5 minutes, 26 (28.3%) patients in 3 minutes and 18 (19.6%) in 10 minutes. It took 1 (1.1%) patient about 15 minutes to complete it (Table 6.3).

Table 6.2 Sociodemographic characteristics of the study participants (n=92)

Variables	Number (%)
Sex	
Male	50 (54.3)
Female	42 (45.6)
Age	
Range	39-78
Median	57.0
Mean	57.7
Medical condition	
Hypertension	59 (64.1)
High cholesterol	2 (2.2)
Angina	2 (2.2)
Heart attack	6 (6.5)
Hypertension and others	23 (25)
Education	
Primary school	10 (10.9)
High school	45 (48.9)
University degree	37 (40.2)
Marital status	
Single	14 (15.1)
Married	63 (67.7)
Divorced	6 (6.5)
Widowed	9 (9.7)
Employment status	
Employed	65 (69.9)
Retired due to health	2 (2.2)
Retired not due to health	21 (22.6)
Self employed	4 (4.3)
Annual income	
E < £10000	19 (20.7)
£10000 <E<£20000	32 (34.8)
£20000 < E <£30000	8 (8.7)
£30000 < E < £40000	23 (25)
E > £40000	10 (10.8)

Table 6.3 Time taken by the participants to complete the SEIP (n=92)

Time (in minutes)	No of participants
2	3 (3.3)
3	26 (28.3)
4	1 (1.1)
5	28 (30.4)
6	9 (9.8)
7	5 (5.4)
8	1 (1.1)
10	18 (19.6)
15	1 (1.1)

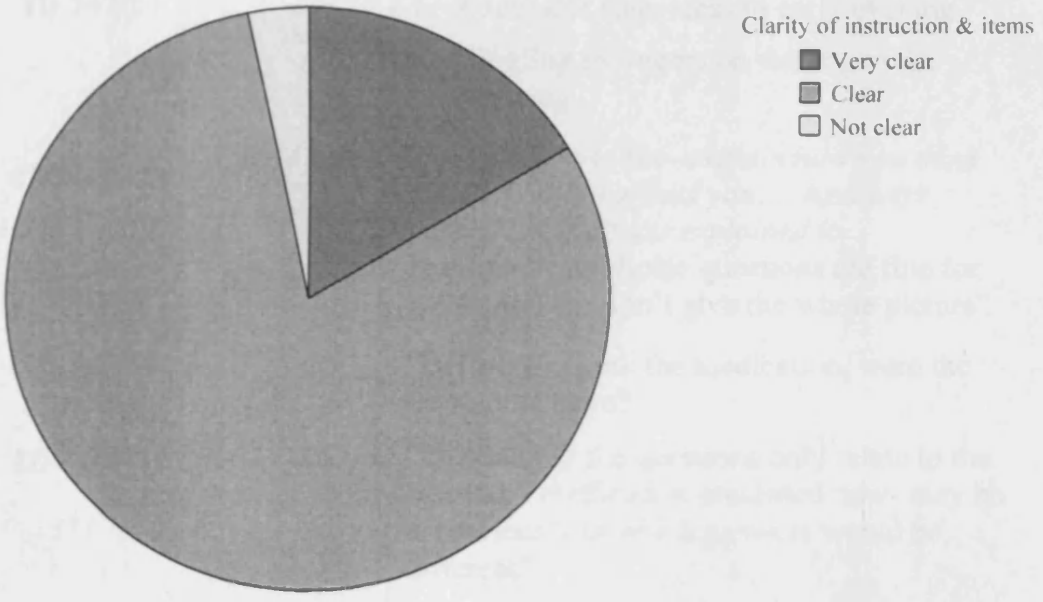
When patients were asked whether the instructions to the questions were clear and understandable, 15 (16.3%, n=92) patients agreed that the questions and instructions were "very clear", 74 (80.4 %,) agreed they were "clear", and 3 (3.2 %,) reported that they were "not clear". Only one patient did not respond to this part of the questionnaire (Figure 6.1).

When they were asked whether the SEIP items were comprehensive enough to measure their social and economic well-being including quality of life, the majority of patients, (73{78.5%}) responded positively. In contrast, 20 (21.5%) patients disagreed with the statement. Those who chose the "No" response option were asked to state any additional questions they would like to be included about the effects of their medications on the quality of life. Table 6.4 lists some suggestions and comments by these participants.

Almost all the patients agreed that hardly any of the questions in the SEIP were unsuitable, difficult or distressing to answer (89 {96.7%} patients). Only 3 (3.3%) patients agreed otherwise. One patient considered the item asking about "annual income" as inappropriate because of its personal nature. Another patient wished the

phrase "do you think" in one of the column in the social interaction and emotional behaviour domain of the SEIP (asking whether respondents think the problems they were experiencing was due to a side effect of their medications) to be changed to "I believe".

Figure 6.1 Patients' perception of clarity of the SEIP items



Test-retest reliability

The reliability of the 19-item SEIP was estimated using the internal consistency while the level of agreement between Test 1 (T1) and retest (T2) was determined using the Wilcoxon Signed Rank test. Overall, the items mean score for each SEIP domain showed that they were not normally distributed. All domains showed negative skewness values indicating that scores were clustered to the right at the high end (Figures 6.2, 6.3 & 6.4). The SEIP item mean scores were high for all categories (Table 6.5).The magnitude of correlation between T1 and T2 would depend on the closeness of the two mean scores of each category. Therefore, if the gap between the two mean scores in test-retest was wider, this would reflect on the correlation coefficient (rho).

Table 6.4 Comments and suggestions from patients who responded "NO" to question3 of the practicality exercise (n=20)

Q3: *Do you think the questions asked are comprehensive enough to measure your social and economic well-being including quality of life?*

Selected samples of "No" respondents	Comments and suggestions of questions to be included
ID 747/29	1. Excessive sleepiness in early evening 2. Tingling in fingers on waking in the morning
ID 6439/14	"I would like to see- *explain how you think the medication affects you....* And *were possible side effects explained to you*...multiple choice questions are fine for symptoms but don't give the whole picture"
ID 747/31	"Before you took the medication, were the symptoms there?
ID 6439/22	"Presumably the questions only relate to the particular medication presented now- may be if previously to which answers would be different"
ID 6547/64	1. Do you regularly swim/walk/other exercise? 2. Do you read books/daily newspaper/do crossword etc daily? 3. Do you engage in any social activity outside your home e.g. dancing, sport, craft, art etc? 4. Do you tend your own garden/home decorating? 5. Do you worry about paying bills? 6. Do you run a car and what is your annual mileage under? 7. Do you go on holiday once, twice, thrice or more times per year?

In this study, the low test-retest correlation coefficients (r_s=0.39 and 0.22) for the two SEIP items (i.e. "slurred speech" and "NHS Direct Number call" respectively) could be explained by the wideness of their T1 and T2 mean scores.

Figure 6.2 Distribution characteristics of "social interaction & emotional behaviors" domain scores for T1

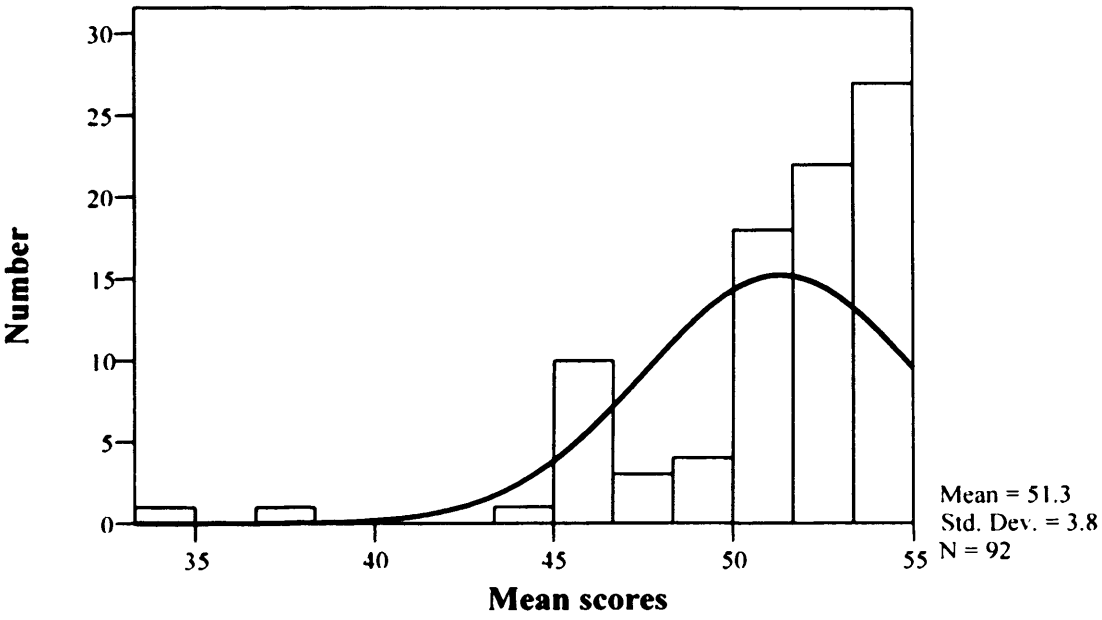


Figure 6.3 Distribution characteristic of "use of healthcare services" domain for T1

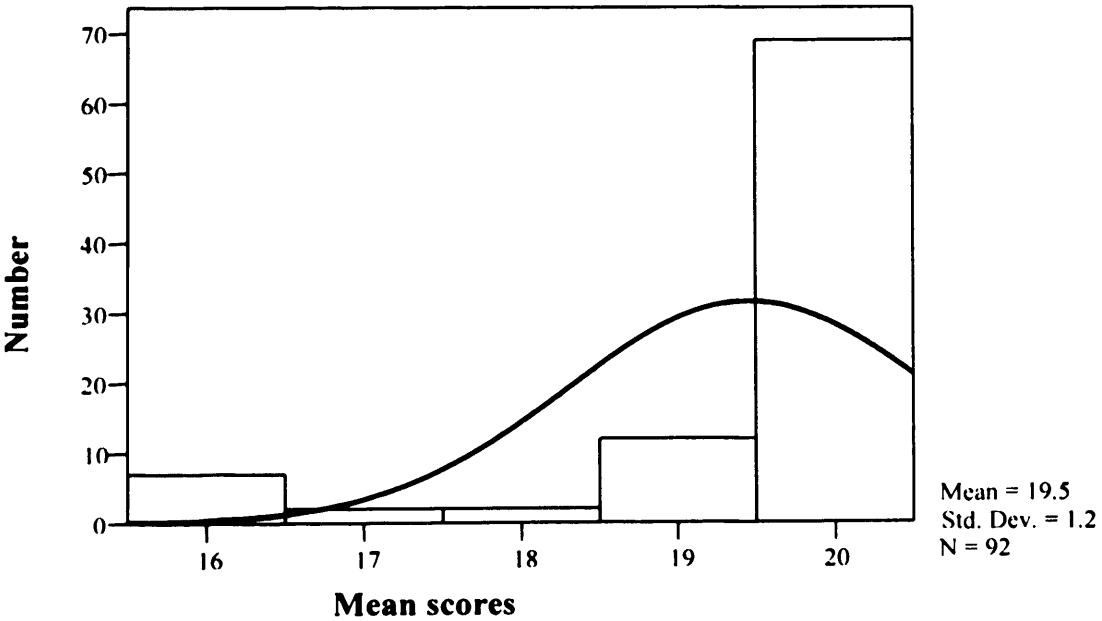
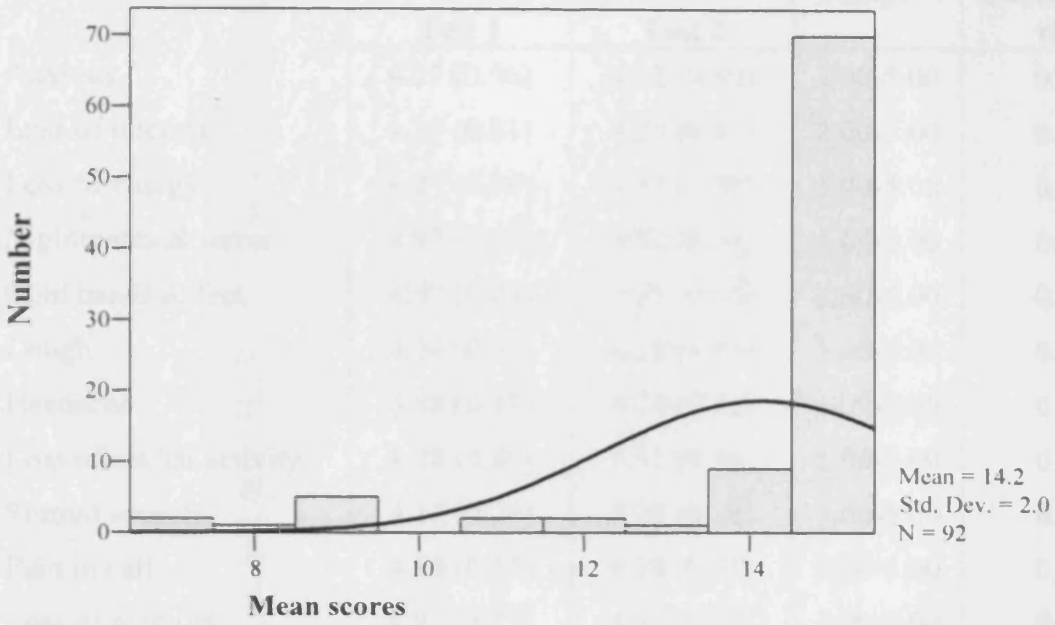


Figure 6.4 Distribution characteristic of "work" domain scores for T1



Based on this result, it was decided to use the non-parametric Wilcoxon Signed Rank test to confirm any significant difference between the SEIP scores of T1 and T2. Results of The Wilcoxon Signed Rank Test showed that there was a significant differences ($P<0.05$) in the SEIP category scores between T1 and T2 (Table 6.6). This significant trend is indicated by the negative direction of the scores probably due to the lower mean SEIP scores of variables at Test 2.

Table 6.5 Correlations between T1 & T2 mean SEIP scores (test-retest reliability of the SEIP) (n=92)

SEIP items	Mean scores (SD)		Score Range*	Spearman's Correlation rho
	Test 1	Test 2		
Anxious	4.25 (0.96)	4.12 (0.89)	1.00-5.00	0.85
Loss of interest	4.37 (0.81)	4.28 (0.83)	1.00-5.00	0.87
Loss of energy	4.27 (0.94)	4.13 (0.93)	1.00-5.00	0.82
Nightmares & terror	4.93 (0.25)	4.82 (0.38)	1.00-5.00	0.90
Cold hands & feet	4.37 (0.79)	4.25 (0.80)	1.00-5.00	0.89
Cough	4.34 (0.91)	4.32 (0.89)	1.00-5.00	0.96
Headache	4.88 (0.47)	4.74 (0.57)	1.00-5.00	0.82
Loss of sexual activity	4.28 (0.89)	4.35 (0.84)	1.00-5.00	0.94
Slurred speech	4.17 (0.24)	3.26 (0.38)	1.00-5.00	**0.39**
Pain in calf	4.86 (0.55)	4.78 (0.51)	1.00-5.00	0.92
Loss of memory	4.91 (0.33)	4.84 (0.43)	1.00-5.00	0.94
Hospital admission	3.89 (0.35)	3.79 (0.44)	1.00-4.00	0.90
Hospital stay	3.89 (0.35)	3.79 (0.44)	1.00-4.00	0.90
NHS Direct Number call	3.99 (0.11)	3.02 (0.38)	1.00-4.00	**0.22**
Appointment with GP	3.86 (0.35)	3.77 (0.42)	1.00-4.00	0.95
Appointment with nurse	3.83 (0.38)	3.79 (0.41)	1.00-4.00	0.97
Work schedule & fatigue	4.63 (0.81)	4.48 (0.90)	1.00-5.00	0.77
Day off sick	4.83 (0.53)	4.68 (0.65)	1.00-5.00	0.77
Work limitation	4.70 (0.89)	4.53 (0.98)	1.00-5.00	0.73

*1 = the lowest possible score and 4 or 5 = the highest possible score

Table 6.6 Test-retest reliability- Comparison* of Test1 and Test 2 (N=92)

	Social interaction & emotional behaviours domain total scores at Test 2 – Test 1	Use of healthcare services domain total scores at Test 2 – Test 1	Work domain total scores at Test 2 – Test 1
Z	-2.33(a)	-2.91(a)	-3.30(a)
Asymp. Sig. (2-tailed)	0.02	0.004	0.001

a Based on positive ranks. * Wilcoxon Signed Ranks Test

Internal Consistency Reliability

The internal consistency reliability as determined by Cronbach's α of the whole 19-item SEIP domains was high for both Test 1 and Test 2. The alpha values ranged between 0.77-0.95 (Table 6.7). The overall internal consistency reliability at T1 and T2 yielded a very high value of Cronbach's alpha coefficient (α=0.91and 0.93 respectively). The Alpha coefficient value of greater than 0.70, supports strong internal consistency reliability of the SEIP.

Table 6.7 Internal consistency reliability of SEIP for Test 1 and Test 2 (n=92)

SEIP domains	Cronbach's α coefficient	
	Test 1	Test 2
Overall SEIP score	0.91	0.93
Social interaction & emotional behaviours	0.87	0.88
Use of healthcare services	0.77	0.95
Work	0.84	0.89

Test 1

The information of interest is the column marked Corrected Item-Total Correlation (Table 6.8), indicating the degree to which each item correlated with the SEIP total score. Generally, low values (< 0.30) indicate that the item is measuring something different to the scale as a whole. Some authors have suggested that if the overall Cronbach's alpha of a scale is less than 0.70, one should consider removing items with low Item-Total-Correlations (Pallant, 2002). In the column headed Cronbach's alpha If Item Deleted, the impact of removing each item from the scale is given. Furthermore, it has been suggested to consider removing any item with higher alpha value than the overall alpha value from the scale (Pallant, 2002). In this study, the Corrected-Item-Total correlations of all 19 items in the SEIP ranged from 0.28 to 0.84. Only question 11 (loss of memory) had a Corrected Item-Total-Correlation value less than 0.30. However, based on Pallant's suggestion, the deletion of this item (loss of memory) did not increase the Cronbach's value (Table 6.8). Thus, it was decided not to remove this question from the SEIP.

Table 6.8 Item correlations of overall SEIP domains with total scores for Test 1

SEIP domains & corresponding items	SEIP Mean if Item Deleted	SEIP Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Social interaction & emotional behaviours				
Anxious	79.79	51.02	0.46	0.91
Loss of interest	79.67	48.75	0.78	0.90
Loss of energy	79.77	47.48	0.76	0.90
Nightmares & terror	79.11	55.57	0.69	0.91
Cold hands & feet	79.67	51.96	0.50	0.91
Cough	79.71	48.39	0.71	0.90
Headache	79.16	52.56	0.80	0.90
Loss of sexual activity	79.76	47.28	0.69	0.91
Slurred speech	79.08	56.97	0.33	0.91
Pain in calf	79.18	51.54	0.81	0.90
Loss of memory	79.13	56.71	**0.28**	0.91
Use of healthcare services				
Hospital admission	80.15	54.42	0.71	0.91
Hospital stay	80.15	54.42	0.71	0.91
NHS Direct Number	80.05	57.63	0.33	0.91
Appointment with GP	80.18	55.43	0.50	0.91
Appointment with nurse	80.22	56.02	0.35	0.91
Work				
Work schedule & fatigue	79.41	50.09	0.65	0.91
Day off sick	79.22	51.58	0.84	0.90
Work limitation	79.35	49.07	0.67	0.91

The social interaction & emotional behaviours domain, with 11 questions such as "loss of interest, nightmares and night terrors" etc, also indicated a good internal consistency with a Cronbach alpha coefficient of 0.87 (Table 6.7). The mean scores ranged between 4.25-4.97 (Table 6.9) while the inter-item correlations ranged from

average (0.30) to excellent at (0.80) (Table 6.10). It was decided not to remove the weaker item in the social interaction& emotional behaviours domain (loss of memory; Corrected Item-Total Correlation=0.30) from the domain as this would have minimal impact on the alpha value. In addition to this, the mean score could be interpreted as showing homogeneity of the items as most of the responses to the questions were similar.

Table 6.9 Social interaction & emotional behaviour domain mean scores for Test 1 (n=92)

	Mean	Std. Deviation
Anxious	4.25	0.96
Loss of interest	4.37	0.81
Loss of energy	4.27	0.94
Nightmares & terror	4.93	0.25
Cold hands & feet	4.37	0.79
Cough	4.34	0.91
Headache	4.88	0.47
Loss of sexual activity	4.28	0.89
Slurred speech	4.97	0.24
Pain in calf	4.86	0.55
Loss of memory	4.91	0.33

The use of healthcare services domain mean scores showed similar trend to the social interaction & emotional behaviours domain, as most responses from the participants were similar. The mean scores ranged between 3.83-3.99 (Table 6.11). The initial Cronbach alpha value was 0.77 and the Corrected-Item-Total correlations also ranged between poor (0.14) to a very good 0.79 (Table 6.12). However, due to the low value of Corrected-Item-Total Correlation of Item 14 of the SEIP (NHS direct number), it was suggested to remove this item from the scale. Interestingly, the Cronbach alpha coefficient of the four remaining components of the use of healthcare services domain improved considerably to 0.82 (Table 6.12).

Table 6.10 Social interaction & emotional behaviours domain item correlations with the total scores for Test 1

Domain 1 items	SEIP Mean if Item Deleted	SEIP Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Anxious	46.18	21.58	0.56	0.87
Loss of interest	46.07	21.18	0.76	0.85
Loss of energy	46.16	19.89	0.80	0.84
Nightmares & terror	45.50	25.81	0.64	0.87
Cold hands & feet	46.07	22.81	0.55	0.86
Cough	46.10	21.67	0.59	0.86
Headache	45.55	23.94	0.73	0.86
Loss of sexual activity	46.15	19.80	0.72	0.85
Slurred speech	45.47	26.58	0.35	0.88
Pain in calf	45.58	23.30	0.74	0.86
Loss of memory	45.52	26.41	0.30	0.87

Table 6.11 Use of healthcare services domain mean scores for Test 1 (n=92)

Domain 2 items	Mean	Std. Deviation
Hospital admission	3.89	0.35
Hospital stay	3.89	0.35
NHS Direct Number	3.99	0.10
Appointment with GP	3.86	0.35
Appointment with nurse	3.83	0.38

Table 6.12 Use of healthcare services domain item correlations with the total scores for Test 1 (n=92)

Domain 2 items	SEIP Mean if Item Deleted	SEIP Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Hospital admission	15.57	0.75	0.79	0.63
Hospital stay	15.57	0.75	0.79	0.63
NHS Direct Number	15.47	1.31	**0.14**	**0.82**
Appointment with GP	15.60	0.86	0.57	0.72
Appointment with nurse	15.63	0.89	0.43	0.78

Similarly, items in the work domain such as "work schedule and fatigue, day off sick, and work limitation" displayed high internal consistency. The Cronbach's alpha value of this 3-item domain was 0.84. The mean scores were also homogeneous and ranged between 4.63-4.83 (Tables 6.13) and the Inter-item-Correlations was from 0.61 to an excellent 0.81 (Table 6.14).

Table 6.13 Work domain mean score for Test 1 (n=92)

	Mean	Std. Deviation
Work schedule & fatigue	4.63	0.81
Day off sick	4.83	0.53
Work limitation	4.70	0.89

Table 6.14 Work domain item correlations with the total scores for Test 1

	SEIP Mean if Item Deleted	SEIP Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Work schedule & fatigue	9.52	1.59	0.81	0.67
Day off sick	9.33	2.57	0.61	0.88
Work limitation	9.46	1.44	0.78	0.71

Retest (Test 2)

In this study of 93 cardiovascular patients who re-completed the SEIP questionnaire at one week interval to the first assessment, data analysis of the retest was based on 92 valid and completed SEIP. One patient was excluded from analysis because of incomplete SEIP data. The internal consistency reliability results for test 2 (α= 0.93) did not show any significant difference to Test 1. Table 6.15 shows the expected SEIP items mean scores for test 2. In addition, Corrected-Item-Total Correlations ranged between 0.44-0.86 (Table 6.16). Compared to Test1, these figures showed similarity in pattern indicating that responses were similar. Internal consistency reliability was also calculated for each domain of the SEIP.

Table 6.15 Expected SEIP mean scores for Test 2 (n=92)

Domains & its items	Mean	Std. Deviation
Social interaction & emotional behaviours		
Anxious	4.12	0.89
Loss of interest	4.37	0.80
Loss of energy	4.13	0.93
Nightmares & terror	4.82	0.38
Cold hands & feet	4.25	0.80
Cough	4.32	0.89
Headache	4.74	0.57
Loss of sexual activity	4.35	0.84
Slurred speech	4.86	0.38
Pain in calf	4.78	0.51
Loss of memory	4.84	0.43
Use of healthcare services		
Hospital admission	3.79	0.44
Hospital stay	3.79	0.44
NHS Direct Number	3.82	0.38
Appointment with GP	3.77	0.42
Appointment with nurse	3.79	0.41
Work		
Work schedule & fatigue	4.48	0.90
Day off sick	4.68	0.65
Work limitation	4.53	0.98

The cronbach's alpha coefficient value for the social interaction & emotional behaviours domain was 0.88 as compared to 0.87 in Test 1. This means that there was no significant difference in response behaviours of participants at both periods. The mean scores also ranged between 4.12-4.85 (Table 6.17) and the Corrected-Item-total correlations were between 0.49-0.76 (Table 6.18). In contrast to the results of Test1, question 11 of the SEIP (loss of memory) showed an increased value of the Corrected-Item-total correlation (0.56), thereby confirming the decision not to remove this item from the SEIP.

The use of healthcare services domain with five items, displayed an excellent internal consistency with Cronbach's alpha coefficient estimated at 0.95.

Table 6.16 Item correlations with the total scores of overall SEIP for Test2 (n=92)

Domains & its items	SEIP Mean if Item Deleted	SEIP Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Social interaction & emotional behaviours				
Anxious	78.12	65.09	0.44	0.93
Loss of interest	77.87	61.63	0.79	0.92
Loss of energy	78.11	60.98	0.71	0.93
Nightmares & terror	77.42	67.14	0.78	0.93
Cold hand & feet	77.99	64.81	0.53	0.93
Cough	77.92	62.81	0.61	0.93
Headache	77.51	65.16	0.72	0.93
Loss of sexual activity	77.89	65.34	0.46	0.93
Slurred speech	77.38	68.68	0.53	0.93
Pain in calf	77.46	65.25	0.81	0.92
Loss of memory	77.41	67.62	0.62	0.93
Use of healthcare services				
Hospital admission	78.45	66.63	0.76	0.93
Hospital stay	78.45	66.63	0.76	0.93
NHS Direct Number	78.42	67.07	0.79	0.93
Appointment with GP	78.47	67.87	0.59	0.93
Appointment with nurse	78.45	67.90	0.61	0.93
Work				
Work schedule & fatigue	77.76	61.63	0.69	0.93
Day off sick	77.56	62.89	0.86	0.92
Work limitation	77.71	60.58	0.70	0.93

The mean scores value ranged between 3.77-3.82 (Table 6.19) and the Corrected-Item-Total Correlations were estimated between 0.83-0.90 (Table 6.20). The Cronbach's alpha coefficients for internal consistency reliability of work domain was 0.89 and the item correlations with the total scores were variable ranging between 0.69-0.88 (Table 6.21). The mean scores pattern was similar to the scores attributable to other domains. The values ranged between 4.48-4.67 (Table 6.22).

Table 6.17 Social interaction & emotional behaviours domain mean scores for Test 2 (n=92)

Domain items	Mean	Std. Deviation
Anxious	4.12	0.88
Loss of interest	4.37	0.79
Loss of energy	4.13	0.93
Nightmares & terror	4.82	0.39
Cold hands & feet	4.25	0.79
Cough	4.32	0.89
Headache	4.73	0.58
Loss of sexual activity	4.35	0.83
Slurred speech	4.85	0.39
Pain in calf	4.77	0.52
Loss of memory	4.83	0.44

Table 6.18 Item correlations with total scores of the social interaction & emotional behaviours domain for Test 2 (n=92)

Domain items	SEIP Mean if Item Deleted	SEIP Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach 's Alpha if Item Deleted
Anxious	45.40	21.83	0.54	0.87
Loss of interest	45.15	20.94	0.76	0.85
Loss of energy	45.39	19.93	0.76	0.85
Nightmares & terror	44.71	24.39	0.66	0.87
Cold hands & feet	45.27	22.09	0.59	0.87
Cough	45.21	21.97	0.52	0.87
Headache	44.79	23.22	0.64	0.87
Loss of sexual activity	45.17	22.19	0.54	0.87
Slurred speech	44.67	25.01	0.49	0.87
Pain in calf	44.75	23.22	0.72	0.86
Loss of memory	44.70	24.48	0.56	0.87

Table 6.19 Use of healthcare services domain mean scores for Test 2 (n=92)

Domain items	Mean	Std. Deviation
Hospital admission	3.79	0.44
Hospital stay	3.79	0.44
NHS Direct Number	3.82	0.38
Appointment with GP	3.77	0.42
Appointment with nurse	3.79	0.41

Table 6.20 Use of healthcare services item correlations with the total scores for Test 2

	SEIP Mean if Item Deleted	SEIP Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Hospital admission	15.18	2.28	0.89	0.93
Hospital stay	15.18	2.28	0.89	0.93
NHS Direct Number	15.14	2.41	0.90	0.93
Appointment with GP	15.20	2.38	0.82	0.95
Appointment with nurse	15.18	2.41	0.83	0.94

Table 6.21 Work domain mean scores for Test 2 (n=92)

	Mean	Std. Deviation
Work schedule & fatigue	4.48	0.90
Day off sick	4.67	0.65
Work limitation	4.52	0.98

Table 6.22 Work domain item correlations with the total score for Test 2 (n=92)

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Work schedule & fatigue	9.20	2.20	0.88	0.75
Day off sick	9.00	3.30	0.69	0.93
Work limitation	9.15	2.02	0.85	0.79

Patients' views about the relationship between side effects and their medication

When patients who completed the questionnaire were asked whether the side effects they experienced were due to their medications, the majority of the respondents did not think the side effects were medication-related (Table 6.23)

Table 6.23 Response rate of participating patients to questions in domain 1 of the SEIP

Type of medication side effects	No. of patients that suffered side effect	No of patients without side effect	Do you think it is due to side effect of your medicine?		
			Yes	No	Unsure
Anxious	54	38	0	28	26
Loss of interest	50	42	0	39	11
Loss of energy	54	38	9	33	12
Nightmares & terror	17	75	0	17	0
Cold hand & feet	52	40	0	31	21
Cough	49	43	8	26	15
Headache	18	74	1	15	2
Loss of sexual activity	39	53	0	24	15
Slurred speech	9	83	0	9	0
Pain in calf	18	74	0	17	1
Loss of memory	14	78	1	11	2

DISCUSSION

As the SEIP was designed for use with community- managed cardiovascular patients on repeat medication therapy, the hypothesis was that there should be no dramatic change(s) in these patients medical conditions, since most of them would have been taking their medication for three months and above and hence have stable medical conditions with minimum or no side effects of drug therapy. With this in mind, the expectation was that SEIP items should be consistent and should measure the same dimensions of impact of medication side effects among these cardiovascular patient groups.

A total of 93 (62.0%) patients returned the questionnaires by pre-paid envelope to both test 1 and 2 in this study. Their sociodemographic characteristics showed that 63.4% were on drug therapy for hypertension, and 24.7% suffered from other medical conditions in addition to hypertension. This is an indication that the majority of these patients were highly involved in the management of their condition. Applicability and practicality results showed that one-third of the respondents actually completed the questionnaires in three minutes and the fact that the mean time taken to complete the questionnaire was 5.7 minutes indicated patients' acceptability of the measure. To support this notion, the majority of the respondents (96.7%) found the SEIP questionnaire to be clear and understandable and 78.5% patients thought that the SEIP questions were comprehensive enough to measure their socioeconomic wellbeing, while almost all the respondents agreed that the SEIP questionnaire was not difficult or distressing to complete. These findings therefore supported the arguments for the practicality of the measure among cardiovascular patients.

The fact that a great majority of the patients who returned the questionnaires completed all parts of the questions indicates its reliability and relevance among cardiovascular patient populations managed in the community setting. The reported overall Cronbach's alpha and the Corrected Item-Total Correlation coefficients in both Test 1 and Test 2 supported the homogeneity of the SEIP in measuring the socioeconomic impacts of medication side effects of cardiovascular drugs. Homogeneity of the items in this scale was further affirmed, as deletion of any items with low Corrected-Item-Total Correlation coefficient yielded negligible improvement in the alpha coefficient (Boyle, 1999).

With regards to the test-retest reliability results measured with the Spearman's correlation coefficients, SEIP demonstrated significant item correlations in both Test 1 and Test 2. Most items showed high Spearman's rho with the exception of two items ("slurred speech" and "NHS Direct Number") that indicated low values of Spearman's rho = 0.39 and 0.22 respectively.

Findings of this study supported the SEIP as a valid and reliable instrument for evaluation of the socioeconomic impacts of medication-related problems of

cardiovascular drugs. The internal consistency reliability results yielded close to perfect correlation coefficients. Such indication of robustness of the SEIP provides an extremely encouraging impetus to build upon in generating confidence for its use in practice.

It should be emphasised that this study tested the psychometric properties of the SEIP among community-managed cardiovascular patients on repeat medication prescriptions with intact cognitive ability. The majority of these patients were hypertensive and were 57 years and above. Limitations therefore exist in generalising the results of this study to other cardiovascular populations who are not community-pharmacy managed and of younger age or with impaired cognitive function.

SUMMARY

- The test-retest reliability property of the SEIP as well as its practicality were carried out in a total of 150 community-managed cardiovascular patients out of which 93 (63.0%) responded.

- The mean time taken to complete the SEIP was 5.7 minutes; the majority of the respondents agreed that the questions were comprehensive, clear and easy to administer.

- Overall, all SEIP domains demonstrated high evidence of internal consistency reliability as well as test-retest reliability.

- Future work should focus on generalising the study to other categories of cardiovascular diseases which are not community managed in order to determine the test-retest reliability of the SEIP and its responsiveness.

The next chapter of this thesis will focus on further psychometric properties of the SEIP such as its validity (discriminant and convergent).

CHAPTER 7

Validation of the Socioeconomic Impact Profile (SEIP) - Convergent and Divergent Validity

INTRODUCTION

The necessity for a comprehensive and yet practical tool with which to assess medication-related socioeconomic problems in community managed cardiovascular patients has prompted development and validation of such measure as described in the previous chapters. Nevertheless, its utility can only be confirmed after relevant psychometric properties for such instrument are established (Guillemin et al., 1993; Bernhard et al., 1996). Any measurement scale or instrument must possess a sound reliability and validity in order to widen its acceptability for use in research as well as in practice routine (Bootman et al., 2005). Chapter 6 described the reliability of SEIP among patients on cardiovascular drugs in the community setting. This chapter will therefore explore its validity.

Validity refers to the extent to which differences in test scores reflect the true differences in individuals under study (Bowling, 2005b). This technique has been well documented in chapter two of this thesis. Moreover, the types of validation necessary and most applicable to health measures should include content, construct and criterion validity. Evidence of content validity of SEIP has been provided in chapter 4 in terms of mean scores for agreement level (1 to 4) for each item of the SEIP and also kappa coefficient (k) for level of agreement among experts panel who validated the instrument. Chapter 5 provides evidence of construct validity of SEIP by using a factor analysis technique to identify items that are highly correlated with each other but exhibit low levels of correlation with other variables in the measure thereby indicating potential underlying structure of the instrument.

Construct validity has been extensively described in chapter 2. Understanding this technique provides knowledge of behaviour of the instrument and its validity. Construct validity is determined by comparisons between measures and examining the relationships between the measure and characteristics of the population being assessed. The following aspects should be considered when establishing construct validity of a new health measure (Walker, 2002):

- The measured variable should display low correlation with related measures but different constructs (divergent validity).
- The measured variable should show positive correlation with related and similar constructs (convergent validity).

Aims of the present study

In this chapter, it is hoped to examine the followings:

- The convergent validity of the SEIP patient scores by comparisons with MIDAS patient scores;
- The divergent validity of the SEIP patient scores by comparison with SF-12 patient scores.
- The relationship between SEIP patient scores and some sociodemographic characteristics such as age, gender and duration of condition;

METHODS

The outcome measures

The outcome measures used in this validity study included the MIDAS and the SF-12. These two health measures have been well described in chapter 2; however, a summary of these will be described here for the purpose of clarity and completion.

The myocardial infarction dimensional assessment scale (MIDAS)

The MIDAS has been fully described in chapter 2. It is a self-administered cardio-specific quality of life instrument measuring seven areas of health status. It takes 5 to 10 minutes to complete using a 5-point Likert scale response option. The MIDAS includes 35 questions grouped into seven domains, namely: physical activities (12 items), insecurity (9 items), emotional reactions (4 items), dependency (3 items), diet (3 items), concern about medications (2 items) and side effects of medications (2 items). The structure and maximum possible score for each domain are shown in Table 7.1. The MIDAS was chosen for use in this study because of its high face, internal and constructs validity and has been validated among the same patient group as this study.

Table 7.1 Structure of the MIDAS

Domain	No of items	Maximum score
Physical activity	12	60
Insecurity	9	45
Emotional reaction	4	20
Dependency	3	15
Diet	3	15
Concerns over medication	2	10
Side effects	2	10
Total	35	175

Medical Outcomes Study Short Form-12 health survey (SF-12)

The SF-12 as described in chapter 2 is an established generic health measure that has been used in cardiovascular patients. It is designed in responding to the need for development of a shorter instrument to the original SF-36. It has been used as a self-administered questionnaire and takes about 2 minutes to complete (Bowling, 2005b). The SF-12 includes eight health concepts such as physical functioning (PF), role functioning physical (RFP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role functioning emotional (RFE), and mental health (MH). Each concept is scored on a 0-100 scale with 0 and 100 corresponding to worst and best HRQOL respectively. These 8 concepts are used to monitor overall physical and mental health outcomes known as the Physical Component Summary (PCS-12) and the Mental Component Summary (MCS-12) respectively. Scale scores are estimated for four of the health concepts (PF, RFP, RFE, and MH) using two items each, whereas the remaining four (BP, GH, VT, and SF) are represented by a single item. All 12 items are used to calculate the physical and mental component summary scores (PCS-12 and MCS-12) by applying a scoring algorithm empirically derived from the data of a US general population survey (Ware et al., 1995). It has been recommended that the US-derived summary scores, which yield a mean of 50 and SD of 10, be used in order to facilitate cross-cultural comparison of results (Gandek et al., 1998).

It should be noted that reverse scoring of four items is required so that a higher item value indicates better health for all SF-12 items and summary scales. Four SF-12 items are therefore reverse scored because higher precoded item values for these items

indicate a poorer health state. The four items that are reversed scored are: GH1 (item 1), BP2 (item 8), MH3 (item 9), and VT2 (item 10). For example, the highest precoded value for the item "How much of the time did you feel calm and peaceful" is "6-None of the time", which indicates a poor health state (Appendix 15).

The 12 items of the SF-12 yield the eight-scale profiles of the SF-36, but with fewer levels and with less precise scores. This has been considered as its limitation in different published studies. The SF-12 was chosen for use in this study on the grounds of its wider acceptability as a generic health measure especially in the cardiovascular patient group. It is also less time consuming to complete with minimum burden on patients. This was an important factor to consider since patient were to be asked to complete three questionnaires.

Study procedure

Cardiovascular patients on repeat prescriptions were recruited from two community pharmacies in South West Wales. The questionnaires were administered with a personalised covering letter to maximise the response rate. Order of completion of the questionnaires was randomised in order to remove training effects on patients. Patients were asked to return the completed questionnaires in a pre-paid envelope included in the pack. All data from the questionnaires were entered into the SPSS 12 data package for analysis.

Data processing and analysis

The data were analysed using SPSS statistical package. Patients' demographic data were entered along with the patient identification number, followed by the response data. Missing values were assigned a score of "999" and a quality control check was carried out to ensure the accuracy of data entry. Validity was measured using non-parametric techniques. The following relationships were examined using appropriate statistical tests:

- The relationship of SEIP scores and other outcome measures scores with patient gender using the Mann Whitney U Test;
- The relationship of SEIP scores and other outcome measures scores with patient age using the Mann Whitney U Test.

- The relationship of SEIP scores and other outcome measures scores with the duration of condition using the Mann Whitney U Test.
- The association between SEIP scores, MIDAS scores and SF-12 scores using Spearman's rank correlation test (r_s values ranging 0.10-0.29 = weak, 0.30-0.49 = moderate, and ≥ 0.50 = strong).

RESULTS

A total of 175 patients were recruited into the study of which 96 returned their questionnaires giving an overall response rate of 54.8%. Table 7.2 shows the demographic characteristics of the respondents. Forty-nine patients (51.0%) were males. The mean age was 63.1 years and the mean duration of condition was 124.4 months. The age of participants ranged from 39 to 84 years with a median age of 63 years. Fifty-nine patients (61.5%) were married, 49 (51.0%) had a high school education, 27 (28.1%) had a university degree and 14 (14.6%) had a primary education. Thirty-seven (38.5%) were employed and over one-third of the participants earned between £10,000 and £20,000 annually. Twenty-four (25.0%) were hypertensive while 43 (44.8%) suffered from another concomitant medical condition. These included diabetes (type1 or type II), asthma, COPD, arthritis and depression.

The SEIP scores

Table 7.3 &7.4 show the mean scores for the SEIP and other outcome measures used in the study. The overall mean score of the SEIP for all patients was 82.4 (91.6%). The mean scores of domain 1 to 3 of the SEIP were 48.61 (88.4%), 19.44 (97.2%), and 13.57 (90.5%), respectively indicating low impacts of MRPs on patients' socioeconomic wellbeing (Figure 7.1). Both MIDAS and the SF-12 displayed high scores out of the maximum possible scores. This indicates that medication-related problems in the observed populations had low negative impacts on their socioeconomic wellbeing. The SF-12 item and summary descriptive statistics are presented in Table 7.4. Four of the items were recoded so that higher scores correspond to better health. The PCS-12 and MCS-12 summary scores were negatively skewed since respondents scored towards the higher end of the health spectrum.

Table 7.2 Demographic characteristics of the study patients

Variables	Number (percentage)
Age (years)	
Mean	63.1
Median	63.0
Range	39-84
Gender	
Male	49 (51.0)
Female	47 (49.0)
Duration of condition (in months)	
Mean	124.4
Median	84.0
Range	3-612
Medical condition	
Hypertension	24 (25.0)
Heart failure	1 (1.0)
High cholesterol	1 (1.0)
Angina	5 (5.2)
Heart attack	8 (8.3)
Heart attack and others	4 (4.2)
Hypertension and others	43 (44.8)
Non cardiovascular –related	5 (5.2)
Education	
None	2 (2.1)
Primary school	14 (14.6)
High school	49 (51.0)
University degree	27 (28.1)
Marital status	
Single	11 (11.5)
Divorced	7 (7.3)
Married	59 (61.5)
Widowed	18 (18.8)
Separated	1 (1.0)
Employment	
Employed	37 (38.5)
Unemployed due to health	8 (8.3)
Unemployed not due to health	1 (1.0)
Retired due to health	23 (24.0)
Retired not due to health	22 (22.9)
Self employed	4 (4.2)
Annual income	
< £10000	38 (39.6)
£10000 < E < £20000	31 (32.3)
£20000 < E < £30000	7 (7.3)
£30000 < E < £40000	10 (10.4)
E > £40000	3 (3.1)

Figure 7.1 The SEIP mean scores

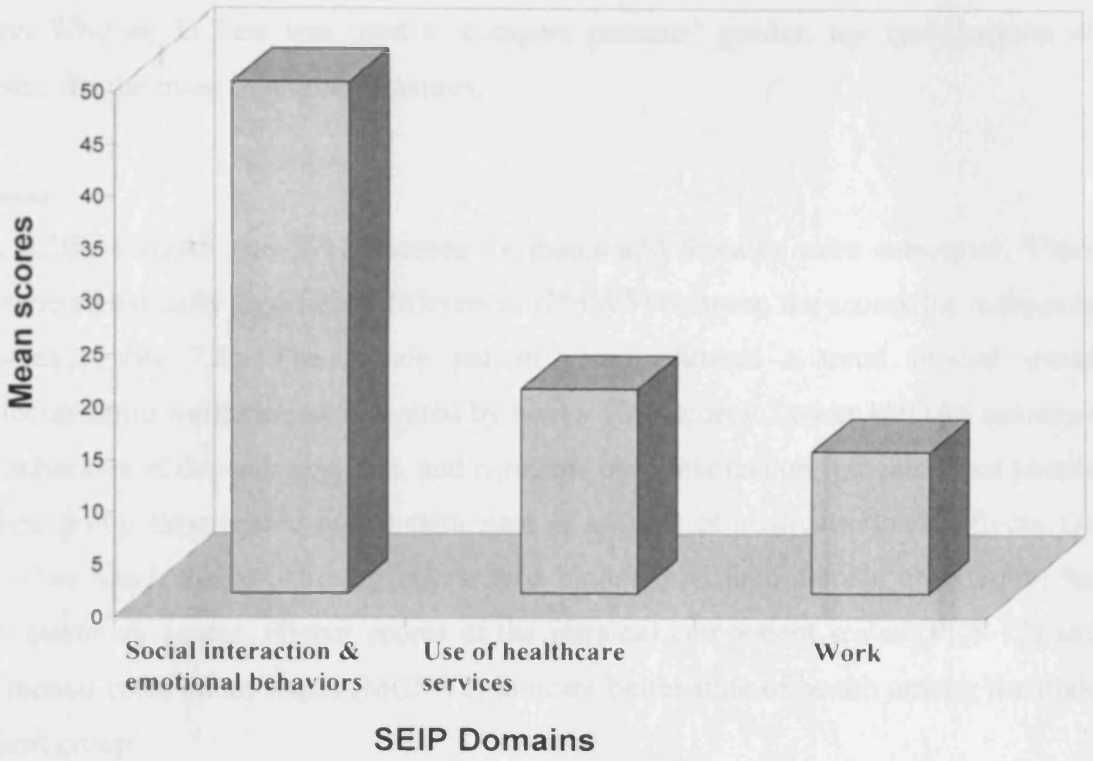


Table 7.3 Mean scores for SEIP & MIDAS (n=96)

Domains	No of items	Mean scores (SD)	Median Range
SEIP			
Social interaction & emotional behaviours	11	48.61 (6.30)	30-55
Use of healthcare services	5	19.44 (1.16)	15-20
Work	3	13.57 (2.73)	3-15
MIDAS			
Physical activity	12	49.82 (10.87)	15-60
Insecurity	9	41.19 (7.53)	11-45
Emotional reaction	4	16.71 (4.13)	4-20
Dependency	3	13.59 (2.64)	5-15
Diet	3	11.59 (2.87)	3-15
Concerns over medication	2	8.63 (2.02)	2-10
Medication side-effects	7	8.43 (1.96)	2-10

Comparisons of patients' demographic characteristics for SEIP, MIDAS and SF-12

Mann Whitney U Test was used to compare patients' gender, age and duration of disease for the three outcome measures.

Gender

The SEIP, MIDAS and SF-12 scores for males and females were compared. There were no statistically significant differences ($P>0.05$) between the scores for males and females (Table 7.5). The female patient group showed a trend toward worse socioeconomic wellbeing as indicated by lower SEIP scores. Lower MIDAS scores of the subscales of dependency, diet, and concerns over medication indicated that female patient group experienced poor health state as a result of medication side effects. On the other hand, males patient group scored higher than their female counterpart for both summary scores. Higher scores of the physical component scales (PCS-12) and the mental component scales (MCS-12) indicate better state of health among the male patient group.

Age

The procedure for performing this analysis involved the splitting of patient age along the median to produce two approximately equal groups. All those aged under 64 years were included in one group and all those that were 64 years and above were included in another group. The SEIP, MIDAS, and SF-12 scores for these two groups were then compared (Table 7.6). No statistically significant differences ($P>0.05$) were observed between the SEIP scores of patients below 64 years and those above 64 years. However, the scores for all three domains of the SEIP were higher for < 64 years. This trend indicated that the patients group under 64 years had better socioeconomic wellbeing than the > 64 years patient group. In contrast, the results showed varying significance levels among scores of MIDAS scales and the SF-12.

Table 7.4 SF-12 item and summary descriptive statistics (n=96)

Item description (scale)	Mean (SD)	Median	Response frequencies (%)					
			1	2	3	4	5	6
Moderate activities (PF)	2.27 (0.76)	2.00	18.8	35.4	45.8	-	-	-
Climb several flights (PF)	1.97 (0.75)	2.00	29.2	44.8	26.0	-	-	-
Accomplished less (RFP)	1.47 (0.50)	1.00	52.1	46.9	-	-	-	-
Limited kind of work (RFP)	1.49 (0.50)	1.00	50.0	49.0	-	-	-	-
Pain interferes* (BP)	3.95 (1.35)	5.00	52.1	13.5	8.3	16.7	5.2	-
Health in general* (GH)	2.70 (0.83)	3.00	1.0	13.5	43.8	32.3	6.3	-
Energy* (VT)	3.59 (1.45)	4.00	4.2	32.3	12.5	22.9	14.6	9.4
Social time (SF)	1.99 (1.38)	1.00	2.1	5.2	9.4	9.4	16.7	53.1
Emotional problem (RFE)	1.24 (0.43)	1.00	76.0	24.0	-	-	-	-
Less work &emotional problem (RFE)	1.22 (0.42)	1.00	74.0	20.8	-	-	-	-
Calm & peaceful* (MH)	4.28 (1.36)	5.00	20.8	30.2	10.4	26.0	6.3	2.1
Felt down / sad (MH)	2.11 (1.27)	2.00	-	5.2	14.6	7.3	27.1	41.7
Summary statistics	**PCS-12**	**MCS-12**						
Mean (SD)	48.42 (1.26)	47.23 (2.15)						
Median	48.00	46.00						
Skewness	-0.23	-0.28						

* Item recoded so that higher scores correspond to better health.

Table 7.5 Comparisons of patients' gender for mean scores of SEIP, MIDAS & SF-12

Outcome measures	Mean rank Scores		Mann Whitney U Test	
	Male	Female	Z*	P value
SEIP				
Social interaction & emotional behaviours	42.96	46.19	+0.59	0.55
Use of healthcare services	50.68	43.39	-1.75	0.08
Work	47.90	42.17	-1.27	0.20
MIDAS				
Physical activity	42.43	46.66	+0.79	0.43
Insecurity	38.40	47.23	+1.80	0.07
Emotional reaction	43.54	49.73	+1.16	0.24
Dependency	47.21	45.73	-0.34	0.73
Diet	45.11	42.81	-0.43	0.67
Concerns over medication	47.14	44.78	-0.46	0.65
Medication side-effects	44.76	48.40	+0.69	0.49
SF-12				
Physical Component Summary (PCS)	48.95	47.44	-0.17	0.87
Mental Component Summary (MCS)	48.10	46.90	-0.33	0.74

Z*= median of distribution

There was a significant difference in the scores of MIDAS subscales physical activity ($P<0.001$), diet ($P<0.04$) and medication side-effect ($P<0.02$). This significant trend may indicate that patients < 64 years do not suffer medication side effects to a degree that will affect their physical activities. Significantly lower mean PCS-12 ($P\leq0.01$) were observed among those above 64 years, compared to those less than 64 years. In contrast, those above 64 years showed higher mean MCS-12 ($P<0.05$) than those less than 64 years. These significant trends are indicative of the discriminative ability of the SF-12 since for every health problem, at least one summary score was significantly lower in the observed group.

Table 7.6 Comparisons of patient age for SEIP, MIDAS, and SF-12 scores.

Outcome measures	Mean rank scores (years)		Mann Whitney U test	
	<64	≥ 64	Z	P value
SEIP				
Social interaction & emotional behaviours	46.55	41.92	-0.85	0.39
Use of healthcare services	50.40	43.22	-1.72	0.09
Work	47.74	41.93	-1.29	0.19
MIDAS				
Physical activity	52.33	35.93	-3.05	**0.001**
Insecurity	43.79	41.01	-0.57	0.57
Emotional reaction	46.96	46.00	-0.18	0.86
Dependency	49.19	43.57	-1.31	0.19
Diet	38.69	49.43	+2.02	**0.04**
Concerns over medication	43.97	48.27	+0.83	0.41
Medication side-effects	52.41	40.06	-2.35	**0.02**
SF-12				
Physical Component Summary (PCS)	45.64	38.71	-2.81	**0.01**
Mental Component Summary (MCS)	42.37	50.43	+2.02	**0.04**

Comparisons of patients' duration of disease for the SEIP, MIDAS, and SF-12

In order to perform this, duration of disease was split along the median to produce two approximately equal groups. All those with duration of medical condition less than 85 months formed one group and those with disease duration of 85 months or more populated the other group. The Mann Whitney U Test was used to perform comparison of SEIP, MIDAS, and SF-12 scores for these two groups (Table 7.7). There were no significant differences (P>0.05) observed between SEIP scores of patients with a duration of condition less than 85 months and those with longer. However, the trend of the scores for the three domains of the SEIP to all move in a negative direction meant those scores for the SEIP domains were lower for patients with a longer duration of disease. This trend may indicate that those with a longer

duration of disease did experience medication side effects with negative impacts on their socioeconomic wellbeing. Similarly, those with longer duration of disease showed lower scores in all subscales of the MIDAS. This is an indication of poor health status among this patient group.

In contrast, there were significant differences between a duration of condition less than 85 months and those that were 85 months and longer for most of the SF-12 subscale including Physical functioning ($P<0.001$), Social Functioning ($P<0.01$), Vitality ($P<0.001$), and Mental Health ($P<0.01$). This indicated that those patients with a longer duration of medical condition showed significantly greater impairment in Physical Component Summary Scales (PCS-12) but did reasonably well with the Mental Component Summary scales (MCS-12). This trend may indicate that those with a longer duration of disease have an intact cognitive status.

Internal validity of the SEIP

The relationships between SEIP items and their domains was examined using Spearman's Rank Order Correlation. When comparisons were made between items in the SEIP and its domains, strong correlations were observed in most cases (Table 7.8). Social interaction and emotional behaviour items (1-11) produced moderate to strong correlations with their own domains (r_s = 0.32-0.86) and in most cases showed weak correlations with the use of health services domain and work domain. Similar trends were observed with items in the other domains. All items (12-16) correlated stronger with the use of healthcare services domain (r_s= 0.40-0.80) than with other domains. In addition, items (17-19) showed stronger correlations (r_s=0.58-0.89) with work domain than other domains of the SEIP. This suggests the internal stability of the SEIP.

Table 7.7 Comparisons of patients' duration of disease for SEIP, MIDAS & SF-12

Outcome measures	Mean rank scores (months)		Mann Whitney U Test	
	<85	≥ 85	Z	P value

SEIP				
Social interaction & emotional behaviours	49.74	40.49	-1.67	0.09
Use of healthcare services	47.88	45.69	-0.51	0.61
Work	46.82	43.11	-0.79	0.43
MIDAS				
Physical activity	49.39	40.70	-1.58	0.11
Insecurity	43.16	41.27	-0.38	0.71
Emotional reaction	47.43	45.15	-0.42	0.68
Dependency	51.01	43.01	-1.81	0.07
Diet	44.52	42.90	-0.29	0.77
Concern about medication	50.62	42.39	-1.55	0.12
Medication side-effects	46.79	45.53	-0.24	0.81
SF-12				
General Health	49.82	44.64	-0.96	0.34
Physical Functioning	59.75	41.45	-3.18	**0.001**
Social Functioning	38.82	52.42	+2.68	**0.01**
Role Functioning Physical	50.52	43.49	-1.61	0.11
Role Functioning Emotional	40.95	48.13	+1.74	0.08
Vitality	56.23	40.18	-3.05	**0.001**
Bodily Pain	43.66	41.33	-1.29	0.19
Mental Health	39.21	52.20	+2.56	**0.01**

Table 7.8 Correlations† between SEIP items and their corresponding domains

SEIP	Social interaction & emotion behaviours domain											Use of healthcare services domain					Work domain		
Domains	**Item 1**	**Item 2**	**Item 3**	**Item 4**	**Item 5**	**Item 6**	**Item 7**	**Item 8**	**Item 9**	**Item 10**	**Item 11**	**Item 12**	**Item 13**	**Item 14**	**Item 15**	**Item 16**	**Item 17**	**Item 18**	**Item 19**
1	0.82**	0.78**	0.86**	0.45**	0.53**	0.40**	0.32**	0.66**	0.43**	0.58**	0.51**	0.28	0.22	0.12	0.10	0.06	0.12	0.28	0.21
2	0.26*	0.38**	0.23	0.38**	0.22	0.22	0.26*	0.31**	0.30**	0.33**	0.03	0.80**	0.80**	0.38**	0.61**	0.40**	0.03	0.18	0.15
3	0.27*	0.30**	0.05	0.21	0.09	0.07	0.17	0.30**	0.16	0.02	0.07	0.26**	0.35**	0.11	0.01	-0.06	0.85**	0.58**	0.89**

†Spearman's rank correlation coefficients (r_s). **P< 0.01; *P< 0.05.

Domain 1= Social interaction and emotional behaviour

Domain 2= Use of health services

Domain 3= Work

Item 1= Anxious, item 2= Loss of interest, item 3= Loss of energy, item 4= Nightmares & terror, item 5= Cold hands & feet

Item 6= Cough, item 7= Headache, item 8= Loss of sexual activity, item 9= Slurred speech, item 10= pain in calf,

Item 11= Loss of memory, item 12= Hospital admission, item 13= Hospital stay, item 14= NHS direct use,

Item 15= Appointment with GP, item 16= Appointment with nurse, item 17= Work schedule & fatigue,

Item 18= Day off sick, item 19= Work limitation.

Convergent validity of the SEIP

The construct validity of some of the SEIP domains was examined by testing their associations with the relevant dimensions of the MIDAS scales (Table 7.9). Most subscales of the MIDAS correlated well ($P<0.05$ to $P<0.01$) with the SEIP domains. The MIDAS subscale relating to physical activity (MIDAS 1) correlated moderately ($r_s= 0.44$; $P<0.01$) with the SEIP 1 (social interaction and emotional behaviour) and weakly with the use of health services domain ($r_s= 0.26$; $P<0.05$) and work domain ($r_s= 0.29$; $P<0.01$) of the SEIP. The insecurity subscale (MIDAS 2), the emotional reaction subscale (MIDAS 3), and the dependency subscale (MIDAS 4) all correlated moderately with the social interaction and emotional behaviour domain of the SEIP ($r_s= 0.32$-0.35; $P<0.01$).

There was no significant correlation observed between the diet subscale of the MIDAS and the social interaction and emotional behaviour domain of the SEIP ($r_s= 0.16$; $P>0.05$). However, a weak correlation was observed between the diet subscale of MIDAS and the work domain of the SEIP ($r_s= 0.26$; $P<0.05$). Furthermore, the medication side effects subscale of MIDAS demonstrated a moderate correlation with the social interaction and emotional behaviour domain of the SEIP ($r_s= 0.31$; $P\leq0.01$).

The insecurity subscale, the emotional reaction subscale, the dependency subscale, the diet subscale and the concerns over medication subscales of the MIDAS all demonstrated poor correlations with the use of health services domain of the SEIP ($r_s= 0.02$-0.19). Furthermore, SEIP domain 3 (work) produced weak correlations with all other scales of the MIDAS ($r_s=0.22$- 0.29; $p<0.05$) except dependency subscale (MIDAS 4) for which correlation was poor ($r_s =0.17$). The result of this exercise suggests that the SEIP possesses an acceptable convergent validity.

Table 7.9 Correlations† between domains of the SEIP and MIDAS subscales

Domains	SEIP 1	SEIP 2	SEIP3	MIDAS 1	MIDAS 2	MIDAS 3	MIDAS 4	MIDAS 5	MIDAS 6	MIDAS 7
SEIP 1	1.00									
SEIP 2	0.34**	1.00								
SEIP 3	0.37**	0.27*	1.00							
MIDAS1	0.44**	0.26*	0.29**	1.00						
MIDAS 2	0.35**	0.19	0.23*	0.72**	1.00					
MIDAS 3	0.35**	0.16	0.23*	0.78**	0.83**	1.00				
MIDAS 4	0.32**	0.16	0.17	0.63**	0.57**	0.69**	1.00			
MIDAS 5	0.16	0.02	0.26*	0.33**	0.38**	0.55**	0.30**	1.00		
MIDAS 6	0.27*	0.09	0.28*	0.34**	0.51**	0.46**	0.28**	0.75**	1.00	
MIDAS 7	0.32**	0.24*	0.22*	0.59**	0.51**	0.63**	0.47**	0.38**	0.30**	1.00

†Spearman's rank correlation coefficients (r_s)
**P<0.01; *P<0.05

Note:
SEIP 1= Social interaction and emotional behaviour SEIP 2= Use of health services domain SEIP 3= Work domain
MIDAS 1= Physical activity domain MIDAS 2= Insecurity domain MIDAS 3= Emotional reaction
MIDAS 4= Dependency MIDAS 5= Diet MIDAS 6= Concerns over medication MIDAS 7= Medication side effects

Divergent validity of the SEIP

Comparisons of scores were made for the SEIP and the Short Form-12 (Table 7.10). Moderate to high correlations (r_s= 0.32-0.45; P<0.01) were observed between the social interaction and emotional behaviour domain of the SEIP and all but one of the SF-12 domains (i.e. physical functioning, general health, social functioning, physical role functioning, role functioning emotional, vitality and mental health). In contrast, domain 2 of the SEIP (the use of health services) did not correlate significantly with any of the categories on the SF-12 (r_s= 0.04-0.21) except the vitality domain which showed a weak correlation (r_s= 0.23; P<0.05). Furthermore, with the exception of the social functioning domain and the vitality domain of the SF-12, all other categories did not show any significant correlations (r_s= 0.02-0.17) with the SEIP domain 3 (work). This indicates that these corresponding domains of the SF-12 are not measuring similar underlying concepts as domain 2 and 3 of the SEIP.

Table 7.10 Correlations† between the SEIP and SF-12 domains

SF-12 health concepts	SEIP		
	Social interaction & emotional behaviours	**Use of healthcare services**	**Work**
General health	0.39**	0.15	0.17
Physical functioning	0.32**	0.20	0.02
Social functioning	-0.40**	0.14	-0.23*
Role functioning physical	-0.45**	0.03	0.08
Role functioning emotional	-0.40**	-0.21	0.01
Vitality	-0.44**	0.23*	0.27*
Bodily pain	-0.01	0.05	-0.03
Mental health	-0.45**	0.04	-0.07

†Spearman's rank correlation coefficients (r_s)
**P<0.01; *P<0.05

DISCUSSION

As suggested by Bootman et al (2005), the development and wider acceptability of any measurement scale or instrument will not be complete without testing of the tool's psychometric properties such as reliability and validity in order to determine whether

the instrument in question can perform as expected before its implementation in the target population at large. The SEIP questionnaire has been shown in the previous chapters of this study to be reliable both in terms of internal consistency and test-retest reliability in the target population of community–managed cardiovascular patients. Content validity of the SEIP has also been addressed in chapter 4 by developing items on the basis of in depth discussions with experts in the area of community pharmacy practice and with cardiovascular patients. The content of the SEIP addresses experiences of great importance to individuals on cardiovascular drug treatment such as lack of energy, depression, insomnia and libido. Such experiences are quite distinctively associated with some cardiovascular medication side effects.

The results in this chapter has undoubtedly demonstrated the validity of the SEIP through measuring what it was intended to measure in patients on cardiovascular drug treatments. In addition to the results of construct validity (factor analysis) described in chapter five, this chapter has further demonstrated evidence of the construct validity, in particular that of convergent and divergent validity.

The high domain scores of SEIP and the two health measures (MIDAS and SF-12) demonstrated that majority of the observed populations did not consider medication-related problems as impediments to their socioeconomic wellbeing. Also, it was shown that neither age nor gender of the observed patients has any significant effect on the impacts of MRPs on their socioeconomic wellbeing. However, the results of the relationship between age and scores of the other two patient-reported outcome measures showed significant correlation for patient age and scales of MIDAS (physical activity, diet and medication side effects) as well as SF-12 domains (physical functioning, social functioning, role functioning emotional, vitality and mental health items). This is not surprising as published studies had demonstrated that both the physical and mental scales (PCS-12 and MCS-12) of the SF-12 are able to discriminate between age groups (Lim and Fisher, 1999), providing evidence of its construct validity. The finding that MCS scores increased with increasing age is consistent with the majority of the literature that notes that MCS scores tend to improve with increasing age (as opposed to PCS scores which generally decline).

Furthermore, the results of the relationship between patient's duration of medical condition and the scores of the other patient-reported outcome measures demonstrated that SF-12 is also able to discriminate between patients' physical and mental scale and duration of condition. In this study, those patients with medical condition longer than 85 months showed worse impairments in Physical Component Summary than those with medical condition less than 85 months but better health status in terms of the scores for the Mental Component Summary.

Further evidence for the validity of SEIP was demonstrated with its comparison with a widely used generic health measure (SF-12) and a cardio-specific instrument (MIDAS). Correlations with the SF-12 were of poor to weak magnitude especially with the use of health services domain and work domain of the SEIP indicating that these domains were measuring distantly related concepts. The social interaction and emotional reaction domain of the SEIP was strongly related with the physical and mental scale of the SF-12 and the physical activity scale of the MIDAS. This demonstrated that these domains were measuring closely related concepts.

Finally, the findings of this chapter have demonstrated that the SEIP, a questionnaire designed to assess socioeconomic impacts of cardiovascular drug-related problems has acceptable validity in the observed cardiovascular patient groups and can be recommended as a patient-reported health outcome measure for use in routine practice and in conjunction with medicine use review (MUR).

SUMMARY

- The observed associations between the social interaction and emotional behaviour domain of the SEIP and the subscales of MIDAS on physical activity, insecurity, emotional reaction, dependency, concern over medication and medication side effects, support the construct validity of the SEIP;

- With the exception of the social interaction and emotional behaviour domain of the SEIP (r_s= 0.32-0.45), the other two domains demonstrated weak to poor

correlation (r_s= 0.02-0.27) with both the physical and mental scale of the SF-12 indicating the divergent validity property of the SEIP.

Chapter 8

General Discussion

The importance of measurement of health-related social and economic wellbeing in patients with cardiovascular conditions has been widely recognised (Treasure, 1999; Dempster and Donnelly, 2000; Smith, et al., 2000), though, to date, systematic attempts to assess social and economic impacts of cardiovascular medication-related problems from the perspective of the patients have been relatively limited. Modern medicines have contributed to longer life spans, improved health and better quality of life. Medication is the most common treatment for many diseases and conditions seen in chronically ill individuals (Donohue and Pincus, 2007). Medicines now not only treat and cure diseases that were untreatable just a few years ago, they aid in the early diagnosis of disease; prevent life-threatening illnesses; relieve pain and suffering, and allow people with terminal illnesses to live more comfortably during their last days (Fillenbaum et al., 2004). However, prescribed medication, over-the-counter medication, social drugs such as alcohol, and herbal remedies/alternative medicines can be a double-edged sword. When not used appropriately, effectively and safely, medication can have devastating consequences.

In the past decade, it has been recognised that a patient's perspective is as important as a clinician's professional opinion in the process of treatment decision taking. As a testimony to this, various techniques have been developed for measuring patients' perspective (Geigle and Jones, 1990; Leplege and Hunt, 1997). In the western world today, the incidence and prevalence of cardiovascular disease is steadily increasing (Carlberg et al., 2004). Not only do these patients suffer from highly distressing symptoms of their medical condition such as fatigue, depression and insomnia, they also experience various medication-related side effects (Westerlund et al., 2003). Cardiovascular drug-related problems if not well managed often cause distress and impairment of social wellbeing for patients and economic burden for the health services. Many people are more likely to suffer medication-related problems (MRPs) as a result of multiple drug therapy due to their condition (Hammerlen et al., 2007). Such situations would have double jeopardy economic consequencies for the health services.

Nevertheless, research has shown that medication-related problems are often preventable. Caregivers can play a key role in helping to identify when an actual or potential MRP is occurring. This assistance can help prevent the costly and unwanted negative consequences of medication use, such as admission to acute care hospitals, assisted living facilities or nursing homes. About one quarter of all nursing home admissions are due at least in part to the inability to take medication correctly (Bell et al., 2006). An important step to preventing problems is for health care professionals, patients and caregivers to understand what medication-related problems are, to recognize the signs and symptoms of actual and potential MRPs, and to identify appropriate steps that can be taken to reduce the incidence of these common and costly problems. It is important to keep in mind that medication effects can directly impact the daily functioning of the chronically ill, such as cardiovascular patients. These effects or "symptoms" of MRPs may include:

- Excessive drowsiness
- Confusion
- Depression
- Insomnia
- Muscle weakness
- Loss of appetite
- Falls and fractures
- Changes in speech and memory.

When these symptoms appear, they should be considered "red flags" to caregivers that an MRP may be happening.

The importance of the need to assess the impact of medication-related problems on patients' social and economic wellbeing has been demonstrated by an increasing call for the incorporation of sound medication-related assessment tools in community practice (Buurma et al., 2007; Hammerlen et al., 2007). Health-related social and economic wellbeing assessment measures have been shown as having the ability to predict treatment outcome and thus, can be used to plan individualised menu driven care and provide comprehensive assessment of therapeutic outcomes (Dixon, et al, 2000). Several studies have demonstrated that compliance with drug treatment is largely dependent on the impact of patients' feelings on well being (Viktil, et al.,

2004). Anecdotal evidence suggests strong correlations between self-reported psychosocial distress and pharmacotheapeutic concordance, as well as hospital re-admission. Furthermore, there is low concordance between the patient and the physician regarding drug treatment and health evaluations due to distressing medication side effects (Testa et al., 1993). In many cases, low concordance has resulted in drug treatment withdrawal or low compliance. Clearly, the impact of MRPs on social and economic wellbeing constitute a major outcome variable and should be measured by means of a valid, reproducible and sensitive instrument.

In the general introduction to this thesis, a number of instruments were reviewed. The shortcomings of these instruments as discussed in chapter one fell into the following categories: some instruments assessed a concept related to but not the same as social and economic impacts of medication-related problems concept. Some measures were too lengthy and burdensome for cardiovascular patient groups. Currently, there are a number of cardio-specific disease instruments available for measuring HRQoL as humanistic outcomes. These play an important role in the long term management of such patient population. However, these instruments were not considered in this present study due to lack of relevance to the overall assessment of MRPs' impact on patients' social and economic wellbeing. As described in chapter two, the existing cardio-specific HRQoL instruments are actually measuring an outcome that is related but different to the concept underpinning socioeconomic impact.

As the incidence and prevalence of medication-related problems in patients on multiple drug therapy increase, costs, both direct and indirect, due to MRPs will also rise dramatically. Incorporating a sound medication-related problem assessment tools as part of multiple strategies will help to reduce the costs of medication-related problems, especially in the community setting. As described in chapter one, the aim of this study was to develop an instrument to assess the social and economic impact of medication-related problems in three cardiovascular patient groups. This was the first attempt to conduct this type of research in such patient groups.

As part of a developmental process of a new instrument, its applicability, practicality, reliability and validity were assessed. Findings of this study therefore supported the SEIP as a valid and reliable instrument for evaluating the social and economic impacts

of medication-related problems of cardiovascular treatments in community setting. As demonstrated in the relevant chapters, this 19-item SEIP questionnaire is easy to administer and has been shown to be reliable (both in terms of internal consistency reliability and test-retest reliability) and valid. More research is of course needed to determine the applicability of this measure to individual patients in secondary care. Nevertheless, in the absence of a standardised, validated, medication-related problems socioeconomic measure, it is hoped that the SEIP would serve as a 'gold standard'. This of course would be possible only on the strength of its robustness, comprehensiveness, and sound measurement properties which in turn would underpin its acceptability and use by researchers as well as practitioners in the field.

As many patients do not know whether the side effects they experience are medication-related or due to their medical condition, the SEIP can be used in clinical judgement because it relates to all aspects of social interactions and emotional behaviour side effects of cardiovascular drugs. Thus, adoption of SEIP in the community setting may improve patients' compliance with their medications.

Chapter one of this thesis deals with issues related to medication-related problems and implementation of its assessment tools. Some of these risk assessment tools have been applied in clinical practice to identify and document medication errors (Westerlund et al., 2003). This chapter also demonstrated that only few of these assessment tools have been used in the community settings to identify and resolve medication-related problems (Hammerlen et al., 2007). Documentation and implementation of these MRPs risk assessment tools in the community setting could possibly be improved by developing pharmacists' versions of some of the existing MRPs risk assessment tools. The overall goal and objectives of developing these risk assessment tools were to facilitate better prescribing and improved outcomes, especially in the community.

For several years, the health policy agenda of many countries around the world has focussed on measuring and assessing the quality of health care services. In Britain for example, this policy was reinforced by the introduction of the National Patient Safety Agency and the commitment of the Department of health to reducing medical error by 40% (Morris et al., 2003). To achieve this, the use of medication-related assessment tools in the community setting is one important starting point. At present in the UK,

as a result of implementation of the new pharmacy contracts, pharmacists, especially those involved in community practice, now face many challenges as their practice changes from providing product centred to patient-oriented services (Van Mil, 2004) such as medication review, medicines management, minor ailment schemes etc in order to minimise negative outcomes of medication-related problems. In addition to all of these new initiatives and challenges, as drug prescribing and its use is increasingly becoming complex resulting in a variety of medication-related problems (Paulino et al., 2004), pharmacists have the responsibility of evaluating appropriateness of medication including dose before dispensing. This of course falls well within pharmacists' theoretical and practical training. Lack of pro-activeness on the part of pharmacists in the community setting may result in dispensing errors/medication errors. In the UK for example, current pharmacy practice is based on re-activeness largely due to pharmacies not having access to patient's notes and health record. This may result in lack of continuity of care which in turn leads to undetected medication-related problems.

The results from chapter three demonstrated that cardiovascular patients on multiple drug therapy do experience medication-related side effects. Many of the pharmacists' interventions were not dependent on the pharmacists possessing specialist knowledge about cardiovascular illness, but rather their ability to review peoples' drug regimens as a whole. Recent literature has highlighted the importance of developing strategies to better manage chronic illness such as cardiovascular disease (Bell et al., 2006). Although most of the medication-related problems, according to Paulino et al. (2004), may seem not to have direct clinical consequences, they could be associated with compliance problems which indirectly may reduce therapeutic benefits. Whenever medications are administered, there are possibilities for occurrence of certain problems that may compromise therapeutic benefits and diminish a patient's quality of life. Based on the results in chapter three, this study has demonstrated that chronically ill patients and hypertensive patients in particular, should be an important target group for pharmacists' interventions.

Chapter four described all stages involved in the development of SEIP and also established its content validity. During the developmental stages of SEIP, the expert panel reviewed the initial 31 items and raised issues related to conceptual and

linguistic aspects of the new instrument. These were subsequently resolved to the satisfaction of the panel members. Furthermore, content validity was addressed by developing items on the basis of a focus group with experts from various professional backgrounds as well as in-depth interviews with patients. The content of SEIP addresses experiences of great importance to cardiovascular patients such as social and emotional impacts of medication side effects, use of healthcare services and the impact of medication side effects on productivity. Such experiences are quite distinctively associated with medication-related problems.

One of the major areas of concern during the developmental stages of SEIP was whether the linguistic tone was fit for purpose. In fact individuals from various socioeconomic backgrounds who participated in the initial study observed no difficulties in comprehending and understanding SEIP statements. Furthermore, chapter four results confirmed that the SEIP is applicable and practical with an acceptable burden to both patients' and professionals' time. The results also confirmed that the use and administration of the SEIP required little explanation other than that given on the cover page of the questionnaire. As no published study had focused on defining social and economic implications of medication-related problems relevant to cardiovascular patients on multiple drug therapy, the content of SEIP was therefore developed primarily from a literature review. SEIP items therefore focused primarily on how patients' perception of medication side-effects impacted their physical, emotional and social functioning.

Since the objective of this study was to construct and validate an instrument to measure the social and economic impact of medication-related problems of cardiovascular drugs in the community setting, the study used both quantitative and qualitative methods to identify items, leading to the establishment of the initial twenty-four-item SEIP, consisting of: a thirteen-item domain covering "medication-related problems and socio-emotional distress"; a six-item domain covering "impacts on healthcare services utility"; a three-item domain focussing on "work and productivity"; a one-item domain covering "change in medication"; and a one-item "satisfaction with change in medication treatment" domain. Principal components analysis was conducted to assess construct validity of this initial 24-item SEIP. As described in chapter five, exploratory factor analysis revealed factors representing

social and emotional burdens of medication-related problems, the impact on healthcare resources utilization and productivity. As Fayers and Hand (1997) suggested, the fundamental aim of factor analysis is to identify groups of highly correlated variables which are relatively independent from other variables. Based on this result, the number of items in the initial version of SEIP was reduced from 24 to 19 and grouped in three domains found important to cardiovascular patients on multiple drug therapy. The scores obtained from the factor analysis were found to be internally consistent with Cronbach's alphas ranging between 0.62 and 0.74.

One important factor that makes SEIP unique among other available health measures is that its first domain includes a column that asks the respondents to comment whether they think the side effects they experience are medication-related or due to their medical condition. Consequently, most of the respondents who experienced medication side-effects did not think that some of the side-effects they perceived were as a result of this drug therapy. In fact, some were unsure as to whether the side-effects were due to their medication or their medical condition.

SEIP questionnaire was developed in order to be sufficiently short and simple in format so that it would be applicable to cardiovascular patients in the community setting as well as acceptable to pharmacy practice professionals. As described in chapter six, cardiovascular patient groups under observation in the study found that SEIP is easy to understand and complete. It only took most of the respondents on average five minutes to complete. The reliability of a new instrument is based on the assumption that the concept being measured remains constant in value. However, according to Bailey (1994), if the concept being measured does change in value, a reliable instrument should detect that change. The reliability of the SEIP was established in this study by internal consistency and test-retest reliability. The results in chapter six demonstrated that all SEIP domains possess high evidence of internal consistency as well as test-retest reliability. The reported Cronbach's alpha and the corrected item-to-total correlation coefficients supported the homogeneity of the SEIP in measuring the construct of an assessment tool. Homogeneity of the items was further affirmed, as deletion of any individual item did not increase the Cronbach's alpha by more than 0.1. Furthermore, the fact that a great majority of the patients who returned the SEIP questionnaire in the reliability study completed all parts of the

questions indicates its reliability and relevancy among cardiovascular patient populations.

Comparing the SEIP with some HRQoL instruments in an effort to evaluate its validity proved to be a challenging pursuit. It should be noted that SEIP was developed to measure the impact of medication-related problems on patients' social and economic wellbeing. Most of the existing health measures today are measuring disease impacts on patients' health-related quality of life. As a result, the choice of another measure for a comparison study with the SEIP was limited. In this study, a generic SF-12 and a cardio-specific MIDAS scales were chosen against which to test the validity of the SEIP. Nevertheless, the validation results of the SEIP described in chapter seven produced an encouraging result in terms of convergent and divergent validity. The validity results also indicated that participants who experienced one or more side-effects did not think these were medication-related. The results described in chapter 7 further demonstrated that the SEIP scores were not influenced by the patients' age and gender. However, the results of the comparison study with MIDAS scales showed that individuals above 64 years were more limited in physical activities and experienced more medication-related side-effects. The results also confirmed the already published hypothesis that both the physical and mental scales of the SF-12 are able to discriminate between age groups.

The daunting prospect of any study of such nature would be ending up with a non-valid instrument, which could compel one to go back to the drawing board. However, in this present study, the level of correlations between domains of the SEIP, SF-12 and the MIDAS left no doubt about the validity of the SEIP. One plausible question however could be: can the MIDAS scale used in the convergent validity of the SEIP be considered as a 'gold standard' measure? Although answering this question would require full re-examination of MIDAS, it suffice to reiterate that MIDAS was considered to be the most closely related measure to the SEIP among all the existing cardio-specific HRQoL measures available at the time. In addition, what is important and must be noted is the consistency of results from different types of validity tests carried out in this study. It is this collective evidence that gives support to the validity claim for the SEIP.

The aging population in Western countries means that the proportion of the population with chronic illness, especially cardiovascular disease, will increase due to lifestyle and environmental factors. This also means that the proportion of the population with cardiovascular disease will increasingly be on multiple drug therapy and inevitably prone to medication–related problems. In such scenarios, pharmacists play an important role in effective management of medication-related problems leading to optimisation of outcomes and improvement in patients' health-related quality of life.

Study Implications

The major outcome of this study was the development of a new instrument to measure social and economic impacts of medication-related side effects of cardiovascular drugs. In the absence of a 'gold standard' instrument of such nature, one of the primary implications of the SEIP will be encouragement of further research in this area of pharmaceutical care in chronic conditions. In addition, due to lack of social and economic assessment tools in this area, it gives an impetus to the use of the SEIP in both research and practice and places the SEIP in an ideal position for further refinement. Undoubtedly, with such background, the SEIP could also play a leading role for development of socioeconomic assessment tools in other chronically ill patients prone to medication-related problems.

Clearly, development of the SEIP has made philosophical contribution to the field of socioeconomic research. Indeed, the most effective way of increasing awareness about the concept of social and economic impacts of medication-related problems, as a patient-focussed outcome measure, would be through its application in community practice. Without well-designed and properly conducted studies, it would be difficult to demonstrate the value of such a novel outcome measure. Clearly, development of the SEIP has set a precedent in terms of influencing some of the attitudinal barriers towards the use of health measures in the community setting.

Study Limitations

Following completion of any piece of research, the hindsight benefits allow one to reflect on the whole events that have taken place. On reflection, any researcher will

think of a number of areas of his/her research that could have been done differently. Thus reflection on this piece of research has produced the following limitations:

- Sample size: the sample size used in chapter 3 and the validity study in chapter 7 was relatively small. A number of community pharmacists who were approached for collaboration did not show positive response probably due to their heavy workload.

- It should also be emphasized that the psychometric properties of the SEIP are established in most of the cases, from sample of elderly patients (≥ 60 years) who had intact cognitive ability. Limitations therefore exist in generalizing the results of this study to other cardiovascular populations who are community dwelling, of younger age (<50years) or with impaired cognitive function.

- As this study presents data obtained from three cardiovascular patient groups with majority of them being hypertensive and are from one to five community pharmacies across South West England and South Wales, caution should be exercised in the extrapolation of these results to other patient groups of cardiovascular disease in other parts of England and Wales.

- Although, the primary objective of this study was to evaluate both social and economic implications of medication-related problems in the community setting, however, this study did not evaluate comprehensively the economic impacts in terms of monetary costs of MRPs, instead it focuses on economic demand of MRPs on health services.

Future work

As the mean age of participants in the validity study was 63 years, future studies need to be conducted on other age group of cardiovascular patients, for example, 40 years hypertensive patients, to further examine the validity of the SEIP. Furthermore, future work should be aimed at promoting the use of the SEIP as part of the new community pharmacy initiatives in the UK for evaluation of treatment outcomes in patients with

medication-related side-effects. In addition, future work on this project should focus on economic evaluations of medication-related problems in terms of its cost implication in the community pharmacy practice.

Notwithstanding the need for additional research, it is hoped that the SEIP will become a useful tool for researchers, especially those in community pharmacy practice and who are interested in understanding the role of medication-related problems in social and economic wellbeing of not only cardiovascular patients, but also other chronically ill patients managed in the community setting. For example, given the findings that majority of the cardiovascular patients in this study did not think that the medication-related side effects have a major impact on their social and economic wellbeing such as the ability to socialise, work or how often they utilise healthcare services such as emergency visits to GP, nurses, pharmacists as a result of medication side-effects. It would be of importance to examine these attributes among other chronically ill patients such as those with asthma, other chronic obstructive pulmonary disease, and diabetes who are largely managed in the community setting.

In conclusion, it is hoped that the work presented in this thesis has made a valuable contribution to the limited existing body of knowledge in this area. In particular, it is believed that this work has enriched the much under-researched area of socioeconomic impacts of medication-related problems of cardiovascular drugs in the community setting. In addition to all efforts made in communicating the findings of this work during the course of this study, a full manuscript is under preparation for publication in reputable scientific journals in the field of community pharmacy practice.

BIBLIOGRAPHY

Acock, A. (2005). Working With Missing Values. *Journal of marriage and Family* **67**:1012-1028.

Adair, C., Marcoux, G., Cram, B. and Ewashen, C. (2007). Development and multi-site validation of a new condition-specific quality of life measure for eating disoders. *Health and Quality of Life Outcomes* **5**:23.

Allenet, B., Bedouch, P., Rose, F-X., Escofier, L., Roubille, R., Charpiat, B., Juste, M. and Conort, O. (2006). Validation of an instrument for the documentation of clinical pharmacists' interventions. *Pharm World Sci* **28**:181 - 188.

Al-Mansoori, E. (2003). The development, validation and application of an Arabic version of a general health-related quality of life measure, the Sickness Impact Profile. Easa Al-Mansoori., in *Pharmacy*, Cardiff University, Cardiff.

Alvarez-de-Toledo, F. (2004). Comment:Drug-Related Problem Classification Systems. *The Annals of Pharmacotherapy* **38**:1543-1545.

American Psychological Association. (1974). Standards for Educational and Psychological Tests, APA, Washington, DC.

Ang, RB. and Huan, VS. (2006). Academic Expectations Stress Inventory: Development, Factor Analysis, Reliability, and Validity. *Educational and Psychological Measurement* **66**:522-539.

Aqil, M., Imam, F. and Hussain, A. (2006). A pharmacovigilance study for monitoring adverse drug reactions with antihypertensive agents at a South Delhi hospital. *Int J Pharm Pract* **14**:311-313.

Asadi-Lari, M., Javadi, H., Melville, M. and Oldridge, N. (2003). Adaptation of the MacNew quality of life questionnaire after myocardial infarction in an iranian population. *Health and Quality of Life Outcomes* **1**:23.

ASCP. (2002). The American Society of Consultant Pharmacists. In : A profile of older Americans.Administraion on Aging,, US Dept. of Health and Human Services., Washington.

ASHP (1993). ASHP statement on pharmaceutical care. *Am J Hosp Pharm* **50**:1720-3.

Avis, N., Smith, K. and Hambleton, R. (1996). Development of the multidimensional index of life quality: a quality of life measure for cardiovascular disease. *Med Care* **34**:1102-1120.

Badia, X., Arribas, F., Ormaetxe, JM., Peinado, R., and De Los Terreros, MS. (2005). Development of a questionnaire to measure Health –Related Quality of Life (HRQOL) in patients with atrial fibrillation (AF-QOL). *Health and Quality of Life Outcomes* **5**:37

Bailey, K. (1994). *Methods of Social Research.* The Free Press, New York.

Bardage, C. (2000). Cardiovascular Disease and Hypertension: Population - Based Studies on Self - Rated Health and Health - Related Quality of Life in Sweden, in *ACTA UNIVERSITATIS UPSALIENSIS* pp 236, Uppsala University Sweden, Uppsala.

Barker, K., Flynn, E. and Pepper, G. (2002). Observation method of detecting medication errors. *Am J Health-Syst Pharm* **59**:2314-6.

Bartlett, MS. (1954). A note on the multiplying factors for various chi square approximations. *Journal of the Royal Statistical Society* **16**:296-298.

Battersby, C., Hartley, K., Fletcher, A., Markowe, H., Styles, W. and Sapper, H. (1995). Quality of life in treated hypertension: a case-control community based study. *J Hum Hypertens* **9**:981-986.

Beard, K. (1992). Adverse reactions as a cause of hospital admission in the aged. *Drugs and Aging* **2**:356-67.

Becker, M., Kallewaard, M., Caspers, P., Visser, L. and Leufkens, H. (2006). Hospitalisations and emergency department visits due to drug-drug interactions: a literature review. *Pharmacoepidemiology and drug safety (in press).*

Beijer, H., and Blaey, C. (2002). Hospitalisations caused by adverse drug reactions (ADR): A meta-analysis of observational studies. *Pharmacy World & Science* **24**: 46-54.

Bell, JS., Whitehead, P., Parisa, A., Mclachlan, AJ., and Chen, TF. (2006). Drug-Related Problems in the Community Setting. *Clin Drug Invest* **26** (7):415-425.

Bernhard, J., Hurny, CDT., Coates, A. and Gelber, RD. (1996). Applying quality of life principles in international cancer clinical trials., in *Spilker, B. Quality of Life and Pharmacoeconomics in Clinical Trials.* (Spilker B ed) pp pp. 693-705, Lippincott-Raven., Philadelphia.

Berry, C. and McMurray, J. (1999). A review of quality of life evaluations in patients with congestive heart failure. *Pharmacoeconomics* **16**:247-271.

Blix, H., Vikti,l K., Moger, T. and Reikvam, A. (2006). Characteristics of drug-related problems discussed by hospital pharmacists in multidisciplinary teams. *Pharm World Sci* **28**:152-158.

Blood Pressure Association. (2007). www.bpassoc.org.uk.

Bootman, J., Townsend, R. and McGhan, W. (2005). *Principles of Pharmacoeconomics*. Harvey Whitney Books Company, Cincinnati.

Borg, WR. and Gall, MD. (1983). *Educational research.* Longman., New York.

Bowling, A. (2005a). Mode of questionnaire administration can have serious effects on data quality. *Journal of Public Health.* **27**:281-291.

Bowling, A. (2005b). *Measuring Health: A review of quality of life measurement scales*. Open University Press, New York.

Boyle, GJ. (1991). Does item homogeneity indicate internal consistency or item redundancy in psychometric scales? In *Personality and Individual Differences*.

Breckenridge, A. (1991). Angiotensin converting enzyme inhibitors and quality of life. *Am J Hypertens* **4**:79S - 82S.

Bremner, A. (2003). Antihypertensive Medication and Quality of Life - Silent Treatment of a Silent Killer? *Cardiovascular Drugs and Therapy* **16**:353 - 364.

Briceland, L., Hamilton, R. and Kane, M. (1993). Pharmacy students' experience with identifying and solving drug-related problems during clinical clerkship. *Am J Hosp Pharm* **50**:294-296.

Brouwer, W., Meerding, W., Lamers, L. and Severens, J. (2005). The Relationship between Productivity and health-related QOL: An Exploration. *Pharmacoeconomics* **23**:209-218.

Buerger, D. (1999). Heading Off Medication-Related Problems, in *American Society of Consultant Pharmacists*.

Bungay, K. and Ware, J. (1993). Measuring and monitoring health-related quality of life, Upjohn, Kalamazo, MI.

Burke, L., Dunbar-Jacob, J. and Hill, M. (1997). Compliance with cardiovascular disease prevention strategies: a review of the research. *Ann Behav med* **19**:239-263.

Buurma, H., Schalekamp, T., Egberts, TCG. and De Smet, A. (2007). Compliance with National Guidelines for the Management of Drug-Drug Interactions in Dutch Community pharmacies. *Ann Pharmacother* **41**:2024-2031.

Carlberg, B., Samuelsson, O. and Lindholm, L. (2004). Atenolol in hypertension: is it a wise choice? *Lancet* **364**.

Carpenter, J. and Kenward, M. (2004) .Guidelines for handling missing data in Social Science Research, www.missingdata.org.uk.

Carter, B. and Zillich, A. (2003). Pharmaceutical care services for patients with hypertension. *The Annals of Pharmacotherapy* **37**:1335-7.

Catell, RB. (1966). The scree test for number of factors. *Multivariate Behavioural Research* **1**:245-276.

Christensen, D. and Hansen, R. (1999). Characteristics of pharmacies and pharmacists associated with the provision of cognitive services in the community setting. *J Am Pharm Assoc* **39**:640-9.

Cipolle, R., Strand, L. and Morley, P. (1998). *Pharmaceutical care practice.* McGraw-Hill, New York.

Clark, L. and Watson, D. (1995). Constructing Validity: Basic Issues in Objective Scale Development. *Psychological Assessment* **7**:309-319.

Classen, D., Pestotnik, S., Evans, R., Lloyd, J. and Burke, J. (1997). Adverse drug events in hospitalized patients. Excess length of stay, extra costs, and attributable mortality. *JAMA* **277**:301-6.

Cline, C., Bjorck-Cinne, A., Israelsson, BY., Willenheimer, RB., and Erhardt, LR. (1999). Non-compliance and knowledge of prescribed medication in elderly patients with heart failure. *Eur J Heart Failure* **1**: 145-149.

Cranor, C., Bunting, B. and Christensen, C. (2003). The Asheville Project: long-term clinical and economic outcomes of a community pharmacy diabetes care program. *J Am Pharm Assoc* **43**:173-84.

Cross, L. and Franks, A. (2005). Clinical Outcomes Associated with Pharmacist Involvement in Patients with Dyslipidemia. *Dis Manage Health Outcomes* **13**:31-42.

Curie, J., Chrischilles, E., Kuehl, A. and Buser, R. (1997). Effect of a training program on community pharmacists' detection of and intervention in drug-related problems. *J Am Pharm Assoc* **37**:182-191.

De Gucht, V., Van Elderen, T., Van Der Kamp, L. and Oldridge, N. (2004). Quality of life after myocardial infarction: Translation and validation of the MacNew Questionnaire for a Dutch population. *Quality of Life Research* **13**:1483-1488.

Dempster, M. and Donnelly, M. (2000). Measuring the health related quality of life of people with ischaemic heart disease. *Heart* **83**:641-644.

De Vaus, D. (2002). Surveys in Social Research. Routledge, London. *Fifth edition.*

Deyo, R. (1984). Measuring functional outcomes in therapeutic trials for chronic disease. *Controlled Clinical trials* **5**:223-240.

Dixon, T., Lim, L-Y., Powell, H. and Fisher, J. (2000). Psychosocial experience of cardiac patients in early recovery: A community-based study. *J Adv Nurs* **31**:1368-1375.

Donohue, J. and Pincus, H. (2007). Reducing the Societal Burden of Depression: A Review of Economic Costs, Quality of Care and Effects of Treatment. *Pharmacoeconomics* **25**:7-24.

Dougherty, CM., Dewhurst, T., Nichol, PW. and Spertus, J. (1998). Comparison of Three quality of Life Instruments in Stable Angina Pectoris: Seattle Angina Questionnaire, Short Form Health Survey (SF-36), and Quality of Life Index-Cardiac Version III. *J Clin Epidemiol.* **51**:569-575.

Douglas, H. and McLay, J. (1996). A comparative review of the adverse effects of calcium antagonists. *Drug safety* **15**:91-106.

Drummond, H., Ghosh, S., Ferguson, A., Brackenridge, D. and Tiplady, B. (1995). Electronic quality of life questionnaires: A comparison of pen-based electronic questionnaires with conventional paper in a gastrointestinal study. *Qual Life Res* **4**:21-26.

Dupuy, H. (1984). The psychological general well-being index., in *Assessment of quality of life in clinical trials of cardiovascular therapies* (Wenger N, Mattson M and Furberg C eds), Le Jacq, New York.

Ellison, J. (2003). Validation of the PCNE Drug-related problems classification (Version 3.01), pp 134, Queen's University Belfast, Belfast.

Ellrodt, G., Cook, D., Lee, J., Cho, M., Hunt, D. and Weingarten, S. (1997). Evidence-based disease management. *JAMA* **278**:1687-92.

Ernst, F. and Grizzle, A. (2001). Drug-related morbidity and mortality: updating the cost-of-illness model. *J Am Pharm Assoc* **41**:192-9.

Farris, KB., Fernandez-Llimos, F. and Benrimoj, S. (2005). Pharmaceutical care in Community Pharmacies: Practice and Research from Around the World. *The Annals of Pharmacotherapy* **39**:1539-1541.

Fayers, P. and Hand, D. (1997). Factor analysis, causal indicators and quality of life. *Quality of Life Research* **6**:139-150.

Fernandez-Llimos, F., Tuneu, L., Baena, M., Garcia-Delgado, A. and Faus, M. (2004). Morbidity and Mortality Associated with Pharmacotherapy. Evolution and Current Concept of Drug-Related Problems. *Current Pharmaceutical Design* **10**:3947-3967.

Ferrans, C. and Powers, M. (1985). Quality of life index: development and psychometric properties. *Adv Nurs Sci* **8**:15-24.

Field, T.S., Gilman, B.H., Subramanian, S. et al,. (2005). "The costs associated with adverse events among older adults in the ambulatory setting." Med Care **43**: 1171-1176.

Fillenbaum, G., Hanlon, J., Landerman, L., Artz, M., O'Connor, H., Dowd, B. and Gross, C. (2004). Impact of Inappropriate drug Use on Health services Utilization Among Representative Older Community-dwelling Residents. *Am J Geriatr Pharmacother* **2**:92-101.

Finch, H. (2006). Comparison of the Performance of Varimax and promax Rotations: Factor structure Recovery for Dichotomous Items. *Journal of Educational Measurement* **43**:39-52.

Fitzgerald, L., Hanlon, J., Shelton, P., Landsman, P., Schmader, K., Pulliam, C. and Williams, M. (1997). Reliability of a modified medication appropriateness index in ambulatory older persons. *Ann Pharmacother* **31**:543-8.

Fletcher, A., Bulpitt, C., Chase, D., Collins, W., Furberg, C., Goggin, T., Hewett, A. and Neiss, A. (1992a). Quality of Life with three antihypertensive treatments. Cilazapril, atenolol, nifedipine. *Hypertension* **19**:499 - 507.

Fletcher, A., Gore, S., Jones, D., Fitzpatrick, R., Spiegelhalter, D. and Cox, D. (1992b). Quality of life measures in healthcare 11: Design, analysis and interpretation. *British Medical Journal* **305**:1145-1148.

Fletcher, A., Palmer, A. and Bulpitt, C. (1994). Cough with angiotensin converting enzyme inhibitors: how much of a problem? *J Hypertens Suppl* **12**:S43 -S47.

Gandek, B., Kosinki, MK., and Ware, JE. (1998). Cross –validation of items selection and scoring for the SF-12 Health Survey in nine countries: Results from

IQOLA Project. International Quality of Life Assessment. *J Clin Epidemiol* **51**: 1171-1178.

Garratt, A., Hutchinson, A. and Russell, I. (2001). The UK version of the Seattle Angina Questionnaire (SAQ-UK): Reliability, Validity and Responsiveness. *Journal of Clinical Epidemiology* **54**:907-915.

Gattis, W., Hasselblad, V., Whellan. D. and O'connor, C. (1999). Reduction in heart failure events by the addition of a clinical pharmacist to heart failure team. *Arch Intern Med* **159**:1939-45.

Gaudet, W. (1998). Pharmaceutical care in a community-based setting: A pilot study of the economic, clinical and health-related quality of life outcomes., in *Pharmaceutical sciences* pp 180, Alberta University, Edmonton, Alberta.

Gaziano. (2007). Reducing The growth Burden of Cardiovascular Disease in The Developing World. *Health Affairs*. **26** (1): 13-24

Geigle, R. and Jones, S. (1990). Outcomes measurement: A report from the front. *Inquiry* **27**:7-13.

Gerstman, B., Jolson, H., Bauer, M., Cho, P., Livingston, J. and Platt, R. (1996). The incidence of Depression in New Users of beta - blockers and Selected Antihypertensives. *J Clin Epidemiol.* **49**:809 - 815.

Gorsuch, RL (1983). *Factor analysis*. Lawrence Erlbaum, Hillsdale, NJ.

Gourley, G., Portner, .T and Bass, G. (1998). Part 3. Humanistic outcomes in the hypertension and COPD arms of a multicenter outcomes study. *J Am Pharm Assoc* **38**:574-85.

Graham-Clarke, E. and Hebron, B. (1999). Hypertension, in *Clinical Pharmacy and Therapeutics* (Walker R and Edwards C eds), Churchill Livingstone, Edinburgh.

Granas, A. and Bates, I. (1999). The effect of pharmaceutical review of repeat prescriptions in general practice. *Int J Pharm Pract* **7**:264-75.

Gravetter, F. and Wallnau, L. (2000). *Statistic for the behavioural sciences.* Wadsworth, Balmont, CA.

Gray, S., Mahoney, J. and Blough, D. (2001). Medication adherence in elderly patients receiving home health services following hospital discharge. *Ann Pharmacother* **35**:539-45.

Guillemin, F., Bombardier, C. and Beaton, D. (1993). Cross-cultural adaptation of health-related quality of life measures: Literature review and proposed guidelines. *Journal of Clinical Epidemiology* **46**:1417-1432.

Guyatt, G. (1993). The philosophy of health-related quality of life translation. *Quality of Life Research* **2**:461-465.

Haase et al., (2006). Heart disease and stroke statistics-2006 update: A report from the American Heart Association Statistics committee and Stroke Statistics Subcommittee. *Circulation.* **113** (6):e85-151

Hammerlen, A., Griese, N. and Schulz, M. (2007). Survey of Drug-Related Problems Identified by Community Pharmacies. *Ann Pharmacother* **41**:1825-1832.

Hanlon, J., Schmader, K., Sams,a G., Weinberge,r M., Uttech, K., Lewi,s I., Cohen, H. and Feussner, J. (1992). A method for assessing drug therapy appropriateness. *J Clin Epidemiol.* **45**:1045-51.

Hanlon, J., Weinberger, M., Sams,a G., Schmader, K., Uttech, K., Lewis, I., Cowper ,P., Landsman, P., Cohen, H. and Feussner, J. (1996). A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy. *Am J Med.* **100**:428-37.

HAWE, E. (2008). Compendium of Health statistics. London: Office of Health Economics. 19th Edition.

Henson, R. and Roberts, J. (2006). Use of Exploratory Factor Analysis in Published Research. *Educational and Psychological Measurement* **66**:393-416.

Hillers, T., Guyatt, G. and Oldridge, N. (1994). Quality of life after myocardial infarction. *J Clin Epidemiol.* **47**:1287-1296.

Ho, K. (1994). The transition to pharmaceutical care on a geriatric unit in a community hospital. *Can J Hosp Pharm* **47**:283-287.

Hobbs, R. and Boyle, A. (2004). Heart failure, in *Medicine Index*, The Cleveland Clinic Foundation.

Hogarty, KY., Hines, CV., Kromrey, JD., Ferron, JM. and Mumford, KR. (2005). The quality of Factor Solutions in Exploratory Factor Analysis: The influence of sample size, Communality, and overdetermination. *Educational and Psychological Measurement* **65**:202-226.

http://wilderdom.com. (2004). Essentials of a Good Psychological Test, http://wilderdom.com.

Hugtenburg, J., Blom, ATG., Gopie, CTW. and Beckeringh, J. (2004). Communicating with patients the second time they present their prescription at the pharmacy: Discovering patients' drug-related problems. *Pharm World Sci* **26**:328-332.

Hunt, S., McKenna, S. and Mcewen, J. (1980). A quantitative approach to perceived health status: a validation study. *J Epidemiol Community Health* **34**:281-286.

Ijben, G., Van Mil, J., Tromp, T. and De Jong-van den Berg, L. (1999). Quantification of communication processes, is it possible? *Pharmacy World & Science* **21**:195-199.

Israili, Z. and Hall, W. (1992). Cough and angioneurotic edema associated with angiotensin - coverting enzyme inhibitor therapy. A review of the literature and pathophysiology. *Ann Intern Med* **117**:234 - 242.

Jackevicius, C., Mamdani, M., and Tu, JV. (2002). Adherence with statin therapy in elderly patients with and without acute coronary syndromes. *JAMA* **288**: 462-7.

Jameson, J. and VanNoord, G. (2001). Pharmacotherapy consultation of polypharmacy patients in ambulatory care. *Ann Pharmacother* **35**:835-40.

Johnson, A., Copas, A. and Erens, B. (2001). Effect of computer-assisted self-interviews on reporting of sexual HIV risk behaviours in a general population sample: A methodological experiment. *AIDS* **15**:111-115.

Johnson, J. and Bootman, J. (1997). Drug-related morbidity and mortality and the economic impact of pharmaceutical care. *Am J Health-Syst Pharm* **54**:554-8.

Julian, D., Prescott, R., Jackson, F. and Szeke,ly P. (1982). Controlled trial of sotalol for one year after myocardial infarction. *Lancet* **1**:1142 - 1147.

Kaasa, S., Hjermstad, M., Jordhoy, M., Wisloff, F. and Loge, J. (1998). Compliance in quality of life data: A Norwegian experience. *Statistic in Medicine* **17**:623-632.

Kaiser H (1970). A second generation Little Jiffy. *Psychometrika* **35**:401-415.

Kaiser, H. (1974). An index of factorial simplicity. *Psychometrika* **39**:31-36.

Karimova, G. and Martin, C. (2003). A psychometric evaluation of the Hospital Anxiety and Depression Scale during pregnancy. *Psychology, Health and Medicine* **8**:89-103.

Kassam, R., Martin, L. and Farris, K. (2003). Reliability of a Modified Medication Appropriateness Index in Community Pharmacies. *Ann Pharmacother* **37**:40-6.

Kline, R.B. (2005). Principles and practice of Structural Equation Modelling. The Guilford Press, ISBN 1-57230-690-4

Ko, D., Hebert, P., Coffey, C., Sedrakyan, A., Curtis, J. and Krumholz, H. (2002). Beta Blocker Therapy and Symptoms of Depression, Fatigue, and Sexual Dysfunction. *JAMA* **288**:351-357.

Koch-Weser, J. and Frishman, W. (1981). Beta-adrenoceptor antagonists: new drugs and new indications. *N Engl J Med* **305**:500 - 506.

Kramer, H. and Bloch, D. (1988). Kappa coefficients in epidemiology: an appraisal of a reappraisal. *J Clin Epidemiol.* **41**:959-68.

Krska, J., Cromarty, J., Arris, F., Jamieson, D., Hansford, D., Duffus, PR., Downie, G. and Seymour, D. (2001). Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care. *Age and ageing* **30**:205-211.

Kulich, K.R., Madisch, A., Pacini, F. et al,. (2008). Reliability and validity of the Gastrointestinal Symptom Rating Scale (GSRS) and Quality of Life in Reflux and Dyspepsia (QOLRAD) questionnaire in dyspepsia: a six-country study. *Health and Quality of Life Outcomes* **6**:12

Lacoste-Roussillon, C., Pouyanne, P., Haramburu, .F, Miremount, G. and Begaud, B. (2001). Incidence of serious adverse drug reactions in general practice: A prospective study. *Clin Pharmacol Ther* **69**:458-62.

Lassetter, J. and Warnick, M. (2003). Medical Errors, Drug-Related Problems, and Medication Errors: A literature Review on Quality of Care and Cost Issues. *J Nurs Care Qual* **18**:175-181.

Lazarou, J., Pomeranz, B. and Corey, P. (1998). Incidence of adverse drug reactions in hospitalized patients. A meta-analysis of prospective studies. *JAMA* **279**:1200 - 1205.

Leal, A., Paiv,a C., Hofe,r C., Amado, J. and Gomes, L. (2005). Evaluative and Discriminative properties of the portuguese MacNew heart Disease Health-related Quality of Life questionnaire. *Qual Life Res* **14**:2335-2341.

Leal, J., Luengo-Fernandez, R., Gray, A. et al,. (2006). Economic burden of cardiovascular diseases in the enlarged European Union. *European heart J* **27** (13):1610-1619.

Lee, D., Yu, D. and Woo, J. (2004). Validation of the Chronic Heart Failure Questionnaire (Chinese version). *Quality of Life Research* **14**:1421-1426.

Leplege, A. and Hunt, S. (1997). The problem of quality of life in medicine. *JAMA* **278**:47-50.

Lim, LL. and Fisher, J. (1999). Use of the 12-item short form (SF-12) health survey in an Australian heart and stroke population. *Quality of Life Research* **8**:1-8.

Lim L-Y, Valenti L and Knapp J (1993). A self-administered quality of life questionnaire after acute myocardial infarction. *J Clin Epidemiol.* **46**:1249-1256.

Loh E, Waruszynski B and Poston J (1996). Costs savings associated with community pharmacist interventions in Canada. *Canadian Pharm J* **2**:43-55.

Lua PL (2002). Health-Related Quality of Life assessment in Palliative cancer care: Development, Evaluation and Cross-cultural comparisons of a new instrument for use in routine clinical practice., in *Pharmacy* pp 288, Cardiff University, Cardiff.

MacCallum R, Wegener D, Uchino B and Fabrigar L (1993). The problem of equivalent models in applications of co-variance structure-analysis. *Psychol Bull.* **114**:185-199.

Machado M, Bajcar J, Guzzo G and Einarson T (2007). Sensitivity of Patient outcomes to Pharmacist Interventions. Part II: Systematic Review and Meta-Analysis in Hypertension Management. *The Annals of Pharmacotherapy* **41**:1770-1781.

Mackay, J., Mensah, G. (2004). Atlas of heart Disease and Stroke. *World Health Organisation.* Geneva.

Madejski R and Madejski T (1996) Cholesterol screening in a community pharmacy. *Am Pharm Assoc* **4**:243-8.

Martin C and Thompson DR (2000). A psychometric evaluation of the Hospital Anxiety and Depression Scale in coronary care patients following acute myocardial infarction. *Psychology, Health and Medicine* **5**:193-201.

Mayou R (1990). Quality of life in cardiovascular disease. *Psychother Psychosom* **54**:99-109.

Mccue P, Martin C, Buchanan T, Rodgers J and Scholey A (2003). An investigation into the psychometric properties of the Hospital Anxiety and Depression Scale in individuals with Chronic Fatigue Syndrome. *Psychology, Health and Medicine* **8**:425-440.

McElnay J (2004). What do researchers need from pharmacy practice?, in *Dialogue: Research meets pharmacy practice* pp 1-48, EuroPharm-PCNE Conference 2004, Pharmakon, Hillerod, Denmark.

McHorney C, Kosinska M, Ware E, Lu J and Sherbourne C (1994). The MOS 36 item short-form.Health survey (SF-36).III. Tests of data quality, scaling, assumptions, and reliability across diverse patient groups. *Med Care* **32**:40-66.

Menzin J, Foster T and Audette R (2004). Socioeconomic Implications of Long-Term Warfarin Use. *Dis Manage Health Outcomes* **12**:385-392.

METRIC. (2005). Critical review of Medication Appropriateness Index (MAI). http://www.measurementexperts.org//instrument/instrument_reviews.asp?detail=61.

Morris C, Cantrill JA and Bates J (2003) How the use of preventable drug-related morbidity indicators can improve medicines management in primary care. *The Pharmaceutical Journal* **271**:682-686.

Morrow D, Weiner M, Deer M, Young J, Dunn S, McGuire P and Murray M (2004) Patient-Centered Instructions for Medications prescribed for the treatment of Heart failure. *The American Journal of geriatric Pharmacotherapy* **2**:44-52.

Mullins C, Sikirica M, Seneviratne V, Ahn J and Akhras K (2004) Comparisons of Hypertension-Related Costs from Multinational Clinical studies. *Pharmacoeconomics* **22**:1001-1014.

Munroe W, Kunz K and Dalmady-Israel C (1997) Economic evaluation of pharmacist involvement in disease management in a community pharmacy setting. *Cli Ther* **19**:113-23.

Murphy, B. and Frig,o L. (1993). Development implementation and results of a successful multidisciplinary adverse drug reaction reporting program in a university teaching hospital. *Hosp Pharm* **28**:1199-1240.

Murray, M. (1997). Medication Appropriateness Index: putting a number on an old problem in older patients. *Ann Pharmacother* **31**:643-4.

Murray, M. and Callahan, C. (2003). Improving medication use for older adults: an integrated research agenda. *Ann Intern Med* **139**:425-429.

NCC-MERP (1998) NCC MERP Taxonomy of Medication Errors, pp 1-20, United States Pharmacopeia office, Rockville.

Nunnaly J (1978) *Psychometric Theory*. McGraw-Hill Book Company, New York.

OBrien B, Novosel S and Torrance G (1995) Assessing the economic value of a new antidepressant: A willingness to pay approach. *Pharmacoeconomics* **8**:34 - 45.

O'Connor B (2000) SPSS and SAS programs for determining the number of components using parallel analysis and Velicer's MAP test. *Behaviour Research Methods, Instruments, & Computers* **32**:396-402.

Oldridge N, Perkins A and Hodes Z (2002). Comparison of three heart disease specific health-related quality of life instruments. *Monaldi Arch Chest Dis* **58**:10-18.

Osoba D (1994). Lessons learned from measuring health-related quality of life in oncology. *journal of Clinical Oncology* **12**:608-616.

Ostergren J, Storstein L, Karlberg B and Tibblin G (1996). Quality of Life in hypertensive patients treated with either carvedilol or enalapril. *Blood press* **5**:41 - 49.

Ozsogut, B. (2001). The Development, Validation and Clinical application of the Turkish Cross - Cultural adaptation of the Sickness Impact Profile (a generic health - related quality of life measure), in *Clinical Pharmacy* pp 298, Cardiff University, Cardiff.

Palaian S, Mishra P, Shankar P, Dubey A, Bista D and Almeida R (2006). Safety monitoring of drugs - Where do we stand? *Kathmandu University Medical Journal* **4**:119-127.

Pallant J (2002). A step by step guide to data analysis using SPSS version 12, in *SPSS Survival manual. 2nd edition* pp 172-193.

Patel P and Zed P (2002). Drug-related visits to the emergency department: how big is the problem? *Pharmacotherapy* **22**:915-923.

Patrick D (2003). Patient-reported outcomes (PROs). An organizing tool for concepts, measures and applications. *Quality of Life Newsletter* **31**:1-5.

Paulino E, Bouvy M, Gastelurruita M, Guerreiro M and Buurma H (2004). Drug related problems identified by European community pharmacists in patients discharged from hospital. *Pharmacy World & Science* **26**:353-360.

Pelton R, LaValle JB, Hawkins EB and krinsky D (1999-2000). Hypertension Drug precautions and Nutrient Depletion, in *Drug-Induced Nutrient Depletion Handbook.*

Pennington D (2003). *Essential personality.* Arnold Edward.

Petrie A and Sabin C (2005). *Medical Statistics at a Glance.* Blackwell, Massachusetts.

Petrilla A, Benner J and Battleman D (2005). Evidence-based interventions to improve patient compliance with antihypertensive and lipid-loweing medications. *Int J Clin Pract* **59**:1441-1451.

Pettersen K, Reikvam A and Stavem K (2005). Reliability and validity of the Norwegian translation of the Seattle Angina questionnaire following myocardial infarction. *Qual Life Res* **14**:883-889.

Piette J, Heisler M and Wagner T (2004). Cost-Related Medication Underuse Among Chronically ill Adults: the treatments People Forgo, How Often, and Who is at risk. *American Journal of Public health* **94**:1782-1787.

Pirmohamed M, James S, Meakin S, Green C, Scott A, Walley T, Farrar K, Park B and Breckenridge A (2004). Adverse drug reactions as cause of admission to hospital: prospective analysis of 18820 patients. *BMJ* **329**:15-19.

Plumridge, R. and R. Wojnar-Horton (1998). A review of the Pharmacoeconomics of Pharmaceutical Care. *Pharmacoeconomics* **14**(2): 175-189.

Priesto, L., Thorsen, H., Juul, K (2005). Development and validation of a quality of life questionnaire for patients with colostomy or ileostomy.

Raybardhan, S., Balen, R., Partovi, N., Loewen, P., Liu, G. and Jewesson, P. (2005). Documenting drug-related problems with personal digital assistants in a multisite health system. *Am J Health-Syst Pharm* **62**:1782-7.

Rector, T. and Cohn, J. (1992). Assessment of patient outcome with the Minnesota Living with Heart failure questionnaire: Reliability and validity during a randomized, double-blind, placebo-controlled trial of pimobendan. *Am Heart J* **124**:1017-1025.

Reio, TG. and Wiswell, AK. (2006). An Examination of the Factor Structure and Construct Validity of the Gregorc Style Delineator. *Educational and Psychological Measurement* **66**:489-501.

Ribera A, Permanyer-Miralda G, Alonso J and Cascant P (2006). Is psychometric scoring of the McNew Quality of Life after Myocardial infarction questionnaire superior to the clinimetric scoring? A comparison of the two approaches. *Qual Life Res* **15**:357-365.

Routledge P and O'Mahony M (2003). Adverse drug reactions in elderly patients. *British Journal of Clinical Pharmacology* **57**:121-126.

Rupp, M. (1992). Value of community pharmacists' interventions to correct prescribing errors. *Ann Pharmacother* **26**:1580-4.

Rupp, M., De Young, M. and Schondelmeyer, S. (1992). Prescribing problems and pharmacist interventions in community Practice. *Med Care* **30**:926-40.

Salek, M. (ed) (2004). *Compendium of Quality of Life Instruments*. Euromed Communications, UK, Haslemere.

Salek M and Luscombe D (1992). Health-related quality of life assessment: A review. *Journal of Drug Development* **5**:137-153.

Samsa G, Hanlon J, Schmader K, Weinberger M, Clipp E, Uttech K, Lewis I, Landsman P and Cohen H (1994). A summated score for the Medication Appropriateness Index:development and assessment of clinimetric properties including content validity. *J Clin Epidemiol.* **47**:891-6.

Santos C and Madeira A (2003). Using the PCNE Classification in Portugal, in *PCNE Conference 2003*.

Schaefer M (2002). Discussing basic principles for a coding system of drug-related problems: the case of PI-DoC. *Pharmacy World & Science* **24**:120-127.

Schmader K, Hanlon J, Landsman P, Samsa G, Lewis I and Weinberger M (1997). Inappropriate prescribing and health outcomes in elderly veteran outpatients. *Ann Pharmacother* **31**:529-33.

Schmader K, Hanlon J, Weinberger M, Landsman P, Samsa G, Lewis I, Uttech K, Cohen H and Feussner J (1994). Appropriateness of medication prescribing in ambulatory elderly patients. *J Am Geriatr Soc.* **42**:1241-7.

Schumock G, Guenette A, Keys T and Hutchinson R (1994). Prescribing errors for patients about to be discharged from a university teaching hospital. *Am J Hosp Pharm* **51**:2288-90.

Scott K, Tobias M, Sarfati D and Haslett S (1999). SF-36 health survey reliability, validity and norms for New Zealand. *Australian and New Zealand Journal of Public Health* **23**:401-406.

Shaw -Phillips M (2002). Voluntary reporting of medication errors. *Am J Health-Syst Pharm* **59**:2326-8.

Smith D, Fassett W and Christensen C (1999). Washington State CARE project: downstream cost changes associated with the provision of cognitive services by pharmacists. *J Am Pharm Assoc* **39**:650-7.

Smith H, Taylor R and Mitchell A (2000). A comparison of four quality of life instruments in cardiac patients:SF-36, QLI, QLMI, and SEIQoL. *Heart* **84**:390-394.

Solomon D, Portner T and Bass G (1998). Part 2. Clinical and economic outcomes in the hypertension and COPD arms of a multicentre outcomes study. *J Am Pharm Assoc* **38**:574-85.

Sorensen L, Grobler M and Roberts M (2003). Development of a quality use of medicines coding system to rate clinical pharmacists' medication review recommendations. *Pharmacy World & Science* **25**:212-7.

Sorensen L, Stokes J, Purdie D, Woodward M, Elliott R and Roberts M (2004) .Medication reviews in the community: results of a randomized, controlled effectiveness trial. *British Journal of Clinical Pharmacology* **58**:648-664.

Spertus J, Winder J, Dewhurst T, Deyo R and Fihn S (1994). Monitoring the quality of life in patients with coronary artery disease. *Am J Cardiol* **74**:1240-1244.

Spertus J, Winder J, Dewhurst T, Deyo R, Prodzinski J, McDonell M and Fihn S (1995). Development and validation of the Seattle Angina Questionnaire: A new functional status measure for coronary artery disease. *J Am Coll Cardiol* **25**:333-341.

Strand L, Morley P, Cipolle R, Ramsey R and Lamsam G (1990). Drug-related problems: their structure and function. *Drug Intell Clin Pharm (Ann Pharmacother)* **24**:1093-1097.

Stroupe K, Teal E, Weiner M, Gradus-Pizlo I, Brater D and Murray M (2004). Health Care and Medication Costs and Use among Older Adults with Heart Failure. *The American Journal of Medicine* **116**:443-450.

Suh D-C, Woodall B, Shin S-K and Hermes-De Santis E (2000). Clinical and Economic Impact of Adverse Drug Reactions in Hospitalized patients. *The Annals of Pharmacotherapy* **34**:1373-1379.

Tabachnick BG and Fidell LS (2001). *Using multivariate statistics 4th edn.* HarperCollins, New york.

Testa M, Anderson R, Nackley J and Hollenberg N (1993). Quality of life and antihypertensive therapy in men. A comparison of captopril with enalapril. *N Eng J Med* **328**:907-913.

Testa M, Turner R, Simonson D, Krafcik M, Calvo C and Luque - Otero M (1998). Quality of Life and calcium channel blockeade with nifedipine GITS versus amlodipine in hypertensive patients in Spain. gastrointestinal Therapeutic System. *J Hypertens* **16**:1839-1847.

Thompson DR, Jenkinson C, Roebuck A, Lewin RJP, Boyle RM and Chandola T (2002). Development and validation of a short measure of health status for individuals with acute myocardial infarction: the myocardial infarction dimensional assessment scale (MIDAS). *Quality of Life Research* **11**:535-543.

Thomsen, L., Winterstein, A., Sondergaard, B., Haugbolle, L. and Melander, A. (2007). Systematic Review of the Incidence and Characteristics of Preventable Adverse Drug Events in Ambulatory Care. *Ann Pharmacother* **41**:1411-1426.

Thurstone, LL. (1947). *Multiple factor analysis.* University of Chicago Press, Chicago.

Treasure T (1999). The measurement of health related quality of life. *(editorial) Heart* **81**:331-332.

Tregaskis B and McDevitt D (1990). Beta-adrenoreceptor-blocking drugs in the elderly. *J Cardiovasc Pharmacol* **16**:S25 - S28.

Tullis D and Guyatt G (1995). Quality of life in cystic fibrosis. *Pharmacoeconomics* **8**:23-33.

Tully MP, Javed N and Cantrill JA (2005). Development and face validity of explicit indicators of appropriateness of long term prescribing. *Pharmacy World & Science* **27**:407-413.

Valenti, L., Lim, L-Y., Heller, R. and Knapp, J. (1996). An improved questionnaire for assessing quality of life after acute myocardial infarction. *Qual Life Res* **5**:151-161.

Van den Bemt, P., Egberts, T., De Jong-van den Berg, L. and Brouwers, J. (2000). Drug-Related Problems in Hospitalised Patients. *Drug safety* **22**:321-333.

Van Mil, J. (1999). Pharmaceutical Care- the future of pharmacy. Theory, research and Practice., in *Dept of Social Pharmacy and Pharmacoepidemiology* pp 264, University of Groningen, Groningen.

Van Mil, J. (2003). The problem of validating DRP classifications, in *PCNE proceedings 2003* pp 33-36.

Van Mil J, Westerlund T, Hersberger K and Schaefer M (2004). Drug-Related Problem Classification Systems. *The Annals of Pharmacotherapy* **38**:859-867.

Van Mil JWF (2004). Dialogue: Research meets pharmacy practice, in *Joint conference EuroPharm-PCNE* pp 47, Pharmaceutical Care Network Europe, EuroPharm Forum, and Van Mil Consultancy, The Netherlands, Pharmakon, Hillerod, Denmark.

Vik S, Hogan D and Patten S (2006). Medication Nonadherence and Subsequent Risk of Hospitalisation and Mortality among Older Adults. *Drugs Aging* **23**:345-356.

Viktil, K., Blix, H., Reikvam, A., Moger, T., Hjemaas, B., Walseth, E., Vraalsen, T., Pretsch, P. and Jorgensen, F. (2004). Comparison of Drug-Related Problems in Different Patient Groups. *The Annals of Pharmacotherapy* **38**:942-8.

Vinks, THAM., De Koning, FHP. and Egbert,s TCG. (2006). Identification of potential drug-related problems in the elderly: the role of the community pharmacist. *Pharm World Sci* **28**:33-38.

Walker, M. (2002). Health-related quality of life assessment in dementia: development of a new instrument for patients and carers., in *Pharmacy*, Cardiff University, Cardiff, Wales.

Wang, P., Bohn, R., Knight, E., Glynn, R., Mogun, H. and Avorn, J. (2002). Noncompliance with antihypertensive medications: the impact of depressive symptoms and psychosocial factors. *J Gen Intern Med* **17**:504 - 511.

Weingarten, S., Henning, J., Badamgarav, E., Knight, K., Hasselblad, V., Gano, A. and Ofman, J. (2002). Interventions used in disease management programmes for patients with chronic illness-which ones work? Meta-analysis of published reports. *BMJ* **325**:1-8.

West, R. (1991). Computing for psychologists. *Char: Harwwod Academic.*

Westerlund, T., Almarsdottir, A. and Melander, A. (1999a). Drug-related problems and pharmacy interventions in community pharmacy. *Int J Pharm Pract* 7:40-50.

Westerlund, T., Almarsdottir, A. and Melander, A. (1999b). Factors influencing the detection rate of drug-related problems in community pharmacy. *Pharmacy World & Science* **21**:245-250.

Westerlund T, Handl W, Marklund B and Allebeck P (2003). Pharmacy Practitioners' Views on computerized documentation of Drug-Related problems. *Ann Pharmacother* **37**:354-360.

Westerlund, T., Marklund, B., Handl, W., Thunberg, M. and Allebeck, P. (2001). Non prescription drug-related problems and pharmacy interventions. *Ann Pharmacother* **35**:1343-1349.

White, T., Arakelian, A. and Rho, J. (1999). Counting the Costs of Drug-Related Adverse Events. *Pharmacoeconomics* **15**:445-458.

Wilson, A., Wiklund, I. and Lahti, T. (1991). A summary index for the assessment of of quality of life in angina pectoris. *J Clin Epidemiol.* **44**:981-988.

Wu, A., Rubin, H., Mathews, W., Ware, J., Brysk, L. and Hardy, W. (1991). A health statusquestionnaire using 30 items from the Medical Outcomes Study: Preliminary validation in persons with early HIV infection. *Med Care* **29**:786-798.

Yaghmaie, F. (2003). Content validity and its estimation. *Journal of medical Education.*

Yee, D., Veal, J., Trinh, B., Bauer, S. and Freeman, C. (1997). Involvement of HMO-based pharmacists in clinical rounds at contract hospitals. *Am J Health-Syst Pharm* **54**:670-3.

Zehnder, S., Beutler, M., Bruppacher, R. and Ehrenhofer, T. (2004). Needs and use of drug information sources in community pharmacies: A questionnaire based survey in german-speaking Switzerland. *Pharm World Sci* **26**:197-202.

Zigmond, A. and Snaith, R. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* **67**:361-370.

Zwick, W. and Velicer, W. (1986). Factors influencing five rules for determining the number of components to retain. *Psychol Bull.* **99**:432-442.

PUBLICATIONS

Conference Presentation

1. Adetomilola Aderounmu, Sam Salek. Development and validation of an instrument to measure socioeconomic impacts of medication-related problems: the socioeconomic impact profile (SEIP)-oral presentation at the 35th European Symposium on Clinical Pharmacy. 18-21 October 2006. Vienna, Austria

2. Adetomilola Aderounmu, Sam Salek. Evaluating medication-related problems of cardiovascular drugs in 5 community settings using the PCNE-DRP system. Poster presentation at the 35th European Symposium on Clinical Pharmacy. 18-21 October 2006. Vienna, Austria

3. Aderounmu AO, Salek MS. Development and Validation of the Socioeconomic Impact Profile (SEIP) - Factor Analysis. Poster presentation at the 36th European symposium on Clinical Pharmacy (ESCP). 25-27 October 2007. Istanbul, Turkey

APPENDIX 1

A copy of the Pharmaceutical Care Network Europe Drug Related Problem Classification Scheme Version 5.00

(PCNE_DRP classification V5)

APPENDIX 1

DRP-Registration Form V5.00 (PCNE Classification)

Age of patient: ..... ☐ Male ☐ Female

Name of medication: ..... ☐ Rx ☐ OTC

Main active substance: ..... ☐ New ☐ Refill
(ATC-Code(s))

No of drugs taken... ☐ According to patient

☐ According to medication record

Problem discovered ☐ by patient
☐ by pharmacy Date: .../.../.....
☐ by physician

Description & comments:

Time spent on evaluation and intervention: .....min.

Date evaluation of outcome:

☐ Problem solved
☐ Problem partially solved
☐ Problem not solved

TYPE OF PROBLEM *(please tick only ONE problem)*

P1. Adverse reactions

- ☐ Side effect suffered (non allergic)
- ☐ Side effect suffered (allergic)
- ☐ Toxic effect suffered

P2. Drug choice problem

- ☐ Inappropriate drug
- ☐ Inappropriate drug form
- ☐ Inappropriate duplication of drug(-group)
- ☐ Contra-indication for drug
- ☐ No clear indication for drug
- ☐No drug but clear indication

P3. Dosing problem

- ☐ Drug dose too low or regimen not frequent enough
- ☐ Drug dose too high or regimen too frequent
- ☐ Duration of treatment too short
- ☐ Duration of treatment too long

P4. Drug Use Problem

- ☐ Drug not taken/administered at all
- ☐ Wrong drug taken/administered

P5. Interactions

- ☐ Potential interaction
- ☐ Manifest interaction

P6. Adverse events

- ☐ Side effect suffered (non allergic origin)
- ☐ Side effect suffered (allergic origin)

P7. Patient related problems

- ☐ Patient dissatisfied with therapy
- ☐ Insufficient awareness of health and disease
- ☐ Unclear complaints. Further clarification necessary
- ☐ Therapy failure (unknown reason)

CAUSE OF DRP *(max. 3 boxes to be ticked)*

C1. Drug or dose selection

- ☐ Inappropriate drug selection
- ☐ Inappropriate dosage selection
- ☐ More cost-effective drug available
- ☐ Pharmacokinetic problems
- ☐ Synergistic/preventive drug required
- ☐ Deterioration/improvement of disease state
- ☐ New symptom/indication revealed
- ☐ Manifest side effect, no other cause

C2. Drug use process

- ☐ Inappropriate timing of dosing
- ☐ Drug underused/ under-administered
- ☐ Drug overused/ over-administered
- ☐ Drug abused
- ☐ Patient unable to use drug/form as directed

C3. Information

- ☐ Instructions for use/taking not known
- ☐ Patient unaware of reason for drug treatment
- ☐ Patient has difficulties reading/ understanding
- ☐ Patient Information Form/Leaflet
- ☐ Patient unable to understand local language
- ☐ Lack of communication between health professionals

C4. Patient/Psychological

- ☐ Patient forgets to use/take drug
- ☐ Patient has concerns with drugs
- ☐ Patient suspects side-effects
- ☐ Patient unwilling to carry costs
- ☐ Patient unwilling to bother physician
- ☐ Patient unwilling to change drugs
- ☐ Patient unwilling to adapt life-style
- ☐ Burden of therapy
- ☐ Treatment not in line with health beliefs

C5. Logistics

- ☐ Prescribed drugs not available
- ☐ Prescribing error (slip of the pen)
- ☐ Dispensing error (wrong drug or dose dispensed)

C6. Others

- ☐ Other cause
- ☐ No obvious cause

TYPE OF INTERVENTION *(Max. 3 boxes to be ticked)*

I0. No intervention

I1. Prescriber level

- ☐ Prescriber informed only
- ☐ Prescriber asked for information
- ☐ Intervention proposed, approved by prescriber
- ☐ Intervention proposed, **not** approved by prescriber
- ☐ Intervention proposed, outcome unknown

I2. Patient/carer level

- ☐ Patient (medication) counseling
- ☐ Written information provided only
- ☐ Patient referred to prescriber
- ☐ Spoken to family member/caregiver

I3. Drug level

- ☐ Drug changed to .....
- ☐ Dosage changed to .....
- ☐ Formulation changed to .....
- ☐ Instructions for use changed to
- ☐ Drug Stopped
- ☐ New drug started

I4. Other

- ☐ Other intervention .....
- ☐ Side effect reported to authorities

OUTCOME OF INTERVENTION *(Tick one box only)*

O1. Solved

- ☐ Problem totally solved

O2. Partially solved

- ☐ Problem partially solved

O3. Problem NOT solved

- ☐ Lack of cooperation of patient
- ☐ Lack of cooperation of physician
- ☐ Intervention not effective
- ☐ No need or possibility to solve problem

INSTRUCTIONS FOR COMPLETING THE DRP (DRUG-RELATED PROBLEM) REGISTRATION FORM.

1. Use only one form for each drug-related problem you detect.

2. You may indicate more than one cause for a particular drug-related problem (max 3)
3. You may indicate more than one intervention made per drug-related problem (max 3)
4. If the patient's age is not known, please estimate the age within a 5 year range

5. The drug(s) involved in the drug-related problem are entered under the 'Name of medication' section

6. If the ATC-code of the drug is not known, please enter the main active substance or approved / generic name of the medicine

7. R_x relates to a prescribed drug, and OTC relates to products purchased without prescription.

8. Complete the section 'New' and 'Refill' only if the medicine involved is a prescribed medicine

9. If the patient initiates the discussion of the drug problem, tick the 'by patient' box in the 'Problem discovered:' section.

   If the drug problem is discovered by a member of the Pharmacy staff, tick the 'by pharmacy' box in the 'Problem discovered:' section

10. The 'Number of drugs prescribed' refers to the number of different prescription drugs taken by the patient, according to the patient medication profile or according
    to the patient

11. The 'Time spent on intervention' is the time spent actively involved in dealing with the drug problem. This includes time from the identification of the drug

problem, time spent in discussion with the patient, with any other health care professional, obtaining information and final communication with the patient at the resolution of the drug-related problem.

APPENDIX 2

Specimen of the letter to Pharmacies inviting them for collaboration with the study

LETTER OF RECRUITMENT OF PHARMACIES

5th April 2005

(Address)

Dear sir/ ma,

Evaluating socioeconomic impacts of medication-related problems of cardiovascular diseases management.

With regard to the above mentioned research project, I am writing to ask for permission to include your pharmacy in this project.

The aims of this research are : 1) to evaluate the impacts of medication-related problems on social and economic status of cardiovascular diseases patients and the role pharmacists are playing to minimize these socioeconomic consequences by their pro-active involvement in medicine use review, prescription interventions and active involvement in medication surveillance.

I am particularly focusing on three cardiovascular diseases patient groups; hypertension and angina patients, post- myocardial infarction patients and congestive heart failure patients. Literature research has been done on this subject and several studies about drug –related problems and pharmacists' involvement in pharmaceutical care have been identified. But so far, there has been little or no published research about pharmacists' involvement in minimizing social and economic consequences of side effects /adverse drug reactions reported by patients.

According to the NICE (2001) clinical guidelines on the treatment of myocardial infarction, heart failure and hypertension, post myocardial infarction patients with or without heart failure are offered long term treatment firstly with beta-blocker and antiplatelet drug such as aspirin, and then with statins and an ACE inhibitor (NICE,

2001). Beta-blockers and ACE inhibitors are also indicated for the management of symptoms of CHD such as angina, and also risk factors, especially hypertension together with other drug groups such as calcium channel blockers, nitrates, potassium channel activators and diuretics.

From the short description of the nature of this research, what I would like from you are: 1) collaboration in identifying patient groups who are on long term treatment with the above mentioned drug groups. They are our potential participants. This will be done through medicine use review (MUR) and prescription intervention service (PIS). Selected patients will be contacted to request for their consents and invited for free medication use review with their pharmacist. As part of my research, patients will be asked to fill SERT (socioeconomic research tool) questionnaires to evaluate impacts of any medication-related problems discovered during medicine use review on their socioeconomic status. This should not take more than 30 minutes with each patient.

I have included a copy of study protocol with this letter with full details about your involvement in the study.

From 1st April 2005, a new pharmacy contract has taken effect giving pharmacists opportunity to offer medicine use review as part of enhanced services for which they will now be fully reimbursed. This is a further development of acknowledgement of pharmacists' role as experts in pharmaceutical care. As a registered pharmacist myself, I will be willing to offer **FREE OF CHARGE** this medicine use review and other pharmaceutical care services for the patient groups involved in my research study at your pharmacy.

Your response is therefore very important to my research and I will be grateful for your interest in it.

If you would like to discuss more about this research proposal, I would be pleased to come to your pharmacy or to discuss with you by telephone. I can be contacted on

029-20668438. You can also contact my supervisor at Welsh school of pharmacy, centre for socioeconomic research Cardiff University.

I look forward to hearing from you,

Sincerely yours,

Tommy Aderounmu, MPharm, PharmD, MRPharmS

PhD research student

Dr Sam Salek
Research supervisor
Reader in Pharmacoepidemiology
Director - WSP Centre for Socioeconomic Research
Director - Postgraduate Course in Pharmaceutical Medicine
Cardiff University
Redwood Building
King Edward VII Ave
Cardiff, CF10 3XF, U

APPENDIX 3

Specimen of the invitation letter to patients for participation in the Medicine Use Review

Invitation letter to patients

Dear sir / ma,

ANNUAL REVIEW OF YOUR MEDICATIONS

From April 2005, a new range of services were introduced in community pharmacies across England and Wales to improve quality of healthcare services offered to people. One of this is called "Medicine Use Review". This service will enable people with long-term condition such as high blood pressure, heart problems etc. to discuss with their pharmacists how they have been getting on with their medications, whether any changes are needed and how they feel in general with their condition.

As part of routine standard of care we offer to our customers, we are inviting you to come forward for this review of your medications as you will surely benefit most from it. All you need to do is bring along all medications prescribed by your doctor and which you regularly take as well as any you might have bought over the counter for any other condition.

This review with your pharmacist should not take more than 30 minutes. Initially the review will be done on Wednesdays and advance booking is therefore necessary. You can make your booking by calling to pharmacy on tel. no ..... , or in case of any inconveniency contact our "medicine use review pharmacist" on mobile no: 07932736616 for alternative arrangement.

Your response is greatly appreciated.

Yours sincerely,

Pharmacy manager

Tesco pharmacy

APPENDIX 4

Specimen of the covering letter to patients in the Reliability and Validity Study

A STUDY TO SEE HOW RELIABLE IS THE SOCIO-ECONOMIC IMPACT PROFILE QUESTIONNAIRE FOR ROUTINE USE

Dear sir / ma,

The Centre for Socioeconomic Research, Cardiff University in collaboration with some community pharmacies in England and Wales is carrying out a study on how any side effects you may experience from your medication(s) is affecting your quality of life in general. We would be most grateful if you could help us by answering some questions about those side effects of your medications.

This study will help us to understand more about medication side effects and also help us to keep track of how you feel and how well we can help to minimise the impact of medication side effects on your life.

We would be most grateful if you could complete the **two enclosed questionnaires**. The first questionnaire is to be completed **today** and the second **7 days after**. Please also fill in the details on the **yellow form** and make any additional comments that you wish in the space provided on the sheet. Please return the questionnaires and the yellow form in the **pre- paid envelope** provided. If for any reason you are not able to complete the questionnaires, then please be assured that this will not affect the quality of care / service we offer you in any way.

All the information collected during this study will be kept strictly confidential. If you have any questions or would like any help in completing the questionnaire, we would be pleased to hear from you. Please feel free to contact Professor Sam Salek (tel. at work: 02920- 876017) or Tommy Aderounmu (tel: 07932736616).

Thank you once again for your assistance and cooperation.

Yours sincerely,

Prof Sam Salek Tommy Aderounmu

APPENDIX 5

Specimen of the Content Validity Assessment Form

CONTENT VALIDATION OF THE SOCIOECONOMIC IMPACT PROFILE

Introduction

Cardiovascular diseases as a leading cause of death especially in developed countries impose significant economic, humanistic and clinical burdens on both the patients and the society as a whole. Majority of patients with this chronic condition are on multiple drug therapy hence are prone to medication-related side effects. There is the need to develop an instrument which will investigate the impacts of medication side effects on a patient's quality of life, which will also include both social and economic consequences.

What is the Socioeconomic Impact Profile (SEIP)?

The Socioeconomic Impact profile (SEIP) questionnaire is a cardiovascular disease specific instrument designed to investigate the impact of medication-related side effects on socioeconomic aspects and quality of life of patients on cardiovascular drugs. As this instrument has not been used before in practice, it is important to test its applicability, reliability and validity in real patient population.

Assessment of Socioeconomic Impact Profile (SEIP)

What do you have to do?

This is the final version of the SEIP questionnaire after several amendments of its different drafts. Your tasks are:

A. to validate the content of this questionnaire by taking into consideration the following criteria listed below:

1) **Clarity** – the items must be clear, unambiguous and straightforward in their intentions.

2) **Completeness of sentence** – the included items must show a degree of relevance and reflect sample areas of interest to the observed patient population.

3) **Linguistic clarity-** the sentences should be clearly understandable, straightforward and simple. This means the sentences should be understood by anyone with a minimum knowledge of reading and writing.

4) **Relevance** – the items in each domain should be relevant to the area of interest. Remember that this instrument is cardiovascular drug specific and is designed to measure the effects of cardiovascular drugs-related side effects on socioeconomic aspects of these patients.

5) **Scaling (response) option** – to derive an overall quality score for each domain, the intention is to use Likert scaling system starting from five points to one point (five for "never", four for "a little of the time", three for "some of the time", two for "most of the time", and one for "all of the time". Total points will be divided by the total possible points (the sum of the maximum points for each item) to yield a fraction between 0 and 1. A score of 1 represents the highest quality.

B. To rate each domain and its content in accordance with a degree of agreement using the above named criteria. Then complete the assessment form included.

CONTENT VALIDITY ASSESSMENT FORM

For each of the item in the questionnaire, please put a tick in the assessment box below.

1) **Title**

	Strongly agree	**Agree**	**Disagree**	**Strongly disagree**
Clarity				
Completeness				

Linguistic clarity				
Relevance				
Scaling option				
Comments and suggestions:				

2) Introduction/Instruction

	Strongly agree	**Agree**	**Disagree**	**Strongly disagree**
Clarity				
Completeness				
Relevance & Scaling option				
Linguistic clarity				
Comments and suggestions:				

3) Global question

	Strongly agree	Agree	Disagree	Strongly disagree
Clarity				
Completeness				
Relevance				
Scaling option				
Linguistic clarity				
Comments and suggestions:				

Source: Pei Lin Lua PhD 2002

Thank you for your time and help

Appendix 6

A copy of the covering letter to patients for the Validity Study

Dear.....,

The Centre for Socioeconomic Research, Cardiff University in collaboration with community pharmacies in England and Wales is carrying out a study to assess the Socioeconomic Impact of heart condition and its treatment on daily life. It has been suggested that assessment of quality of life should be integrated into health care services in order to allow optimal patients' care.

I would be most grateful if you could complete the **three enclosed questionnaires** in the presented order (1, 2 and 3) and return them to the pharmacy in the **envelope** provided at your earliest convenience. If for any reason you are not able to complete the questionnaires, then please be assured that this will not affect the quality of care / service we offer you in any way.

All the information collected during this study will be kept strictly confidential. If you have any questions or would like any help in completing the questionnaire, I would be pleased to hear from you.

Thank you once again for your help and cooperation.

Kind regards,

Massoud

Appendix 7

Specimen of the Practicality questions

Socioeconomic Impact Profile Questionnaire

Patient ID: Date:

The questions below refer to the Socioeconomic Impact Profile questionnaire which you have just completed. Please give your best possible answer to each question.

1) How much time (in approximate minutes) did you take to complete the questionnaire?

2) How clear and understandable were the instructions and questions to you in general?

☐ Very clear ☐ Clear ☐ Not clear ☐ Very unclear

3) Do you think the questions asked are comprehensive enough to measure your social and economic well-being including quality of life?

☐ Yes ☐ No

4) If your answer to no 3 is NO, please state what additional questions would you like us to ask/ know about the effects of your medications on your quality of life?

5) Did you find any question(s) to be unsuitable, difficult or distressing to answer?

☐ Yes ☐ No

6) If yes, can you state which?

Thank you very much for your time and participation.

Appendix 8

A copy of the Myocardial Infarction Dimensional Assessment Scale (MIDAS)

Patient Identification number.....

MIDAS Quality of life questionnaire

INSTRUCTIONS

This survey asks for your views about how you have been feeling during the last 2 weeks and in what ways these affect your quality of life in general.

All responses will be treated ***in the strictest confidence.***

Answer every question by ticking the appropriate box, if you are unsure about how to answer a question, please give the best answer you can and feel free to make comments as you wish.

A Physical activity

Please tick only one circle for each question

Since your medical condition, how often during the last week have you.....

	Never	Occasionally	Sometimes	Often	Always
	5	4	3	2	1
1. Thought twice before you undertook physical activity (e.g. housework or going to the shops)?	O	O	O	O	O
2. Had angina symptoms (e.g. chest pain or tightness)?	O	O	O	O	O
3. Had angina (chest pain or tightness) that affected your life?	O	O	O	O	O
4. Felt slowed down?	O	O	O	O	O
5. Had no energy?	O	O	O	O	O
6. Been breathless?	O	O	O	O	O

7. had chest pain or tightness when undertaking physical activity?	O	O	O	O	O
8. Felt frustrated at your limitations?	O	O	O	O	O
9. Needed to rest more?	O	O	O	O	O
10. Felt you have a reduced social life?	O	O	O	O	O
11. Felt you cannot perform your domestic duties	O	O	O	O	O
12. Found the weather made your pain worse?	O	O	O	O	O

B **Insecurity**

Please tick only one circle for each question

Since your medical condition, how often during the last week have you.....

	Never	Occasionally	Sometimes	Often	Always
13. Felt frightened you will have another heart attack?	O	O	O	O	O
14. Felt isolated?	O	O	O	O	O
15. Felt lonely?	O	O	O	O	O
16. Felt anxious about travelling?	O	O	O	O	O
17. Felt vulnerable?	O	O	O	O	O
18. Felt insecure?	O	O	O	O	O
19. Felt your confidence has been affected?	O	O	O	O	O
20. Felt anxious about dying?	O	O	O	O	O
21. Worried or felt anxious about the future?	O	O	O	O	O

C Emotional reaction

Please tick only one circle for each question

Since your medical condition, how often during the last week have you.....

	Never	Occasionally	Sometimes	Often	Always
22. Felt irritable?	O	O	O	O	O
23. Felt down or depressed?	O	O	O	O	O
24. Felt bad tempered?	O	O	O	O	O
25. Felt stressed?	O	O	O	O	O

D Dependency

Please tick only one circle for each question

Since your medical condition, how often during the last week have you.....

	Never	Occasionally	Sometimes	Often	Always
26. Felt your family or friends are over protective?	O	O	O	O	O
27. Felt you have lost your independency?	O	O	O	O	O
28. Felt you have to rely on others?	O	O	O	O	O

E Diet

Please tick only one circle for each question

Since your medical condition, how often during the last week have you.....

	Never	Occasionally	Sometimes	Often	Always
29. Felt concerned about your diet?	O	O	O	O	O
30. Felt concerned about your cholesterol level?	O	O	O	O	O
31. Felt worried about your weight?	O	O	O	O	O

F Concerns over medication

Please tick only one circle for each question

Since your medical condition, how often during the last week have you.....

	Never	Occasionally	Sometimes	Often	Always
32. Worried about taking tablets?	O	O	O	O	O
33. Worried about side effects from your tablets?	O	O	O	O	O

G Side effects

	Never	Occasionally	Sometimes	Often	Always
34. Felt the cold more?	O	O	O	O	O
35. Experienced side effects (e.g. cold hands or feet / going to toilet at night) from your medications?	O	O	O	O	O

Appendix 9

A copy of the Short Form-12 health survey questionnaire

Short Form Health Survey Questionnaire
SF-12

1. In general, would you say your health is

   O Excellent
   O Very good
   O Good
   O Fair
   O Poor

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Limited a lot	**Limited a little**	**Not limited at all**
2. Moderate activities such as moving a table, pushing a vacuum cleaner, bowling or playing golf.	O	O	O
3. Climbing several flights of stairs.	O	O	O

4. During the past four weeks, have you accomplished less than you would like as result of your physical health?

   O No
   O Yes

5. During the past four weeks, were you limited in the kind of work or other regular activities you do as a result of your physical health?

   O No
   O Yes

6. During the past four weeks, have you accomplished less than you would like to as a result of any emotional problems, such as feeling depressed or anxious?

   O No
   O Yes

7. During the past four weeks, did you not do work or other regular activities as carefully as usual as a result of any emotional problems such as feeling depressed or anxious?

O No
O Yes

	Not at all	slightly	moderately	Quite a bit	Extremely
8. During the past four weeks, how much did pain interfere with your normal work, including both work outside the home and housework?	O	O	O	O	O

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
9. How much time during the past 4 weeks have you felt calm and peaceful?	O	O	O	O	O	O
10. How much of the time during the past 4 weeks did you have a lot of energy?	O	O	O	O	O	O
11. How much time during the past 4 weeks have you felt down?	O	O	O	O	O	O
12. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities like visiting with friends, relatives etc?	O	O	O	O	O	O

Thank you for your time and help