

A Community Pharmacist Delivered Therapeutics  
Outcome Monitoring Service for Hyperlipidaemia-  
(Project Number 2002-024)

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## EXECUTIVE SUMMARY

## **EXECUTIVE SUMMARY**

### **Aim of research project**

This project aimed to develop a new remunerable cognitive service in community pharmacy. The service focused on providing therapeutic outcomes monitoring to consumers with hyperlipidaemia, with the goal of enhancing medication adherence and lipid control.

### **Methods**

One hundred and eighty pharmacies in the Hawkesbury, Bankstown, Canterbury, Central, Western, and Nepean Divisions of general practice were contacted by telephone and invited to be part of the study. Pharmacies that expressed interest were sent a letter outlining the study and then re-contacted. If they remained interested, they were enrolled into the study. A total of 38 pharmacies enrolled in the study, and were randomly allocated to intervention and comparison groups (19 in each group). Pharmacists in all participating pharmacies were trained in the conduct of the study, and given continuing professional education in the area of lipid management.

Pharmacists recruited patients for the study using a variety of methods (n=142). Initial recruitment was conducted via advertising in the pharmacy using leaflets and flyers, telephone recruitment based on dispensing records, and direct contact as patients came to fill their anti-hyperlipidaemic prescriptions. Most of the pharmacies experienced difficulty recruiting their ten patients. Therefore advertorials were placed in local newspapers appropriate for the pharmacies catchments, and some pharmacists mailed letters out to their customers inviting them to participate. Twenty seven pharmacies were able to recruit at least some patients using these methods. However, out of the original 38 pharmacies only 17 remained in the study. A total of 97 patients completed the study (48 in intervention group and 49 in comparison group)

Patients in the intervention group attended the pharmacy approximately every three months at which time they had their total blood lipid levels measured using the Accutrend GC™ manufactured by Roche Diagnostics. After the lipid levels were taken and the result fed back to the patient, the patient completed a multi-part questionnaire (including a measure of adherence to their anti-hyperlipidaemic medication), with the help of the pharmacist. The pharmacist and the patient discussed any adherence and medication related issues arising on the basis of the questionnaire. Appropriate interventions were devised and recorded on sheets for both the patient to take home and for the pharmacist to keep as a record, and to serve as a data sheet for the study. Comparison group patients also attended the

pharmacy, had their blood lipid levels read and fed back to them, and completed the questionnaire, but they did not discuss issues arising out of the questionnaire with the pharmacist. Furthermore, interventions were not devised for them to aid adherence to therapy. Questionnaires were collected personally at the pharmacy by the project coordinator at which time some debriefing and further training of the pharmacists also took place.

All data were entered into, and analysed using the Statistical Package for the Social Sciences. Descriptive statistics were compiled for all quantitative data. Data were compared using a two-group independent t-test or equivalent (for non-parametric data sets). Chi-squared analysis was conducted to compare independent proportions. The *a priori* level of significance was set at 5%. Other multivariate techniques, such as repeated measures Analysis of Variance, were also used to determine changes in outcome variables over the study period.

## **Results**

### ***Clinical outcome***

Patients in the intervention group achieved a significantly greater reduction in total cholesterol levels (0.5 mmol/L) compared to those in the comparison group (0.01 mmol/L) over the study period ( $F_{(2,196)} = 5.97$ ,  $p < 0.05$ ). Thus, a principal objective of the study was achieved.

There was a 9% reduction in the total cholesterol levels of the intervention group. Taking into account the baseline difference in cholesterol levels between the two study groups, the cholesterol levels of the intervention group decreased by 6.65%. Using the data published by Gould *et al* (1998), this reduction in cholesterol levels translates to approximately 10% reduction in coronary heart disease mortality risk and an expected approximately 7% reduction in total mortality risk.

### ***Adherence measures***

Two measures of adherence were used in the study, the Brief Medication Questionnaire (BMQ), and the Medication Adherence Report Scale (MARS). Neither of these instruments, however, specifically identified information about adherence to anti-hyperlipidaemic medications. The number of people identified by the BMQ as at risk of non-adherence (ie by having a score greater than zero on any of the subscales) was low. However, this may partly be an artefact of data collection as dispensing records were not used in interpretation as the patients were not restricted to using one pharmacy throughout the study, and many used

different pharmacies. The only significant difference found between groups on the much shorter MARS scale appeared to contradict other results from the study, (clinical outcomes and patient perceptions), by indicating that by the end of the study the intervention group patients were more likely to alter their dose against medical advice than those in the comparison group. It is posited that this result may indicate that the intervention patients became more willing to report difficulties with medication adherence due to the increased strength of their bond with the pharmacists as a result of the counselling sessions.

### ***Interventions used by the pharmacists***

Although the number of interventions used by pharmacists was quite small overall, and the number of interventions declined during the period of the study (as expected with the regular contact with patients), by the end of the study pharmacists reported that the interviews conducted with the intervention group patients were still taking approximately 15 minutes to complete. This was shorter than the initial interview but similar in length to subsequent interviews. At the initial interviews the types of interventions offered usually concerned the provision of information, such as offering Consumer Medicine Information, or based on memory/routine aids to medication adherence. However, during the course of the study and for the subsequent interviews, the types of interventions changed to being more patient perception and lifestyle based.

### ***Patient perceptions***

At the start of the study there were virtually no differences in the study measures of perceptions between those in the comparison group and those in the intervention group, as measured by the study questionnaire. By the end of the study, however, those in the intervention group tended to think that they had less trouble remembering their medications, found that their medications were more convenient to take, were less likely to let side effects stop them taking their medication, had less trouble affording their medications, and were less likely to think that an organiser was likely to help them take their medications more regularly. Intervention group patients' perceptions of pharmacists and health professionals also changed over the course of the study compared to those of the comparison group. Intervention group patients felt more comfortable asking their pharmacist questions about their medications, felt that they better understood their health professionals' explanations of their anti-hyperlipidaemic medications, and felt that they had a better understanding of why they were taking their anti-hyperlipidaemic medications compared to those in the comparison group.

These changes in the intervention group would clearly be expected to promote adherence,

and better use of health professionals' expertise.

### ***Extraneous factors that may have affected lipid levels***

Patients were asked about a number of lifestyle and mood factors as well as those factors that directly related to their use of anti-hyperlipidaemic medication. Patients in the intervention group reported that compared with comparison group patients they had increased the amount of weekly exercise that they undertook during the course of the study. Patients were also asked about changes in their diet relating to 21 specific foods, including lipid lowering spreads. Those in the intervention group reported an increased use of skim milk and meat compared to those in the comparison group. There were no other differences and these small differences do not offer a strong explanation of the change in total blood cholesterol levels seen as a result of this study. However, they may indicate that the patients were in a better mindset to make better choices in general about their lifestyle which we could not capture, but may have made a difference to their cholesterol levels.

### ***Economic analysis***

There were no differences between the two groups' hospital admissions and GP visits during the course of the study, and as a result the economic analysis was conducted strictly on a cost basis.

The cost of delivering the service was between \$195 and \$236 per patient depending on the training method, and including startup costs. Once the startup costs have been discounted and the service is ongoing, the cost of the service would be approximately \$118. For this group of patients, who were reasonably well controlled at the start of the study with an average blood lipid reading of approximately 5 mmol/L, the cost to achieve an average 10% lowering of cholesterol (accounting for the differences in baseline cholesterol levels) was between \$293 and \$356 including startup costs, and approximately \$178 for an ongoing service delivery. It is posited that this is less than the cost of health service provision if the patient's blood cholesterol levels are not lowered.

## **OUTCOMES AND RECOMMENDATIONS**

1. A potentially remunerable community pharmacy based therapeutic outcomes monitoring service model for hyperlipidaemia (incorporating an adherence promoting service) was developed and evaluated.
2. Trained community pharmacists were able to deliver a therapeutic outcomes monitoring service to their patients on anti-hyperlipidaemic medications which

resulted in a lowering of their total blood cholesterol levels.

3. It is feasible to lower the total blood cholesterol levels of patients by instituting a Cognitive Pharmaceutical Service in community pharmacies.
4. The results gained suggest that the therapeutic outcomes monitoring service outlined in this study may have positive impacts, and warrants further evaluation in community pharmacies.
5. If the type of service outlined in this report is instituted or studied further, the length of the questionnaire and frequency of lipid readings used in this study should be reduced. It is posited that this would have the effect of increasing patient retention, increasing pharmacist satisfaction and reducing the cost of delivering the service.
6. If the type of service outlined in this report is instituted or studied further that the instrumentation used should be capable of taking blood lipid fractions and, if possible delivering a Framingham risk assessment. It is thought that the addition of these measures would enhance patient motivation and retention and extend the efficacy of the protocol.





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# INTRODUCTION



# 1 INTRODUCTION

## 1.1 Background

In recent years a significant proportion of the work undertaken in pharmacy research has been conducted around advances in pharmacy practice that would shift the focus of pharmacists away from product supply and toward patient-centred service delivery (Nelson, *et al.* 1984; Hepler and Strand 1990; Savage 1999; Young *et al.* 1999; Harding and Taylor 2001). A term that is commonly used to describe these types of services is cognitive pharmaceutical services (CPS) (which means that the service delivery centres on the patients' thoughts in regard to the effects and efficacy of their medications). The intention of this shift in focus is to develop cost effective services that can add value to the traditional role of the pharmacist and help create an improved health service delivery to patients. In other words, CPS seeks to utilise the professional training, experience and market position of community pharmacists. Such services can be disease specific, such as in the area of cardiovascular diseases.

Hyperlipidaemia is a major risk factor for coronary heart disease (CHD). The direct association between cholesterol levels and CHD risk was initially established by evidence from several longitudinal epidemiological studies (Anderson, Castelli & Levy 1987; Marin, Hulley & Browner 1986). More recently, trials of cholesterol-lowering therapy, (ie statins), which have included data from 30,817 patients in total, have demonstrated a near linear relationship between elevations in cholesterol level and CHD events such as angina, myocardial infarction, or sudden death (4S Group 1995; Shepherd *et al* 1995; Sacks *et al* 1996). The benefits of treating hyperlipidaemia have also been investigated by a number of large-scale randomised controlled trials. Overall, these have shown that lowering cholesterol with medication resulted in significant reductions in mortality and other cardiovascular events as well as stroke, especially in patients with established CHD (Barter *et al.* 2001).

A key issue in the management of hyperlipidaemia is ongoing adherence to therapy. Research has shown that discontinuation of lipid-lowering therapy is a significant problem (40-60% discontinuation rates 1 year after commencement of therapy: (Simons, Levis, & Simons 1996, Avorn & Monnette 1998)) with the likelihood increasing with the duration of therapy (Insull 1997). Patient non-adherence has many implications for both the individual patient and the health care system. Non-adherence can lead to reduced therapeutic outcomes or failure (Lipids Research Clinics Program 1984; Ary *et al* 1986; Inui, Yourtee, & Williamson, 1976), increased morbidity and mortality, financial costs for the patient and hospitalisation rates (Cowen *et al* 1981); changes to medication dosages (Svarstad, 1986),

wastage of medicines; higher drug costs; and an overall increase in health care costs (Murphy & Coster, 1997). It is therefore important to enhance the appropriate use of medicines through an increased understanding of the factors leading to non-adherence, and the strategies needed to address these issues.

Patients may be intentionally or non-intentionally non-adherent (Berg *et al*, 1993). Many factors have been identified which influence patient adherence (Cameron 1996; Raynor 1992). They fall under three broad categories: complexity of the medication regimen; patient understanding of the disease and therapy; and the patient-health professional relationship, including establishment of a concordant therapeutic partnership between the health care professional and the patient. Selected strategies (Osterberg and Blaschke 2005) that have already been shown to increase adherence to lipid lowering therapy include initiation of therapy in hospital, provision of clear and direct messages about the importance of adherence, inclusion of patients in the decision making about treatment and goals, using behavioural strategies, assessing adherence at each visit and the use of reminder systems (e.g. phone calls, Barter *et al* 2001). Additionally, in a meta-analysis of medication adherence, Hall, Roter and Katz (1988) found that there was a positive relationship between patient participation in the doctor/patient relationship and adherence to the medication regimen prescribed within the bounds of the participatory therapeutic relationship.

Pharmacies and pharmacists enjoy a number of advantages that places them well to deliver CPS and to develop concordant health management solutions with their clients/patients. Pharmacists are a frequent and easy point of contact in the local community, unlike General Practitioners (GPs) there is no need for appointments, for example. Additionally, consumers are more likely to take advice and to reach agreement on health management from someone they trust. In surveys of trustworthiness Australians consistently rate pharmacists amongst the most trusted members of the community (Pharmaceutical Society of Australia 2002; Sydney Morning Herald 2004). Technological advances also mean that point of care testing devices can be used in pharmacies to allow the pharmacist to be directly involved in management of lipid lowering therapies while giving patients a quick and direct measure of their cholesterol levels which can then be used to guide their therapy in relation to clinical guidelines.

Horne (1998) identified three main approaches to the study of adherence to medication; atheoretical approaches, the communication model and social cognition models. Atheoretical approaches rely on personality or demographics and have little supporting evidence in the published literature (Sackett and Haynes 1976, Bosley, Fosbury and

Cochrane 1995). Horne (1998, p286) states that communication models are not “explicitly theory driven” but draw on “implicit theory and the quality of the patient interaction with the health professional”. This approach appears to be analogous to the concept of the therapeutic alliance in which the relationship of the patient and the health professional is seen as a working alliance aimed at improving the patient’s wellbeing. The only large scale study that Horne states addresses the effect of communication model on adherence (Stewart and Ware 1992) concluded that the socio-demographic characteristics of the patients and doctors had no influence on adherence. However, socio-demographic factors are not client relationship factors, and it would appear that this measure is more suited to being a measure of the atheoretical approach than a communication model.

The communication model, Social Cognition models, including the health beliefs model (HBM) and the theory of planned behaviour (TPB) have shown that patient beliefs can alter their behaviour in relation to adherence rates (Cummings *et al* 1981, Kelly *et al* 1987) and that patients may be weighing the benefits of a regimen against the barriers (Cummings *et al* 1981). Another model of adherence behaviour that incorporates the beliefs of the patient to predict adherent behaviour is the self regulatory model of Leventhal (Leventhal, Zimmerman and Gutmann, 1984). This model has special relevance when the aim is to increase adherence to antihyperlipidaemic medication as it incorporates a feedback loop where the patient uses the medication’s effect on symptoms to assess the usefulness of the treatment and therefore their degree of adherence. Meyer, Leventhal and Guttman (1985) demonstrated that although 80% of patients in their study agreed with the statement “people cannot tell when their blood pressure is up”, 90% of patients believed that they could tell when their own blood pressure is up. Clients are not relating the objective clinical information to their own circumstances. Hyperlipidaemia, like hypertension, is asymptomatic, and in the absence of reliable feedback patients may still feel that they are able to tell when they are well or unwell, i.e. when lipid levels are low or high. A lack of reliable feedback coupled with client mis-perceptions would act as a barrier to action and may apply equally to each condition. Within this model this barrier would be addressed by providing objective feedback (monitoring devices for example), and by gaining the confidence of the patients so the patient applies the clinical information to their own circumstances. However, at the start of his overview on all of these interventions to enhance medication adherence, Horne (1998, p292) states “on reviewing the interventions literature it quickly becomes apparent that although one finds particular interventions which appear to have improved adherence in specific situations, no single intervention seems to stand out as being consistently effective”. This suggests that no one cognitive model or technique is able to account for all of the factors relating to adherence, and that different models may suit different practitioners and

patients better than others. Hence it is the therapeutic relationship, in the provision of accurate objective feedback on particular conditions that is important in determining behavioural outcomes.

On the basis of evidence from psychological studies, the counselling model chosen is not of great concern, but it is of great importance that the client is actively engaged in their treatment, feel that they have a good therapeutic alliance with their practitioner, and that in this process their beliefs in regard to their treatment are elicited. While the lack of a clearly defined successful model with which to proceed may not appear to be a positive attribute for the implementation of CPS in pharmacies, it does mean that counselling methods need not be thoroughly elucidated and pharmacists need not be highly trained in any particular psychological theory to implement CPS. Thus, years of psychological training are not necessary for successful implementation. However, pharmacists must, as a part of the process of the interview, be more sensitive to the patient's beliefs, needs and experiences and to accommodate these during the therapeutic encounter. A pharmacist who focuses on these points to establish a bond of trust and professionalism with the patient will increase their chances of a successful outcome. On the negative side for implementation it may be that some pharmacists may not generally be able to establish excellent therapeutic relationships with the majority of their patients, and it is certain that none will be able to establish excellent therapeutic relationships with all of their clients. Implementation of a therapeutic alliance approach may mean a special challenge for those pharmacists who have preferred to stay near the back of the pharmacy behind a high counter checking prescriptions.

In order to intervene to alter adherent behaviour the level of patient adherence must be measured. Both direct and in-direct methods are used to detect non-adherence (Osterberg and Blaschke 2005). Direct methods involve testing bodily fluids (usually blood or urine) for drugs, metabolites or marker substances. This has the advantage of being an objective measure. However, it is not possible to tell whether the patient has been taking the drug consistently or has just taken it prior to the testing, or whether lifestyle changes have resulted in the changed results. However, in the case of antihyperlipidaemic medication the 'lag time' between taking the medication and the effect of lowering cholesterol is unlikely to be known by the patient and thus it is unlikely that taking a dose before testing would be an effective strategy, although lifestyle changes, or medication changes may alter the tested cholesterol level. Prescription refills are another measure, but many patients use more than one pharmacy, and thus prescription refills are an unreliable measure. There are medication container caps that record the time and frequency of their being opened, however, even this

expensive measure is imperfect as a patient who does not want the medical professional to know that they are non-adherent will be able to open the cap at the correct times and still not take the medication. Self-report is an indirect measure and there are a number of scales that can be used as self-report measures for example the Brief Medication Questionnaire (Svarstad *et al* 1999) and the Medication Adherence Report Scale (Horne 2003). However, these self-report measures are subject to bias, the patient may not feel able to report the truth, or the patient may over or under estimate their adherence. Without these admittedly imperfect guides to medication adherence, doctors are generally poor at identifying non-adherence in their patients and their professional judgement in these issues has been found to be similar in reliability to tossing a coin (Becker 1985). Thus, it is true that there is no entirely accurate or simple method for identifying non-adherence (Osterberg and Blaschke 2005). However imperfect these measures of medication adherence are, it is likely that a mixture of direct and non-direct measures would be a more reliable guide than the pure guesswork that must occur in the absence of such measures.

## **1.2 Rationale for the research**

Anti-hyperlipidaemic medications are amongst the most prescribed medications in Australia, as well as one of the groups of medications with adherence issues. As such, they represent a good opportunity for the development of a remunerable Cognitive Pharmaceutical Service for community pharmacies focusing on adherence to therapy. The delivery of a service that improves adherence to anti-hyperlipidaemic medication would require the establishment of a therapeutic alliance between the practitioner and the patient coupled with regular objective feedback regarding the patients' lipid levels. All of which should be based on a sound cost benefit basis.

Pharmacists, by virtue of their roles and responsibilities, are ideally placed and skilled to provide an adherence promoting service. Such a service would include an assessment of patient adherence to therapy, identification of barriers to adherence and concordance; provision of appropriate interventions to address and promote patient adherence and concordance; and ongoing monitoring of adherence.

Similar services / interventions delivered by pharmacists have been reported in the literature (Ibrahim *et al* 1990; Shibley and Pugh 1997; Tsuyuki *et al* 1999; Nola *et al* 2000; Alldred *et al* 2001; Peterson *et al* 2004) (see Section 4.1). However, these studies have several limitations, such as small sample sizes, service delivered by hospital pharmacists, service delivered to patients discharged from a hospital on lipid lowering therapy, service delivered from a single community pharmacy, and interventions that are not based on a concordant

approach to counselling. Thus, there is a gap in the literature for a remunerable cognitive service in community pharmacy, focused on providing therapeutic outcomes monitoring to consumers with hyperlipidaemia, with the goal of enhancing medication adherence and lipid control, and based on a concordant relationship between the pharmacist and the patient.

An investigation of the impact of pharmacists in assessing and monitoring patient adherence to drug therapy and the resulting benefits to the individual patients and the health care system in general, is a crucial step to establishing a pharmacy delivered adherence service as a value-added remunerable activity.

### **1.3 Aims of research project**

This project aimed to:

- ◆ develop, implement and evaluate a new cognitive service in community pharmacy for conducting therapeutic outcomes monitoring in consumers with hyperlipidaemia, to promote patient adherence to drug therapy;
- ◆ conduct a cost-effectiveness analysis of the delivery of this service by pharmacists.

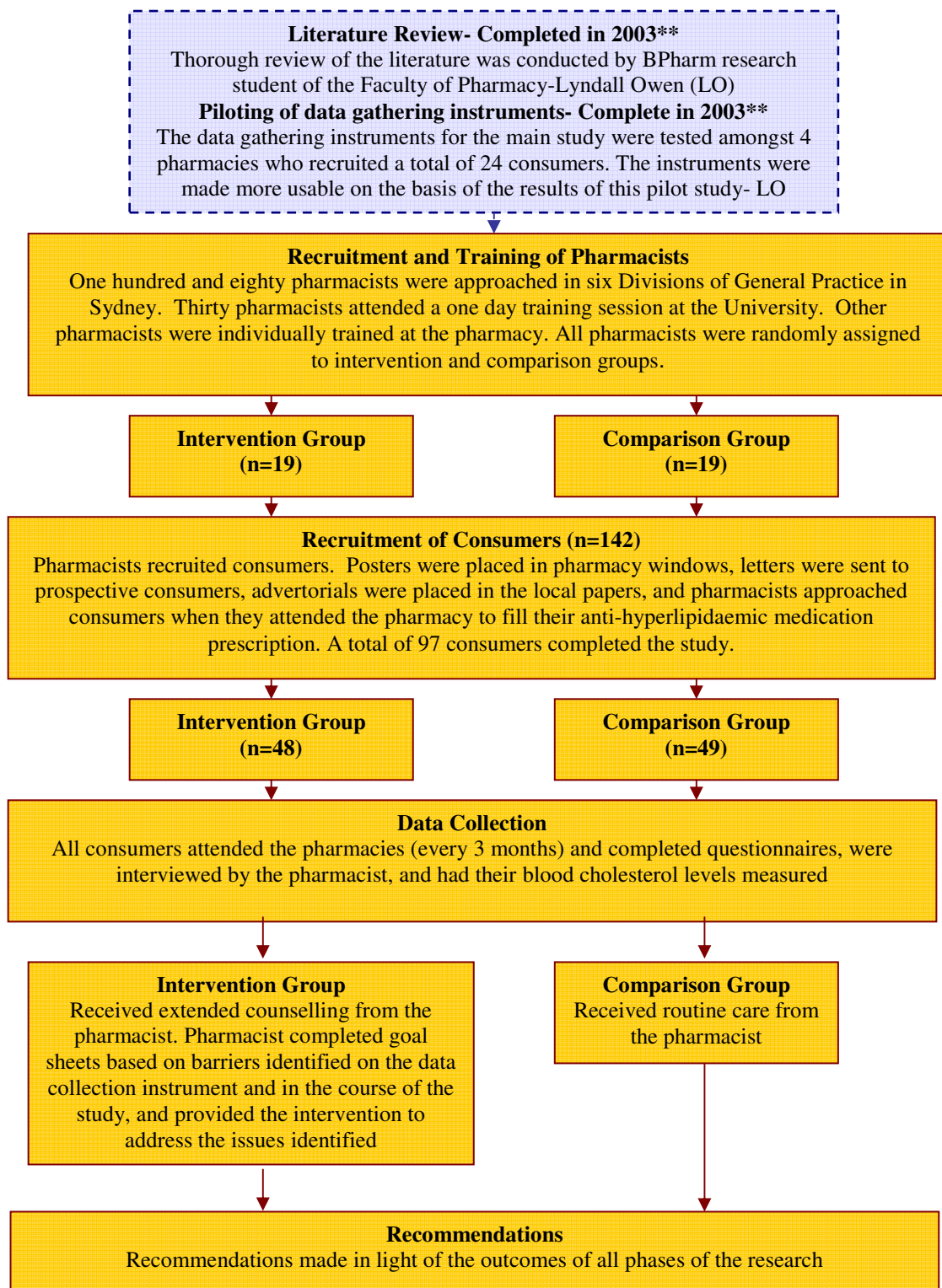
### **1.4 Objectives of research project**

The specific objectives of this research study were to:

- ◆ Develop protocols for a community pharmacy based therapeutic outcomes monitoring and medication adherence service;
- ◆ Train pharmacists in the successful delivery of the intervention.
- ◆ Implement a community pharmacy based therapeutic outcomes monitoring and medication adherence service;
- ◆ Evaluate the impact of the service on patient adherence and clinical outcomes;
- ◆ Conduct a cost-effectiveness analysis of the delivery of this service by pharmacists;

## 1.5 Research project outline

Figure 1: Research Project Outline



*\*\* Not part of the Grant, included as Appendix 1 and 2*

## **2 METHODS**

### **2.1 Target population**

#### **2.1.1 Pharmacists**

The target population consisted of pharmacists who practised in community pharmacies in the Central, Western, and Nepean Divisions of General Practice in the greater Sydney area. All community pharmacies in these divisions were invited to participate in the research project.

#### **2.1.2 Patients**

The target population consisted of patients / consumers who were currently on lipid lowering drug therapy and who presented at the participating community pharmacies with a prescription for a lipid lowering medication for themselves.

### **2.2 Sample**

#### **2.2.1 Pharmacists**

A total of 165 community pharmacies were approached in the Central, Western, and Nepean Divisions of General Practice. A further 15 pharmacies from the Hawkesbury, Bankstown and Canterbury Divisions of General Practice were also contacted. The list of the pharmacies was obtained from the Pharmacy Guild of Australia (QCPP accredited pharmacies) and separated according to Division of General Practice.

#### **2.2.2 Patients**

All participants in the study were identified by the pharmacists as taking anti-hyperlipidaemic medication. Patients were recruited by participating pharmacists according to the following inclusion criteria:

- at least 18 years of age
- able to fluently speak and read English
- taking an anti-hyperlipidaemic medication

Participants were not restricted on the basis of gender or age, nor, within the restriction imposed by the necessity to read and write English, were they restricted on the basis of ethnicity.



## **2.3 Sample size calculation**

Adherence to chronic regimens has been estimated as 10-50% (Cramer, 1995; Salzman, 1995). A 50% rate of non-adherence in the target population, and a decrease to 30% as a result of the community pharmacy based intervention was assumed. Based on these assumptions, the required sample size was 103 patients per study group ( $p=0.05$ , 80% power) (Epicentre Software, 1995). Allowing for a design effect of 1.5 owing to the clustered nature of the design, the required sample size was 150 patients from each group. To achieve this sample size we needed to recruit 30 community pharmacies (15 per study group) and enrol 10 patients per pharmacy.

## **2.4 Study procedure**

Three Divisions of General Practice were conveniently selected, and all community pharmacies within the divisions were contacted by telephone, and invited to take part in the study. The divisions selected were Central, Western and Nepean. These divisions were selected, as at the time of the study no other research projects from the Faculty of Pharmacy, University of Sydney, were being conducted in these divisions. Therefore, there was no risk of “overloading” the community pharmacies with research projects, which could in turn impact recruitment and participation in projects.

Participating pharmacists were informed of the study aims and methods. They were randomised into the two study groups: Group 1 or Intervention group, and Group 2 or Comparison group. Pharmacists recruited patients; attended training (group 1 had extended training); provided the study intervention (group 1 only); and collected data where necessary (including conducting blood cholesterol tests). The same data were collected in both groups to allow comparison of clinical and economic outcome variables. Data were collected at baseline, when the patient was first recruited into the study and then at 3 monthly intervals for a period of 9 months (that is, a total of four data collection times for each patient).

## **2.5 Recruitment process**

### **2.5.1 Pharmacists**

All community pharmacies in the Central, Western, and Nepean Divisions of General Practice in the greater Sydney area were contacted. Initial contact was via telephone call, after which informational letters were sent to interested pharmacists. A follow up telephone call was then undertaken to discuss the information with the pharmacist and to commence

enrolment into the project if the pharmacist was willing to take part. Of those 165 pharmacies approached thusly, 30 pharmacies enrolled in the study and were trained via the methods outlined in Figure 1.

Once the study had been underway for a number of months it became apparent that a number of pharmacists were unable for a number of reasons to continue in the study. It was necessary, therefore, to recruit extra pharmacies into the study. A further 15 pharmacies from the Hawkesbury, Bankstown and Canterbury Divisions of General Practice were contacted. The recruitment procedure followed was the same as for the first wave and a further 8 pharmacies were recruited into the study. All participating community pharmacists received a Subject Information Sheet about the study and completed a consent form (Appendix 4).

Of the 38 pharmacies which had commenced in the study, 11 were unable for a number of reasons to enrol any patients in the study. A further 10 pharmacies enrolled some patients in the study but were unable to continue the study until the end. There were thus 17 pharmacies that were able to usefully complete the study (take three or more readings/completed questionnaires from patients).

### **2.5.2 Patients**

Pharmacists were asked to recruit patients for the study from amongst their customer pool. To assist the pharmacists the university supplied posters and flyers (Appendix 3) and it was suggested that pharmacists also use their dispensing records to identify suitable candidates for the research. Pharmacists typically approached customers when they attended the pharmacy to have their anti-hyperlipidaemic prescriptions filled, or the customer approached them after seeing a poster advertising the study in the shop window. However, this method was not successful for many pharmacists and one pharmacist composed a letter (Appendix 3) and sent it out to those on their dispensing list. This method was successful for a further group of pharmacists; however, again, not all pharmacists benefited from this method and for those pharmacists an information article (Appendix 3) was supplied to local newspapers in the Richmond, Bankstown, and Auburn areas. The contact details of all pharmacists were included in the article if there was more than one study pharmacist in the distribution area of the paper. All papers ran the article without the need to be paid for running an advertorial.

The 27 pharmacies which were able to recruit, recruited a total of 142 patients. The number of patients enrolled varied from 3 to 10 per pharmacy. The average number of patients

within each pharmacy was 6.25 with a median of 6.5. All participating patients received a Subject Information Sheet about the study and completed a consent form (Appendix 4).

## **2.6 Training of pharmacists**

The majority of pharmacists were trained at the Faculty of Pharmacy, University of Sydney in a one-day training session (referred to as off-site training). All pharmacists attended the morning session, at the end of which pharmacists were told to which group they had been randomised. The comparison group pharmacists left and the intervention pharmacists stayed for the afternoon session which trained them in the theory and mechanics of the intervention. Follow-up training was given to all pharmacists over the telephone, by mail and in person at the pharmacy when required. Pharmacists who were unable to attend the training day were trained individually in their pharmacy or at a quiet location nearby (referred to as on-site training). These pharmacists were also afterwards given support by mail, telephone and in person.

The morning training session (Appendix 5), attended by pharmacists in both study groups consisted of:

- Introduction to the research project, concordance, adherence and measures of adherence- delivered by Dr Parisa Aslani.
- Continuing professional education on Lipids and Ischemic Heart Disease- delivered by Associate Professor Ines Krass.
- Project methods and the collection of data using the study questionnaires- delivered by Dr Grenville Rose.
- Using Accutrend GC™ in measuring total blood cholesterol levels- delivered by Roche diagnostics.

The afternoon training session, attended only by pharmacists in the intervention group consisted of the following and was delivered by Dr Parisa Aslani (Appendix 5):

- More detailed information on factors influencing adherence to therapy, strategies to address non-adherence to therapy, and components of a service to improve patient adherence to therapy.
- Focus on the delivery of a community pharmacist delivered therapeutic outcomes monitoring service (See Section 2.6.1), utilising the concept of concordance. The components of the service discussed were:
  - Assessment of the patient's adherence to therapy;
  - Assessment of the barriers and facilitators of adherence to therapy for the

patient;

- Addressing barriers to adherence;
- Delivery of targeted interventions (including tools) to promote adherence;
- Follow-up of the patient;
- Assessment of patient adherence and clinical outcomes.

Those pharmacists who were unable to be trained at the University, received one-to-one training from Dr Grenville Rose using the same training material as above (Appendix 5), including a videotape of the continuing education presented by Associate Professor Ines Krass.

### **2.6.1 Therapeutic outcomes monitoring service**

The therapeutic outcomes monitoring service was based on the literature (Appendix 1 and Du Pasquier, 2005) and findings of an earlier research project which investigated consumers' and community pharmacists' opinions about, and expectations of an adherence support service (Du Pasquier, 2005). The participants were informed that they were to receive training on the key components of the service, to acquire the knowledge and skills necessary to deliver a therapeutic outcomes monitoring service, tailored to the needs of each consumer. In delivering the service, the pharmacists were required to assess each consumer individually, and develop a strategy or intervention appropriate for the consumer to address their barriers to medication adherence, and improve their response to therapy.

The service delivered by the intervention group pharmacists included the following:

1. Assessment of the patient's adherence to therapy- Pharmacists assessed adherence through the use of the BMQ and MARS. The adherence was monitored over the course of the study.
2. Assessment of clinical outcomes- Pharmacists measured the patients' total blood cholesterol levels using the Accutrend GC™, and monitored these levels during the study period.
3. Assessment of the barriers and facilitators of adherence to therapy- Pharmacists were able to identify barriers to medication taking as well as strategies used by patients to facilitate their adherence, by using the BMQ, MARS and BMU questionnaires. They were also able to monitor changes in barriers and facilitators over the course of the study.
4. Addressing barriers to adherence- Once the barriers and facilitators to adherence were identified, the pharmacists discussed these with the patient, and reassessed

the value and impact of the strategies used by the subject (where applicable). Where appropriate they reinforced the use of the strategies, and where necessary they provided advice on alternative strategies to improve medication taking (see below).

5. Delivery of targeted interventions (including tools) to promote adherence- During this step, the pharmacists provided strategies specific to the issues raised by the patient as well as other interventions that the pharmacist felt were appropriate for the patient, such as life style and dietary advice.
6. Follow-up of the patient- Subjects were followed up three times over a period of 9 months, and all measurable study outcomes were monitored.

In summary, steps 1-3 of the service relating to subject assessment, and step 6 relating to subject follow-up, were similar for all enrolled consumers. Step 4 and 5, however, were individualised to each subject's needs.

## **2.6.2 Reimbursement of pharmacists**

Pharmacists were reimbursed for the cost of their travel to the University of Sydney for training. However, none of the participating pharmacists requested reimbursement.

Pharmacists in the intervention group received \$100.00 per patient who completed the study, while the pharmacists in the comparison group received \$25.00 per patient who completed the study.

## **2.7 Data Collection**

Data (questionnaires and total cholesterol levels) were collected at baseline and at approximately three monthly intervals for a minimum of six months, and a maximum of nine months.

### **2.7.1 Questionnaires and data sheets**

Previously validated instruments were used in collecting data from patients (Appendix 6):

- Brief Medication Questionnaire (BMQ) (Svarstad *et al* 1999)
- Medication Adherence Report Scale (MARS) (Horne 2003)
- modified version of Barriers to Medication Use Questionnaire (BMU) (Simpson *et al* 2002) which has not been validated in its present form
- shortened version of the SF12 Quality of Life questionnaire
- a demographic questionnaire based on previous questionnaires used by the Faculty of Pharmacy

- a food frequency questionnaire that was devised by the project co-ordinator, who has 10 years background in food use research. The foods selected for the questionnaire were, largely, those that had high fat and low variants, and as such would be expected to be an indicator of patients' consumption of all types of fats.
- questionnaire on visits to general practitioner and hospital admissions (to aid in the cost analysis)

The BMU as modified for this study is not validated but is based on a heart failure specific instrument (Simpson *et al* 2002). This instrument was tested on a sample of 128 subjects and demonstrated modest internal consistency in two of the five barrier domains and weaker internal consistency in the remaining three. In the original study, the relationships between BMU scores and adherence, and BMU scores and health-related quality of life were examined to test the construct validity. A negative correlation was observed between BMU and adherence, and, although not statistically significant, the authors concluded that this provided some evidence for the construct validity of the BMU questionnaire.

For this study, the BMU was modified by removal of the social support barrier domain, as this was specific to heart failure. Several questions in other domains, relating to heart failure or United States health care system were also removed. The modified questionnaire then consisted of four domains - Patient Knowledge, Previous Medication Experience, Communication and Health Care Professionals. There were 22 multiple choice questions and two open ended questions in the BMU. These asked about what information consumers are given regarding their medications and which health care professionals provide the information, practical factors affecting adherence (eg. side effects, cost of medications), how consumers receive and understand information about their condition and their relationship with their health care professionals.

The BMQ (Svarstad *et al* 1999) assesses consumer adherence to medications and problems that consumers may have with taking their medications. The different types of barriers assessed by the BMQ and the BMU warrant the use of both instruments in this study. The BMQ is a general tool which examines a consumers' whole medication regimen and assesses barriers which may impair adherence to any of the medications – for example, whether the consumer can remember to get their repeats on time, whether they can read the print on the medication labels or whether the number of medications they are taking is overwhelming. The BMU is more specific to the medications that the consumer is using to lower cholesterol – it assesses consumer attitudes towards these medications, knowledge of side effects and drug interactions and non-adherent behaviours specific to lipid lowering

drugs (eg. taking extra doses to compensate for fatty meals). The additional use of the MARS (Horne 2003) instrument acts as a check on the adherence patterns of the study participants.

The Short Form-12 Quality of Life Survey (SF-12) was used in the pilot study for the project (Appendix 2), and the results were not different from a normal population. As hyperlipidaemia is asymptomatic this is a result which could be expected and it was decided to use questions from the SF12 that indicate general mental state; peacefulness, sadness and energy levels. As exercise levels may affect total blood lipids the subjects were also asked about the number of hours of exercise they took in the month prior to the pharmacy visit.

The patient demographic questionnaire consisted of questions compiled from previous surveys used by researchers in the Faculty of Pharmacy (University of Sydney). It included items on gender and age, languages spoken at home, level of education, occupation, employment status and current medical conditions.

### ***Pharmacist data sheet***

In addition to the questionnaires administered to the patients, a pharmacist-specific instrument (the data sheet) was produced to record the strategies used by the pharmacists in response to the information gathered from the patient questionnaires.

## **2.7.2 Total blood cholesterol levels**

Total blood cholesterol levels were measured using near patient cholesterol testing by pharmacists using the Accutrend GC™ in their pharmacies. The equipment and test strips were supplied to the pharmacies as part of the research project. Accutrend GC™ has high precision and accuracy over the total blood cholesterol range of 3.88-7.75 mmol/L (Knappe, Pacht & Hattemer 1999).

All pharmacists using the Accutrend GC™ were provided with training by the company, Roche Diagnostics, to ensure the correct use of the machine. The report, "Evaluation of near patient cholesterol testing using the Cholestech LDX" (August 2001), prepared by the Department of Health and Ageing's Medical Services Advisory Committee, identified several potential benefits of using near patient cholesterol testing:

- Reductions in the number of patients lost to follow-up;
- Improved compliance to, and reduced discontinuation from, lipid-lowering medication;

- Improved lipid control;
- Alterations in the number of tests conducted; and
- Improved process-of-care and patient quality of life.

### **2.7.3 Economic evaluation**

To assist in calculating the cost/benefit of the intervention the subjects were also asked about hospital admissions and GP visits in the year prior to their taking part in the study, as well as during the period of the study.

Economic evaluation took the form of a cost effectiveness analysis in which the costs and health consequences of implementing the new adherence service were compared to “standard” care. The health consequences included in the cost effectiveness analysis were scores on BMQ and clinical measures. The costs examined included pharmacists salaries, and overhead costs including equipment, telephone calls, postage and stationery.

An incremental cost effectiveness analysis was performed. Net costs and net effectiveness associated with the Community Pharmacist Delivered Therapeutic Outcomes Monitoring Service for Hyperlipidaemia were compared with those associated with the conventional service.

As enhanced control of cholesterol has been shown to correlate with a reduction in risk of ischaemic heart disease, the measure of effectiveness used in this study was percentage reduction in total cholesterol. The main outcome measure was the incremental cost per additional 10% reduction from baseline in total cholesterol. The evaluation was conducted from the perspective of the health care provider. Only direct health service costs were considered.

Resource use was documented and unit costs for all resources provided, combined with resource volumes. In this way a net cost per patient over the study period was calculated.

## **2.8 Data analysis**

All quantitative data were entered into, and analysed using the Statistical Package for the Social Sciences, and descriptive statistics were compiled. All variables were compared at baseline and where the variables were continuous independent samples *t* tests were used to detect any differences between groups at baseline, and where the data consisted of frequency counts the  $\chi^2$  test (with Fishers exact variant used when there were small cell



sizes), was used to assess baseline differences between the study groups.

Repeated measures analysis of variance was used to assess the change in perceptions of the patients over time (the BMU results), and any differences between the study groups over time. Data from the MARS tool were also analysed using repeated measures analysis of variance. The between group differences on the scores on the BMQ were analysed using the Mann-Whitney U test with Fishers Exact Test correction due to the low numbers of subjects in each group. Independent samples *t* tests were used to assess differences in cholesterol levels between groups at baseline and repeated measures analysis of variance was calculated to assess any differences between groups over the period of the study. Where differences were observed, significant effect contrasts were calculated to determine the specific reason for the difference.

Analysis of Covariance (ANCOVA) was used to test for significant effects where it was necessary to control for co-variance (eg. where there were baseline differences).

Frequency counts were completed for hospital admissions and GP visits, but due to small numbers of patients identified with hyperlipidaemia-related hospital admissions no inferential statistics were calculated on these results. Interventions were tabulated and only a minimal amount of aggregation of the intervention descriptors was performed as the presentation of the complete set of interventions was more informative of the specific interventions delivered than aggregated results.

### ***Null Hypotheses***

The following null hypotheses were tested:

There was no statistically significant difference in the

- ❖ rates of adherence
- ❖ total blood cholesterol levels
- ❖ mean Quality of Life scores

between the comparison and intervention groups, over the study period.

### 3 RESULTS

#### 3.1 Patient recruitment and retention

A total of 142 patients were recruited into the study, however, only 97 completed the study. Of these 48 were in the intervention group and 49 in the comparison group (Table 1).

**Table 1: Patient recruitment**

Study stage	Study group	n
Non-completers	Intervention	24
	Comparison	21
Completers	Intervention	48
	Comparison	49

The mean age of the initial sample was 61 years and, as can be seen from the confidence intervals in Table 2 there are no differences between the age groups on the basis of completion/non-completion of the study, or the groups to which the participants were randomly assigned. All patients (completers vs non-completers, and intervention vs comparison groups) were compared in terms of their demographics (see Section 3.2)

**Table 2: Age of study participants**

Study stage	Study group	Mean age	95% confidence interval	Minimum	Maximum
Overall		61.4	59.5-63.3	35	85
Non-completers	Intervention	64.3	60.5-68.1	40	78
	Comparison	61.7	56.6-66.8	37	81
Completers	Intervention	58.0	55.2-60.8	35	75
	Comparison	63.6	60.1-67.1	37	85

#### 3.2 Patient demographics

The initial sample had a male bias, and had a substantial proportion of participants who were born overseas (Table 3). However, even though many participants were born overseas, the study requirement that subjects must read and write English meant that most people spoke English in the home. The average age of the initial participants was 61 years and this meant that a substantial proportion of participants were retired. In keeping with their age, and the fact that they were taking lipid-lowering medication, slightly more than one third of participants stated that they had a history of heart disease not including high cholesterol. Most did not smoke, but the incidence of diabetes in the sample was nearly 20%. The male bias evident in the initially enrolled sample remained amongst those who stayed enrolled in the study, as those who did not complete the study were nearly evenly divided between male

and female. Sixty four percent of patients who completed the study were male, and the same percentage was born in Australia, with 87% of patients speaking English at home as a main language.

While 142 people started in the study (72 intervention and 70 comparison) only 97 participants completed the study (49 comparison and 48 intervention), it is possible that the patients who stayed within the study differed from the group dropped out of the study. A comparison of the demographics of patients who stayed in the study and those who dropped out, showed that they were mostly similar. Cross tabulation using Fishers Exact Test (two sided) found that there were differences between the two groups on only one variable. People who stayed in the study were more likely to have diabetes (Table 4). An independent samples t test found that the mean age of discontinuing groups was 63 against 60 years for the continuing group ( $t_{140}=1.256$ ,  $p>0.05$ ). As the mean age for people in the study was similar, the higher incidence of diabetes is not due to a higher age amongst the continuing group. Although a higher incidence of diabetes suggests that the continuing group was less well than the non-continuing group, there were no differences on the other health indicators measured (heart disease and smoking, see Appendix 7) and therefore little support for that line of reasoning.

A statistical comparison of the demographics of patients in the intervention and comparison groups was conducted. Cross tabulation using Fishers Exact Test (two sided) found that there were no statistically significant differences between the intervention and comparison groups on any demographic measure (see Appendix 8), and thus only the overall data are presented in the main body of the report.

**Table 3: Description of sample**

Descriptors		Initial Sample (n=142)		Completed study (n=97)		Did not complete study (n=45)	
Demographic	Category	Frequency	%	Frequency	%	Frequency	%
Gender	Male	84	59	62	64	22	49
	Female	58	41	35	36	23	51
Country of birth	Australia	83	58	62	64	21	47
	Overseas	59	42	35	36	24	53
Main language	English	119	86	83	87	36	82
	Other	20	14	12	13	8	18
	Missing	3		2		1	
Other languages	English	40	31	27	31	13	30
	Other	16	12	10	11	6	14
	None	75	57	50	57	25	57
	Missing	11		10		1	
Highest level of education	None	1	1	1	1	0	0
	Primary	22	16	16	17	6	13
	Year 10	42	30	29	31	13	29
	Year 12	20	14	14	15	6	13
	Trade	34	24	24	25	10	22
	Tertiary	21	15	11	12	10	22
	Missing	2		2			
Occupation	Managers	8	6	4	4	4	10
	Professional	24	18	15	17	9	21
	Trades	26	20	18	20	8	19
	Clerical	12	9	7	8	5	12
	Production / transport	10	8	8	9	2	5
	Service	11	8	7	8	4	10
	Labourers	5	4	4	4	1	2
	Homemaker	23	18	19	20	5	12
	Student	5	4	2	2	3	7
	Other	7	5	6	7	1	2
	Missing	11		8		3	
Job status	Full time	39	32	25	32	14	32
	Part time	18	15	15	19	3	7
	Retired	51	42	27	35	24	55
	Unemployed /health reasons	11	9	8	10	3	7
	Unemployed	2	2	2	3	0	0
	Missing	21		20		1	
Familial disease	Cholesterol	35	35	28	41	7	23
	Heart disease	64	65	41	59	23	77
Have diabetes	Yes	27	19	24	25	3	7
	No	115	81	73	75	42	93
Had heart disease	Yes	50	35	38	40	12	27
	No	91	65	58	60	33	73
	Missing	1		1			
Smoker	Yes	27	19	22	23	5	11
	No	114	81	74	77	40	89
	Missing	1		1			

**Table 4: Significant differences between continuing and non-continuing study participants**

		Left study	Stayed enrolled	Total	Exact test
Do you have diabetes	Yes	3	24	27	$p=0.011$
	No	42	73	115	
	Total	45	97	142	

### 3.3 Pharmacy and Pharmacist Demographics

The 38 pharmacists who enrolled in the study were evenly divided between intervention and comparison groups, tended to be female, young and the pharmacy was situated in a shopping mall or strip pharmacy. The situation of four pharmacies was unknown as these pharmacists withdrew from the study before the investigator visited their pharmacy (Table 5).

**Table 5: Demographics of initially enrolled pharmacists and pharmacies**

Characteristic	Category	n
Study Group	Intervention	19
	Comparison	19
Gender	Male	15
	Female	23
Age Group (years)	Under 35	11
	35-50	18
	Over 50	8
	Unknown	1
Pharmacy Location	Shopping mall	10
	Strip	23
	Stand alone	1
	Unknown	4

The 17 pharmacists who completed the study (nine in intervention group, eight in comparison group) tended to be male, under 50 years of age and their pharmacies were mainly situated either in a shopping strip or shopping mall. Although not statistically significant, the intervention pharmacists tended to be younger and their pharmacies situated in shopping malls compared to the comparison group pharmacists (Table 6).

The data for patient completions of the 17 pharmacists who remained in the study are presented in Table 7.

**Table 6: Demographics of completing pharmacies and pharmacists**

Demographics	Study Group	
	Intervention Group (n=9) n (%)	Comparison Group (n=8) n (%)
Pharmacist gender		
Male	6 (67)	4 (50)
Female	3 (33)	4 (50)
Pharmacist age group in years		
Under 35	6 (67)	1 (12.5)
35 – 50	1 (11)	5 (62.5)
Over 50	2 (22)	2 (25)
Pharmacy Location		
Strip	5 (56)	6 (75)
Shopping Mall	4 (44)	1 (12.5)
Stand Alone	0	1 (12.5)

**Table 7: Number of patients who completed the study by pharmacy group**

Condition	Mean	Median	Minimum	Maximum
Intervention	6	6.5	3	9
Comparison	6.5	6.5	3	10

### 3.4 Clinical outcome- total blood cholesterol levels

The clinical measure of adherence in the study was the level of total cholesterol as measured in the pharmacy using the Accutrend GC™ near patient testing device, and this measure is thus the main outcome measure of the study.

The average number of days between measurements was 108,102, and 99 days for the first, second and third readings, respectively. Analysis of the baseline cholesterol scores showed that, even though pharmacies, and thus patients, were randomly allocated to intervention and comparison groups, there was a difference between the mean cholesterol levels of the two groups at baseline (Table 8 and Appendix 9).

**Table 8: Mean total cholesterol levels for each group (mmol/L) at baseline, middle and end of study.**

Time	Intervention (n=48)		Comparison (n=49)		Difference between groups	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
Time 1- baseline	5.10	4.88-5.32	4.81	4.57-5.05	0.29	-0.04-0.62
Time 2- middle of the study	4.95	4.69-5.21	4.73	4.47-4.99	0.22	-0.14-0.58
Time 3- end of study	4.63	4.37-4.89	4.80	4.54-5.06	0.17	-0.19-0.53

The intervention group started with a slightly higher cholesterol level, (intervention/comparison, 5.10/4.81 mmol/L,  $t_{150}=2.015$ ,  $p<0.05$ ) and thus had more possibility of lowering their cholesterol during the course of the study. Hence two different analyses were performed on the results over time. The first was an Analysis of Covariance (ANCOVA), which corrects for the differences in the baseline readings, but does not allow for problems specific to repeated measure analysis (eg. autocorrelation). The second analysis conducted was a repeated measures Analysis of Variance (ANOVA). ANCOVA showed that there was a difference between the intervention and comparison groups and that there were differences between the covariates at the 95% confidence level (Table 9).

**Table 9: ANCOVA results for differences in cholesterol differences between the intervention and comparison groups**

Source	df	F	Sig.
Corrected Model	3	51.94842	0.00
Intercept	1	15.21617	0.00
2 <sup>nd</sup> reading	1	23.25101	0.00
3 <sup>rd</sup> Reading	1	31.96298	0.00
Group	1	6.842553	0.01
Error	96		

Repeated measures ANOVA showed that there was a significant difference in mean cholesterol readings between the intervention and comparison groups across the course of the study ( $F_{(2,196)}=5.97$   $p<0.05$ ), that the two groups differed in the way their scores changed during the course of the study ( $F_{(2,196)}=6.168$   $p<0.05$ ), and that this difference was due to the cholesterol levels of the intervention group dropping significantly between Time 2 and 3 ( $F_{(1,98)}=11.3$ ,  $p<0.01$ ). Intervention subjects in the study, then, significantly lowered their cholesterol over the time periods measured whereas those in the comparison group did not. There has, thus, been a significant positive outcome of the intervention.

Thus, the study hypothesis, that there were no statistically significant differences found in the mean total blood cholesterol levels between and within the two study groups over the course of the study, is rejected.

### **3.5 Adherence measure outcomes**

#### **3.5.1 Brief Medication Questionnaire**

Measures of adherence were the Brief Medication Questionnaire (BMQ), and the Medication

Adherence Report Scale (MARS). There were few patients who were identified by the regimen subscale of the BMQ as having a potential problem with non-adherence, a total of only 17 instances during the study (Table 10). A Mann-Whitney U test using Fishers Exact test correction on this small number of cases revealed no significant difference between the two groups ( $U=16.05$ ,  $p>0.05$ ) during the study period.

The very low numbers of patients identified as having a potential problem with their regimen means that it is impossible to conduct meaningful statistics on differences between groups at each time point. However, inspection of Table 11 reveals that there is little difference between groups at any of the intervals.

**Table 10: Total number of instances of intervention and comparison patients identified as potentially having an adherence problem with the BMQ**

BMQ Regimen Subscale Score	Intervention (n)	Comparison (n)
2	3	3
3	3	2
4	0	1
5	0	2
7	0	2
8	0	1
<b>Total</b>	6	11

**Table 11: BMQ Regimen subscale score for each time interval**

Time interval	BMQ Regimen Subscale Score	Intervention (n)	Comparison (n)
1	2	1	1
	3	1	1
	7	0	1
	8	0	1
	<b>Total</b>	2	4
2	3	1	1
	4	0	1
	5	0	1
	7	0	1
	<b>Total</b>	1	4
3	2	2	2
	3	1	0
	5	0	1
	<b>Total</b>	3	3

The means, medians and confidence intervals reflect this very low scoring on the BMQ



regimen subscale (Table 12)

**Table 12: Mean, median and confidence intervals of the BMQ regimen subscale scores at each interval**

	Time 1			Time 2			Time 3		
	Mean	Median	95% CI	Mean	Median	95% CI	Mean	Median	95% CI
Intervention	0.19	0	0.06-0.32	0.18	0	0.02-0.34	0.23	0	0.06-0.40
Comparison	0.25	0	-0.02-0.52	0.38	0	0.07-0.69	0.11	0	-0.01-0.23

There were very few patients who had a significant score on the belief screen of the BMQ, a total of 10 instances across the entire study. The breakdown for each interval is shown in Table 13.

**Table 13: Numbers of patients who had a significant score on the BMQ belief screen**

Time	Intervention (n)	Comparison (n)	Total
1	3	1	4
2	1	0	1
3	1	4	5

The means, medians and confidence intervals for the belief subscale support the small numbers of patients found to have a positive score on the belief subscale of the BMQ (Table 14).

**Table 14: Mean, median and confidence interval of the BMQ belief subscale**

	Time1			Time 2			Time 3		
	Mean	Median	95% CI	Mean	Median	95% CI	Mean	Median	95% CI
Intervention	0.24	0	0.10-0.38	0.02	0	-0.03-0.07	0.17	0	0.07-0.27
Comparison	0.20	0	0.08-0.32	0.11	0	0.01-0.21	0.16	0	0.08-0.24

There were 21 patients (10 of whom were comparison patients) who stated at least one concern about using their anti-hyperlipidaemic medication. The main concerns that people had were: the general health effects of having to take medicines all the time, side effects and the inconvenience of having to take the medicine (Table 15).

**Table 15: Patient concerns about anti-hyperlipidaemic medication use over the study period**

Concern	Number of patients
General health worries	7
Muscle aches	3
Other side effects	9
Inconvenience	2

Regarding the recall questions: as anti-hyperlipidaemic medications are generally given as a single daily dose, there were few participants who were on a multiple dose regimen, nine people in total, across both groups. Of these nine people there was one subject, who was in the intervention group, who also thought that they had trouble remembering to get their repeats on time, and thus had a positive score on the recall screen of the BMQ. These very low numbers are supported by the means and medians of the complete set of scores for subjects at each time interval (Table 16).

**Table 16: Means, medians and confidence intervals of patient scores on the BMQ recall subscale of the BMQ**

	Time 1			Time 2			Time 3		
	Mean	Median	95% CI	Mean	Median	95% CI	Mean	Median	95% CI
Intervention	0.09	0.0	0-0.18	0.25	0.00	0.11-0.39	0.21	0.00	0.06-0.36
Comparison	0.17	0.0	0.08-0.26	0.08	0.00	0.01-0.15	0.16	0.00	0.05-0.27

### 3.5.2 Medication Adherence Report Scale

The MARS, a 5 question measure of patient adherence behaviour and beliefs, was also used as an additional measure of patient adherence. There were two questions on the MARS tool that showed significant differences (Appendix 10). Table 17 shows that patients were less likely to report that they would take less than the prescribed dose after the first time interval (main effect  $F_{2,178}=4.3$ ,  $p<0.05$ , contrast  $F_{1,89}=5.7$ ,  $p<0.05$ ).

**Table 17: Mean reported likelihood of taking less than the required dose (1= always, 5=never)**

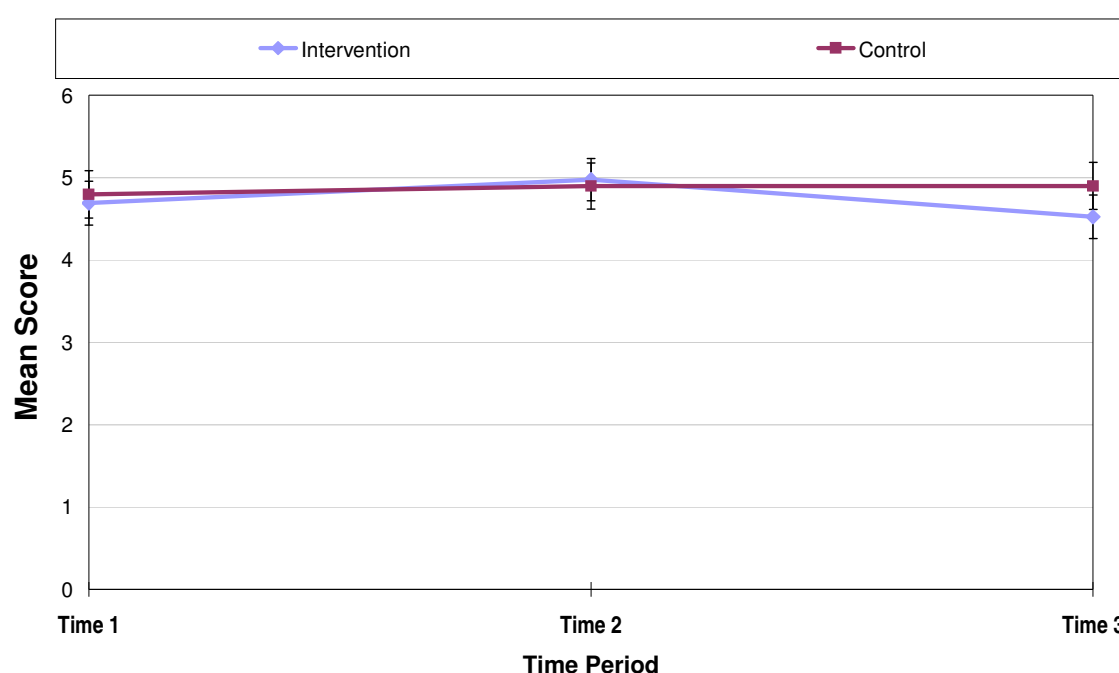
	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
Intervention (n=42)	4.57	4.44-4.70	4.93	4.89-4.97	4.86	4.80-4.92
Comparison (n=49)	4.88	4.76-5.00	4.96	4.92-5.00	4.94	4.89-4.99

Analysis of the patient's reported tendency to alter the dose that was recommended by their

general practitioner (GP) (**Figure 2**) shows that there were overall differences across the different time intervals ( $F_{2,178}=4.26$   $p<0.05$ ), and that this main effect was due to differences between the mean scores at the first and second readings ( $F_{1,89}=7.03$   $p<0.05$ ). However there was also a significant difference in the way the groups responded at the three time intervals ( $F_{2,178}=3.68$   $p<0.05$ ) and this was due to the intervention group reporting that, compared with the comparison group, they were more liable to alter the dose of their medication at the third reading compared to the second reading ( $F_{1,89}=4.97$   $p<0.05$ ).

**Figure 2: Reported tendency of patients to alter the dose recommended by their GPs**

(1= Always, 5=Never)



The power of the study was reduced to 44% ( $p=0.05$ , 2 sided, non-adherence reduced from 50% to 30%) (Epicentre Software, 1995) as a result of the total number of subjects recruited into the study ( $n=97$ ).

Based on the results of the BMQ and MARS, and the smaller than expected sample size of participants, it was not possible to test the study hypothesis that there were no statistically significant differences in the adherence rates, between or within, the two study groups.

### 3.6 Interventions delivered by pharmacists

The pharmacists in the intervention group used the results of the Barriers to Medication Use Questionnaire (BMU) and the shortened version of the SF12 Quality of Life Questionnaire, to

provide the interventions to the patients.

At Time 1, all of the 48 subjects in the Intervention group who completed the study received an intervention with only 4 subjects receiving 4 documented interventions (Table 17a). By Time 3, only 16 of the 48 subjects received an intervention, and 1 subject received 4 interventions.

**Table 17a: Number of interventions received by number of subjects in the Intervention group**

Time	Number of subjects receiving intervention(s)			
	Received 1 intervention	Received 2 interventions	Received 3 interventions	Received 4 interventions
1	48	23	12	4
2	21	6	2	1
3	16	1	1	1

### 3.6.1 Baseline (Time 1)

There were a total of 87 interventions delivered by pharmacists at baseline for the 51 patients in the intervention group. The most common intervention at baseline (1<sup>st</sup> time period) was discussing the use of a reminder or discussing a routine to assist patients in taking their medication regularly (Table 18).

**Table 18: Memory based reminders used at baseline (Time 1)**

Intervention used	Number of times used
Routine and triggers for reminding	6
Reminder when repeat is due	5
Medication reminders	1
Monthly reminder suggested due to forgetting to take meds	1
Suggested organiser, but patient declined	1
Suggested time of day	1
Organiser discussed	1
Encourage routine	1
Flow chart given for routine	1
<b>TOTAL</b>	<b>18</b>

The next most common intervention used by the pharmacists was to provide information about the individual patient's need for taking their anti-hyperlipidaemic medication. These were information/cognitive interventions that would be expected to influence patients' beliefs about the need/effectiveness of their medication use and are largely targeted at patient

beliefs about the medication that may be caused by the asymptomatic nature of hyperlipidaemia (Table 19).

**Table 19: Informational/cognitive interventions regarding asymptomatic nature and natural history of the condition used at baseline (Time 1)**

<b>Intervention used</b>	<b>Number of times used</b>
Long term advantage of cholesterol medicines explained	8
Disease state discussed	2
Counselled on correct cholesterol level target re National Heart Foundation	1
Counselled on need for cholesterol medicines	2
Counselled on need for cholesterol medicines in light of expressed belief that a cholesterol level of 5.3 mmol/L was good	1
Long term effects of high cholesterol discussed	1
Explained reasons for taking medicines	2
<b>TOTAL</b>	<b>17</b>

Consumer Medicine Information (CMI), verbal information and other written information, was also frequently used to assist patients in taking their medication. This information was directly related to the medicines themselves and would be expected to influence patient beliefs by more fully informing the patient about their medication. CMI was sometimes given in response to patient request during the course of the interview (Table 20).

**Table 20: Consumer Medicine Information interventions used at baseline (Time 1)**

<b>Intervention used</b>	<b>Number of times used</b>
CMI discussed	4
CMI discussed with specific emphasis on side effects	1
CMI provided	4
Verbal information and CMI given	1
CMI reviewed	1
Reviewed CMI with patient in response to interview	1
Verbal and written information given as a result of patient request	1
<b>TOTAL</b>	<b>13</b>

The focus of the study was on adherence to medication, and there was no suggested intervention in the study regarding diet. Nevertheless, a number of pharmacists, in an effort to improve the health of their patients, recommended dietary and exercise-based changes. There were a total of eight dietary and exercise recommendations made, and these interventions are shown in Table 21.

**Table 21: Dietary and exercise interventions used at baseline (Time 1)**

<b>Intervention used</b>	<b>Number of times used</b>
Diet and exercise advice offered	2
Recommended exercise	2
Healthy diet reinforced as patient reported no concerns about medicines	1
Dietary advice provided	1
Dietary change suggested	1
No problems identified, dietary and exercise advice given	1
<b>TOTAL</b>	<b>8</b>

There were, in addition, another 31 miscellaneous interventions used. These included discussion of side effects (7), referral back to GP (7), encouragement to become more involved in consultations with GP (4) and a small assortment of other interventions (Table 22).

**Table 22: Miscellaneous interventions used at baseline (Time 1)**

<b>INTERVENTION USED</b>	<b>NUMBER OF TIMES USED</b>
Patient encourage to become more involved in discussing their condition with doctors	4
Referred to GP	8
Side effects discussed	7
Safety net	4
Label lettering discussed	1
medicine brands reviewed	1
Medication pack reviewed due to patient concerns	1
Correct use of medicines explained	1
Pill boxes discussed	1
Provided information (details not specified)	2
Patient indicated difficulty in opening bottle, brand change or assistance from partner suggested	1
<b>TOTAL</b>	<b>31</b>

### 3.6.2 Time 2

There was a sharp fall in the number of interventions used at Time 2, with only 30 interventions given. This is less than the number of intervention subjects and thus there were a number of subjects who received no formal intervention at this time. The general trend of interventions used remained similar to those at the first reading, although mention of CMI reduced markedly, whereas the interventions used were still those based on memory, informational and dietary/exercise reminders (Table 23).

**Table 23: Interventions used at Time 2**

<b>INTERVENTION USED</b>	<b>NUMBER OF TIMES USED</b>
Advised to increase dose, referred to GP	4
Applying for healthcare card on basis of intervention	1
Cholesterol medicines changed because of side effects	1
Counselled on benefits of adherence	1
Counselled on need for cholesterol medicines in light of high reading after non-compliant episode	1
Dietary change suggested	3
Discussed medicines and side effects, referred back to GP	1
Doctor giving medicine samples to assist with cost	1
Explained diet and Logicol <sup>®</sup> margarine	1
Explained long term benefits of cholesterol meds	1
Flow chart given for routine	1
General encouragement given	1
Informed patient of need for medicines in response to patient concerns	1
Long term advantage of cholesterol medicines explained	1
Non-compliance partly due to Alzheimer's addressed	1
Patient has changed medication routine	1
Patient purchased own cholesterol measuring device	1
Recommended exercise	1
Recommended relaxation based on interview	1
Reminded about doctor	1
Repeat reminders used	1
Routine and triggers for reminding discussed	1
Routine supported	1
Verbal and written information given	1
Written information provided	1
<b>TOTAL</b>	<b>30</b>

### 3.6.3 Time 3

At the final reading there were only 19 interventions given and, again these showed a tendency to be focussed on lifestyle factors, on raising or lowering doses of medications, and on medicine information. There was less focus on the patient's routine and medicine taking, and forgetting than there was at the first interview (Table 24).

**Table 24: Interventions used at Time 3 (final reading)**

INTERVENTION	NUMBER OF TIMES USED
Asked about generic variants	1
Ceased med on GP advice (cholesterol 6.2mmol/L)	1
Cholesterol meds changed due to higher reading	1
Counselled on lifestyle factors	1
Counselled on need for meds due to patient concerns	1
Diet and lifestyle advice offered	2
Discussed forgetting meds	1
Flow chart given for routine med taking	1
Informed about possible interaction due to patient request	1
Patient counselled on likelihood of severe side effects from meds	1
Patient dissatisfied with brand of med, and is changed to preferred brand to enhance adherence	1
Patient expressed inability to walk for exercise due to back problems- alternatives discussed	1
Patient reported no problems with meds during interaction	1
Patient started Xenical®- counselling provided	1
Recommended increase in Lipitor® dose	1
Referred to GP to reduce med dose	1
Safety net program explained as patient indicated that meds were expensive	1
Safety net reached and med cheaper now- aid adherence	1
<b>TOTAL</b>	<b>19</b>

### 3.7 Lifestyle changes

#### 3.7.1 Change in exercise

The mean exercise scores for the subjects and the changes over the study period are shown in Table 25 (also Appendix 11). Repeated measures ANOVA of the data showed that the overall change in exercise was not significant ( $F_{2,168} = 1.83$ ,  $p > 0.05$ ), but that there was a significant interaction between study groups and the time interval ( $F_{2,168} = 3.82$ ,  $p < 0.05$ ), and that this effect was most strongly found as a quadratic effect ( $F_{1,84} = 8.68$ ,  $p < 0.05$ ). That is, the group differences were mainly due to the increase in exercise by the intervention group patients at the second time period.

**Table 25: Mean exercise score by group**

(0= no exercise, 5= more than 10 hours of exercise a week)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	2.63	2.43-2.83	3.39	3.21-3.57	3.12	2.88-3.36
<b>Comparison (n=49)</b>	2.73	2.53-2.92	2.51	2.33-2.69	2.89	2.66-3.12



### 3.7.2 Change in diet

Of the 21 foods listed in the food questionnaire and tested with the patients, only changes in skim milk and meat consumption were found to be statistically significant amongst the subjects in the study (Tables 26 and 27, Appendix 11). Repeated measures ANOVA of skim milk consumption showed that there were significant differences across the study period ( $F_{2,166} = 3.9$   $p < 0.05$ ) and that the behaviour of the two groups was different ( $F_{2,166} = 4.4$   $p < 0.05$ ). Examination of contrasts showed that the effect was a quadratic effect and that the difference was due to the intervention group using more skim milk at the time of the second measurement ( $F_{1,83} = 10.05$   $p < 0.05$ ).

**Table 26: Mean score of frequency of use of skim milk per week**  
(1=every day, 5= Never)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	2.64	2.35-2.93	1.85	1.57-2.13	2.95	2.66-3.24
<b>Comparison (n=49)</b>	2.58	2.31-2.85	2.89	2.63-3.15	2.96	2.70-3.22

The other difference in food use was that the intervention group increased their consumption of meat slightly across the study period and the comparison group decreased consumption slightly (Table 27). Neither change by itself was significant, but as Table 27 shows, the combination of the two changes meant that there was a significant interaction in differences between the two groups ( $F_{2,176} = 3.4$ ,  $p < 0.05$ ).

**Table 27: Mean scores for frequency of consumption of meat per week**  
(1=every day, 5= Never)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	2.02	1.92-2.12	1.92	1.81-2.03	1.75	1.62-1.88
<b>Comparison (n=49)</b>	1.76	1.67-1.85	1.74	1.64-1.84	1.92	1.81-2.03

It therefore appears that the interventions provided by the pharmacists in the intervention group may have had an impact on the food consumption of the patients, improving their food intake to aid in lowering their cholesterol levels.

### 3.8 Patient self-perceptions of health and wellbeing

Patients were asked to rate their own health at each time period and were asked how calm, energetic, and sad (blue) they felt. Overall patient's perceptions of their health did not vary over the time period of the study (Table 28, Appendix 12). However, again, there was a

difference in the direction in which patient perceptions differed across time in the two study conditions. Subjective health perceptions of those in the intervention group improved slowly over the study period relative to those of the comparison group ( $F_{2,176} = 3.5$ ,  $p < 0.05$ ).

**Table 28: Average patient perceptions of their own health**  
(1=Excellent, 5=Poor)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	3.17	3.02-3.32	2.93	2.79-3.07	2.76	2.62-2.90
<b>Comparison (n=49)</b>	2.92	2.78-3.06	2.96	2.84-3.08	3.04	2.91-3.17

The only other wellbeing score on which there was a significant change was the measure of patients' feelings of being 'down or blue' (Table 29). Although there was no significant difference between any scores at any time, there was a significant quadratic effect due to intervention patients' rating themselves as being down less often at the second time interval compared with the first and third time intervals, and compared to the perceptions of the comparison group ( $F_{1,90} = 6.9$ ,  $p < 0.05$ ).

**Table 29: Patient self ratings of how often they have felt 'down or blue' in the last 4 weeks**  
(1=all of the time, 6= none of the time)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	4.57	4.18-4.96	5.02	4.65-5.40	4.62	4.30-4.94
<b>Comparison (n=49)</b>	4.76	4.39-5.12	4.61	4.27-4.96	4.90	4.60-5.20

Based on the data obtained, the study hypothesis of no statistically significant differences in the mean Quality of Life scores between and within the two groups over the course of the study was rejected.

### 3.9 Hospital admissions/GP visits

As may be expected when investigating a condition that is indicative of the development of a long term illness, and is largely being treated amongst a population that is more aged than the general populace, there were a number of hospital and emergency admissions, but very few that were related to the focus of the present investigation, hyperlipidaemia.

In the 12 months prior to the study, patients in the intervention group had a total of 8 hospital admissions, only one of which, atheroscopy, was possibly related to hyperlipidaemia. The comparison group had a higher number of admissions in the 12 previous months, 13 admissions, again with only one admission that might possibly be related to hyperlipidaemia,

a pulmonary oedema.

During the study the intervention group had 15 admissions, including 2 atheroscopies, and the comparison group had 18 admissions, with one admission for heart attack and one admission for pulmonary oedema.

The intervention and comparison groups reported 222 and 209 GP visits, respectively, in the 12 months prior to the study. During the course of the study the intervention group had another 80 GP visits, and the comparison group another 98. There were no statistically significant differences in the proportion of GP visits between the groups ( $\chi^2_3=5.65, p>0.05$ ). There is also no evidence that any of the visits were related to the condition of interest, hyperlipidaemia.

### **3.10 Economic analysis**

As there were no meaningful differences in hospitalisation or GP visits the appropriate unit of economic measurement for this study was the cost of delivering the service per 10% decrease in total lipids.

As the comparison group procedure was not part of a normal practice of pharmacy (eg completion of questionnaires and blood lipid tests), it did not make a useful comparison to the cost of the intervention group, and therefore the cost of the therapeutic outcomes monitoring service was calculated without including the time spent filling the prescription in the normal fashion.

As previously mentioned, different pharmacists used different methods of recruitment for the study. The main method used was to simply approach people as they came in to fill their prescriptions, but a minority of pharmacists did their own mail-out and more found it useful to mail reminders to their customers when it was time for a re-test. As such, with these pharmacists, there were also the extra mail costs and the time of an assistant to perform the mail-outs. These extra costs were also included together with the time and costs of training the pharmacists and costs of delivery of the service per patient.

Initial training was conducted in the majority of cases off site at the University of Sydney, and for those who started late in the study training was conducted one-on-one at the pharmacy in a quiet room or at a convenient location. This one-to-one training took an average of 1 hour 15 minutes, and half the pharmacies trained in this fashion subsequently withdrew from the study, which was similar to the average number of withdrawals in the overall study.

However, those who stayed in the study, supplied an additional 14 patients who lowered their cholesterol by an average of 0.69 mmol/L. This average decrease was above the 95% confidence interval of the average change in cholesterol across the entire study (average = 0.47 mmol/L  $\pm$  0.18). Thus, the outcome achieved by pharmacists who were trained individually in their own pharmacies was average or above the average of intervention pharmacists in the study.

Two analyses of service delivery costs were calculated, one using training costs based on group delivery off-site (Table 30), and one based on one-to-one delivery to each participating pharmacist (Table 31). The former training method has lower trainer costs, but the latter has lower pharmacist costs. Assuming that a pharmacist is paid \$70 per hour, amortising the start-up costs across the median number of patients per pharmacy of 6.5, the cost for delivering the service to each patient in the study was \$236.48 (Table 30). The start-up costs when training pharmacists in the field are slightly lower at \$194.91 (Table 31). Once start-up costs are removed, such as the cost of the machine and training, the ongoing cost for delivering the service to each patient was \$118.40 (Table 32). Where the training is conducted off site at the University these costs are for training the pharmacists in a group training exercise at the University. Facilities costs, either for the lecture theatre for the training day or for a space within the pharmacy to conduct the interviews, have not been included in these analyses.

**Table 30: Start-up costs per pharmacy when pharmacists are trained in a group at the University**

<b>Cost per pharmacy</b>	<b>Item</b>
\$7.50	Postage (15 letters/pharmacy average)
\$40.00	2 hrs preparation of mail-out by pharmacy assistant
\$490.00	Cost for day training at the University of Sydney for intervention pharmacist
\$25.20	Cost for trainer for one day- for on-site follow-ups
\$509.60	Pharmacist time to deliver intervention-3 sessions, initial session 35 min, subsequent 15 min- for 6.5 patients
\$82.50	Cost of strips
\$180.00	Cost of machine
\$30.00	Paper/printing
\$22.33	Cost of food for participants on training day
\$50.00	Cost of preparation of training and study materials
\$100.00	Cost of subsequent training/data collection
<b>\$1537.13</b>	<b>TOTAL COST FOR 6.5 PATIENTS</b>
<b>\$236.48</b>	<b>TOTAL COST PER PATIENT (sum of cost per pharmacy/6.5)</b>

**Table 31: Cost per patient when pharmacists are trained individually in the field**

<b>Cost per pharmacy</b>	<b>Item</b>
\$7.50	Postage (15 letters/pharmacy average)
\$40.00	2 hrs preparation of mail-out by pharmacy asst
\$105.00	Cost for day training for intervention pharmacist (\$70/hr*1.5)
\$140.00	Cost for trainer to visit pharmacy for initial training
\$509.60	Pharmacist time to deliver intervention-3 sessions initial session 35 min subsequent 15min-6.5 patients
\$82.50	Cost of strips
\$180.00	Cost of machine
\$30.00	Paper/printing
\$22.33	Cost of food on training day
\$50.00	Cost of preparation of training and study materials
\$100.00	Cost of subsequent training/data collection
<b>\$1266.93</b>	<b>TOTAL COST FOR 6.5 PATIENTS</b>
<b>\$194.91</b>	<b>TOTAL COST PER PATIENT(sum of cost per pharmacy/6.5)</b>

**Table 32: Ongoing cost per pharmacy once training is completed**

<b>Cost per pharmacy</b>	<b>Item</b>
\$7.50	Postage (15 letters/pharmacy average)
\$40.00	2 hrs preparation of mail-out by pharmacy asst
\$509.60	Pharmacist time to deliver intervention-3 sessions initial session 35 min subsequent 15
\$82.50	Cost of strips
\$30.00	Paper/printing
\$100.00	Cost of ongoing training
<b>\$769.60</b>	<b>TOTAL COST FOR 6.5 PATIENTS</b>
<b>\$118.40</b>	<b>TOTAL COST PER PATIENT(sum of cost per pharmacy/6.5)</b>

The mean drop in total cholesterol for the intervention group was 0.47 mmol/L, whereas the mean drop for the comparison group was 0.1 mmol/L. Adjusting the mean drop in total cholesterol for the intervention group to take into account the difference from the comparison group means that the average percentage drop achieved during the study over and above that which the comparison group achieved was 9%. Multiplying the cost figures above by 10/9 gives an approximate cost for lowering total cholesterol by 10%.

However, as there was a baseline difference in cholesterol readings the standardised beta coefficient of the baseline cholesterol reading is the adjusted difference between groups. Analysis of covariance resulted in a standardised beta of 0.739, meaning that the adjustment

needed is 0.739 of 9%, which results in a 6.65% average difference in cholesterol levels at the costs above. Assuming a linear relationship between costs of service and lowering of cholesterol, the costs in the tables above can be multiplied by 10/6.65 to yield the cost to lower cholesterol by an average 10% per patient. These costs are \$355.61, \$293.10, and \$178.05 for off-site, on site and ongoing costs, respectively.

### 3.11 Differences in perception changes towards healthcare professionals

At baseline there was only one score on which there was a difference between the comparison and intervention groups' perceptions towards their healthcare professionals. Patients allocated to the intervention group disagreed less strongly with the statement "These people do not seem interested in what I have to say about my illness" ( $t_{143}=4.24$ ,  $p<0.05$ ), with means of 3.8 and 4.3 for the intervention and comparison groups respectively (where 1 means agree strongly and 5 means disagree strongly). Otherwise there were no differences in perceptions between the groups at baseline (Appendix 13).

### 3.12 Problems with anti-hyperlipidaemic medications

Table 33 shows that whilst most patients felt that they had no trouble remembering to take all of their medications, the intervention group tended to think that it was easier to remember their medications by the end of the study than it was at the start compared to the comparison group ( $F_{2,188}=5.07$ ,  $p<0.05$ ). No other statistically significant differences were found between or within the two groups over the study time period in relation to other problems associated with taking anti-hyperlipidaemic medications (Appendix 14).

**Table 33: Difficulty of remembering to take medications**  
(1=very difficult, 3=not at all difficult)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	2.72	2.66-2.78	2.96	2.92-3.00	2.94	2.91-2.97
<b>Comparison (n=49)</b>	2.92	2.86-2.98	2.90	2.86-2.94	2.96	2.93-2.99

### 3.13 Barriers to Medication Use (BMU)- Patient Knowledge

Table 34 shows that participants in both groups generally agreed that they knew why they were taking their anti-hyperlipidaemic medications, however there was a significant trend over the course of the study for intervention group participants to agree more strongly with the statement that they knew exactly why they were taking their anti-hyperlipidaemic

medications compared with those in the comparison group ( $F_{2,196}=3.86$ ,  $p<0.05$ ).

**Table 34: I know exactly why I am taking my anti-cholesterol medications**  
(1=strongly agree, 5=disagree strongly)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	1.60	1.51-1.69	1.40	1.33-1.47	1.28	1.21-1.35
<b>Comparison (n=49)</b>	1.46	1.37-1.54	1.46	1.39-1.53	1.42	1.35-1.49

No other statistically significant differences were found between or within the two study groups over the time period in relation to the other statements in the patient knowledge section of the BMU (Appendix 15).

### 3.14 Barriers to Medication Use (BMU)- Previous experience

Table 35 shows that during the course of the study the perceptions of the two groups with regards to the 'previous experience' section of the BMU changed. Those in the intervention group became less likely than those in the comparison group to say that the side effects of their anti-hyperlipidaemic medication prevented them from taking those medications at the end of the study compared to the start of the study ( $F_{2,174}=5.75$ ,  $p<0.05$ ).

**Table 35: Side effects prevent me from taking my medication properly**  
(1=strongly agree, 5=disagree strongly)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	3.87	3.74-4.00	4.40	4.29-4.51	4.33	4.21-4.45
<b>Comparison (n=49)</b>	4.34	4.20-4.48	4.16	4.14-4.28	4.18	4.05-4.31

It can be seen in Table 36 that over the course of the study those patients in the intervention condition tended to think that their medications were more affordable, contrasting with those in the comparison group who tended to change in the direction of thinking that they were less affordable. Although neither of these tendencies was significant by itself, the interaction of the tendencies of the two groups was significant ( $F_{2,188}=8.3$ ,  $p<0.05$ ).

**Table 36: Averaged responses to "I cannot afford my anti-cholesterol medications"**  
(1=Agree strongly, 5=Disagree strongly)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	3.96	3.81-4.11	4.31	4.19-4.43	4.31	4.17-4.45
<b>Comparison (n=49)</b>	4.35	4.20-4.50	4.00	3.88-4.12	3.85	3.71-3.99

Whilst overall subjects disagreed when asked whether they had to make sacrifices to afford their anti-hyperlipidaemic medications, it can be seen from Table 37 that, in a similar fashion to responses regarding the affordability of the medication, patients in the intervention group tended to think that they had to make less sacrifices over the course of the study, and those in the comparison condition tended to move in the opposite direction ( $F_{2,190}=4.02$ ,  $p<0.05$ ).

**Table 37: Averaged responses to "I always have to make sacrifices to afford my anti-cholesterol medications"**

(1=Agree strongly, 5=Disagree strongly)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	4.10	3.97-4.23	4.49	4.36-4.62	4.31	4.18-4.44
<b>Comparison (n=49)</b>	4.43	4.30-4.56	4.00	3.88-4.12	3.96	3.83-4.06

Relative patient perceptions of the two groups also changed in regard to the inconvenience of taking anti-hyperlipidaemic medications (Table 38). The perception of the intervention group altered towards thinking that their anti-hyperlipidaemic medication as more convenient compared to those in the comparison condition ( $F_{2,190}=4.02$ ,  $p<0.05$ ).

**Table 38: Averaged responses to "The times for taking my anti-cholesterol medications are inconvenient"**

(1=Agree strongly, 5=Disagree strongly)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	4.08	3.93-4.23	4.46	4.31-4.55	4.44	4.35-4.53
<b>Comparison (n=49)</b>	4.39	4.25-4.53	4.27	4.18-4.36	4.25	4.16-4.34

Interestingly, Table 39 shows that over the course of the study, those in the intervention group, particularly at the time of the second measurement, grew more likely to disagree with the statement that an organiser acts as a reminder for their anti-hyperlipidaemic medication in relation to the comparison group ( $F_{2,178}=3.69$ ,  $p<0.05$ ). This suggests that the interventions given by the pharmacists negated the need or desire for medication organisers.



**Table 39: Averaged responses to "A medication organiser helps to remind me about taking my anti-cholesterol medications"**  
(1=Agree strongly, 5=Disagree strongly)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	3.32	3.14-3.50	3.87	3.70-4.04	3.45	3.28-3.62
<b>Comparison (n=49)</b>	3.52	3.33-3.71	3.20	3.03-3.37	3.23	3.06-3.40

No other statistically significant differences were found between or within the two study groups over the time period in relation to the other statements in the previous experience section of the BMU (Appendix 16).

### 3.15 Barriers to Medication Use (BMU)- Communication

Although, again, there were no significant differences at any one point, it can be seen in Table 40 that the intervention group steadily increased their confidence about which questions to ask pharmacists, in relation to the comparison group, who did not ( $F_{2,190}=5.66$ ,  $p<0.05$ ).

**Table 40: Averaged responses to "I'd like to ask questions but I never know what to ask my pharmacist about my anti-cholesterol medications"**  
(1=Agree strongly, 5=Disagree strongly)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	3.73	3.58-3.88	3.92	3.77-4.07	4.22	4.09-4.35
<b>Comparison (n=49)</b>	4.23	4.08-4.38	3.73	3.58-3.88	3.96	3.83-4.09

Gratifyingly the average patient agreed with the statement that doctors and pharmacists explained the information about their anti-hyperlipidaemic medication in a way that they could understand. Table 41 also shows that those in the intervention group were likely to agree more strongly that the information was conveyed clearly by the end of the study in relation to the comparison group ( $F_{2,194}=3.72$ ,  $p<0.05$ ).

**Table 41: Averaged responses to "My doctor/pharmacist explains information about my anti-cholesterol medication in a way that I can understand"**  
(1=Agree strongly, 5=Disagree strongly)

	Time 1		Time 2		Time 3	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
<b>Intervention (n=48)</b>	2.05	1.80-2.30	1.68	1.43-1.93	1.68	1.38-1.98
<b>Comparison (n=49)</b>	1.86	1.63-2.09	2.08	1.85-2.31	1.90	1.64-2.15

No other statistically significant differences were found between or within the two study

groups over the time period in relation to the other statements in the communications section of the BMU (Appendix 17).

### 3.16 Open Ended Responses

Each time patients had their cholesterol measured and completed a questionnaire they were given the opportunity to give responses to two open ended questions on the questionnaire:

- Is there anything you have done that makes it easier for you to take your medications, and
- Is there anything that makes it hard for you to take your cholesterol medication in the way that your doctor wants you to?

Table 42 shows that the two main factor that intervention group patients identified as making it easier to take their anti-hyperlipidaemic medication were routine (28 responses) and a Dosette<sup>®</sup> box (18 responses). These two issues comprised 46 responses out of the total of 52 responses.

**Table 42: Number of open ended responses from intervention group patients to the question: Is there anything you have done that makes it easier to take your medications.**

Response	n
Changed to Ezetrol <sup>®</sup> from Questran <sup>®</sup>	1
Dosette <sup>®</sup> box/Webster Pack	18
Getting into a routine	2
Habit	1
Keeping them on the bedside table	1
Make them visible	3
Before going to bed	1
Put tablets in pill box at night	1
Put them on the kitchen table	2
Reminder clock	1
Routine	3
Same time each day	2
Tablet box for one week's tablets	1
Take after breakfast	1
Take at regular times, place medication strip in plain view, and replace when empty	1
Take at same time	3
Take it all at once with a daily activity	1
Take them all at once	1
Take them last thing at night	1
Take with food	1
Take them in the morning	1
Sometimes think I know better than the pharmacist	1
Laminated card for instructions	1
Get them delivered by the chemist	2
Exercise and diet	1

Table 43 shows that virtually all of the responses in regard to what made it easier for the comparison group patients to take their medication were concerned with getting into a routine. Even when a pill box was referred to, it still carried the mention of a daily reminder or routine. This contrasted with the responses of patients in the intervention group who mentioned Dosette® style boxes extensively. This may be because the pharmacists in the intervention group were mentioning these devices to their patients during their interactions. The number of responses (about Dosette® style boxes) that the intervention patients made after the first reading, that is, after they had had more than one conversation with the pharmacist, supports this contention. Thirteen of the 18 responses were made after the first interview. If this is indeed the case it is of some concern as one of the other findings of the present research was that the intervention patients became less inclined to believe that Dosette® style boxes would be of help to them in taking their medication properly compared to comparison group patients over the course of the study.

**Table 43: Number of open ended responses from comparison group patients to the question: Is there anything you have done that makes it easier to take your medications.**

Response	n
Ask questions	1
Changed dosage times and increased fibre	1
Daily reminder/pill container	4
Eat more fibre/tried changing drug	1
Get in the habit	2
Getting into a routine	1
Have them with a meal	1
Have them with a meal/remembering to take them at all is a feat in itself	1
Leave near bottle of water	1
Make them visible	2
Pill organiser	3
Printed schedule/routine	2
Put tablets somewhere visible	1
Put them out each day	1
Remembering	1
Routine	9
Same time after dinner	1
Same time each day	5
Same time each night	2
Suck it till it gets smaller	1
Take if before bed	1
Take in the morning/trouble sleeping	1
Take with breakfast	1
Use special pill box and take at same time	1
Weekly pill box	1
Written schedule	2

A smaller number of responses (23) were given when intervention patients were asked to nominate the factors that made it hard to take their medication rather than what made it easier. Forgetfulness and side effects were nominated most commonly as the things that made it hard to adhere to therapy (Table 44).

**Table 44: Open ended responses by intervention group patients to the question "is there anything that makes it hard for you to take your cholesterol medication in the way that your doctor wants you to"**

<b>Response</b>	<b>n</b>
Doctor and specialist disagree that this is the best medication	1
Don't believe they work	1
Forget when busy	1
Forgetfulness and alcohol	1
Remembering to take it at the same time each day	1
Memory	1
No self discipline	1
Side effects	4
Leg pains	1
Keeps me awake	2
They keep me awake if I have them at night	1
Too dry to swallow	1
Too many pills	1
When I eat fatty food	1
Taking them with me when I go out	2
Taking it before bed	1
Pharmacist's admonition	1
Working in remote areas	1

Comparison group patients also nominated a small number of factors that made it hard for them to take their medication (Table 45). These comments also focussed on forgetfulness and side effects, although one patient in this group noted at this point that they were not sure why they were taking an anti-hyperlipidaemic medication.

**Table 45: Number of comparison group patient responses to the question "is there anything that makes it hard for you to take your cholesterol medication in the way that your doctor wants you to"**

<b>Response</b>	<b>n</b>
Forget to take before food	2
Taking before food	2
Memory	2
Not sure why taking it	1
Side effects	1
Side effects/ constipation	1
Fluid retention and nausea	1
Don't sleep well if taken at night	1
Constipation and liver damage	1
Hard to swallow	1
Dislike taking tablets	1
Too busy	1

## **4 DISCUSSION**

### **4.1 Clinical outcome**

The main outcome of the study was that patients in the intervention group lowered their total blood cholesterol level by an average 0.5 mmol/L, more than those in the comparison group. There was a 9% reduction in the total cholesterol levels of the intervention group. Taking into account the baseline difference in cholesterol levels between the two study groups, the cholesterol levels of the intervention group decreased by 6.65% over the study period. Using the data published by Gould *et al* (1998), this reduction in cholesterol level translates to approximately 10% reduction in coronary heart disease mortality risk and an expected approximately 7% reduction in total mortality risk.

Although the total cholesterol level of the intervention group was higher at baseline than that of the comparison group the results showed that the change in cholesterol levels of the intervention group was still statistically significant even when this was taken into account. As the only difference between the intervention and comparison groups was the provision of the intervention (which included counselling and advice giving about the disease, medication, medication use, adherence and lifestyle measures) by the pharmacist, then the significant difference in total cholesterol levels between the two groups by the end of the study was most probably due to the interventions.

These findings support previous studies which have demonstrated the positive impact of pharmacy based cholesterol monitoring programs. Although the programs reported in the literature are not identical to the interventions delivered by pharmacists in this study, there are similarities which allow comparison of some of the outcomes.

The most similar study, both in terms of the research methods and the intervention delivered, has been that conducted by Peterson *et al.* (2004) in Tasmania, Australia. The authors evaluated an educational and monitoring program delivered by pharmacists which aimed to promote adherence to anti-hyperlipidaemic medications as well as promote dietary and lifestyle changes. The study consisted of a similar but lower, number of patients as the current project, 39 in the intervention group and 42 in the control group. The authors showed a decrease in the total blood cholesterol levels of the intervention group as a result of the intervention delivered by the pharmacist. The most notable differences between the two studies were that the patients in the Tasmanian study were recruited from a hospital, discharged on lipid lowering therapy and visited at their home monthly by the study pharmacist.

Although a small study with only two participating community pharmacies and 25 patients, Shibley and Pugh (1997) also demonstrated a significant reduction in lipid levels after 12 months compared to baseline and after 6 months of receiving an intervention from pharmacists. The intervention centred on counselling about non-drug approaches, measurement of lipids, blood pressure and weight, and referral for therapy if needed. Improvements were also observed in other outcomes such as patient satisfaction and quality of life. Patients saw a dietician as part of this study which may have a more positive impact on the study outcomes than if the pharmacist was the only health professional delivering the intervention.

The study by Ibrahim *et al* (1990) is also similar to the current research project in terms of the intervention delivered. Similar to the current study, the pharmacist measured total blood cholesterol levels, delivered patient education on lipids and health, provided explanations of heart disease factors and provided follow-up. However, the study did not include a control group and only one pharmacy participated. Furthermore, the study lasted 6 months. Despite these differences and limitations, the authors showed a significant decrease in total cholesterol levels after the intervention was delivered, but not over the 6 month duration of the study.

The pharmacist's role in reducing total blood cholesterol levels through an intervention program focussing on information about previous and current lipid lowering therapy, tolerance and adherence to therapy has been demonstrated in a recent British study (Alldred *et al* 2001). Even though the setting was in a hospital, the results demonstrated the positive impact that pharmacists can make.

A recent study from Chile published after the completion of this project has also shown similar results (Paulos *et al* 2005). The authors showed that a short term pharmaceutical care program developed and delivered in community pharmacy, resulted in improved blood lipid levels as well as cardiovascular disease risk factors (which were not measured in the current project) and patient's quality of life. However, the Chilean study was conducted in only one community pharmacy by one pharmacist, with a smaller sample size, 42 patients (23 in the intervention group and 19 in the control group).

Improvements in lipid levels as a result of a community pharmacist delivered intervention have also been demonstrated by Nola *et al* (2000). A randomised control trial evaluated the impact of an intervention focusing on dietary, exercise and medication advice, compared to the usual care delivered by pharmacists, on patients lipid levels as well as other outcomes

(51 patients in the intervention and 26 in the control group). A short coming of this study however, was that, like the study above, it was limited to only one community pharmacy. Furthermore, unlike the current study, the patients were not identified based on lipid medication use, but based on using specific medications in hypertension and diabetes.

In a Canadian study, 54 community pharmacies participated in a randomised control trial to evaluate the impact of interventions delivered to patients at high risk of cardiovascular events (Tsuyuki *et al* 1999). A total of 565 patients participated. Improvements were observed in lipid profiles, addition or changing of lipid lowering therapy, patient satisfaction and quality of life. However, the intervention delivered was not similar to the current study. The focus was on the provision of written information on cardiovascular risk factors, as well as preparation of a referral form to the patient's physician about patient risk factors, medications and other recommendations as a result of a patient interview.

Therefore, although there have been other studies in the literature reporting improvements in patients' total blood cholesterol levels, the interventions delivered by the pharmacists and the settings where the interventions have been delivered are not wholly comparable with those of this study.

#### **4.2 Adherence measures**

In this study, the BMQ was not able to detect many instances of non-adherence in either the comparison or intervention groups and, therefore, was not able to detect any differences in non-adherence either over the course of the study or between the two study groups. It should also be noted at this point, that as the patients in the study were not tied to any one pharmacy, the adherence problems detected by the BMQ were only those that were reported by the patient.

A recent similar Australian study evaluating the impact of an intervention delivered by community pharmacists on medication use in patients with type 2 diabetes demonstrated a significant decrease in self-reported non-adherence rates (using BMQ as the measure of adherence) (Krass *et al* 2005). It is possible that the BMQ may be a more sensitive measure of adherence in patients on multiple dosing and / or multiple therapies.

The BMQ also tests for patient's beliefs about the efficacy of their medications (which has been linked with adherence (Cummings *et al* 1981; Kelly *et al* 1987)), as well as having a recall screen that assesses the difficulty of adhering to the medication regimen. As with the regimen screen of the BMQ, neither of these scales identified a significant number of



individuals who had a possible problem on either of these screens.

Other possible reasons for the results observed with the BMQ may be the patient sample size. The more likely explanation however is the medication regimen, that is, the once daily dosing of nearly all of the anti-hyperlipidaemic medications. Non-adherence in a group of patients on chronic anti-hyperlipidaemic medications may be low when the patients have been on therapy for some time as opposed to patients who have recently been prescribed and commenced anti-hyperlipidaemic medications (Simons, Levis, & Simons 1996; Avorn & Monnette 1998).

The MARS similarly yielded little information and what information it did give, on the surface at least, contradicted the positive results obtained with the cholesterol readings (that is lowered total blood cholesterol levels in the intervention group). The only significant difference between the two study groups was that the intervention group reported a slightly higher tendency to alter the dose of their prescribed anti-hyperlipidaemic medication. This is the reverse of that which would be desired and expected given that the fall in total cholesterol levels suggests that intervention group patients lowered their cholesterol on average. It is possible that intervention patients became more likely to actually report behaviour that was happening, which would explain the direction of this change, however there is no direct support from the data for this idea, and it must therefore remain conjecture.

A further reason for not detecting any changes in adherence levels may be the low power of the study. This has been further discussed in Section 4.7 (Study limitations).

Although a direct measure of adherence did not yield good information, the indirect method, that is the assessment of patients' clinical response (total blood cholesterol levels) did (Osterberg and Blaschke 2005).

### **4.3 Interventions delivered by pharmacists**

Analysis of the types of interventions used by pharmacists showed that the number of interventions delivered by pharmacists, although high at the initial interview / consultation at baseline, fell markedly after the first interview. This could be due to pharmacists believing that they had covered most, if not all, issues at the first interview for many patients. The principal intervention that was discontinued after the initial session was the mention of CMI, and over the course of the study the types of interventions used changed from being information and memory/routine related, to lifestyle information with focus on dietary and exercise recommendations. This suggests that the patient was asking for more from the

pharmacist than the daily routine and information on the medications that they were taking, and that once these issues were discussed, some patients were willing to explore other areas with the pharmacist.

Patient education is one of the main categories of interventions reported in the literature to improve adherence (Osterberg and Blaschke 2005), and which can improve adherence (Osterberg and Blaschke 2005; Van Wijk *et al* 2005). It includes educating patients about their disease, medication therapy and other factors that impact adherence eg lifestyle changes. Improving dosing schedules is the second most important and common intervention aimed at improving adherence (Osterberg and Blaschke 2005). Changes such as medication boxes, cues to remind patients to take their medications and establishing a routine fall within this category.

It is worth noting that even though there were few interventions delivered in the latter interviews, these interventions still took an average of 15 minutes. This may be due to several reasons: patients and pharmacists were establishing a trusting relationship and rapport, which allowed the patient to discuss more issues at length with the pharmacist; or pharmacists were becoming more comfortable in questioning patients about their adherence and delivering patient-focused counselling. The change in the information delivered over time (that is from medication and disease focus to lifestyle measures) may also support this.

Peterson *et al* (2003) conducted a meta-analysis of research studies that evaluated the impact of interventions on medication adherence levels. They found that the intervention resulted in an overall increase of 4-11% in adherence rates. However, there was no single strategy that was revealed to be the best. Thus a combination of strategies addressing various factors that influence adherence, as was the case in this study (a combination of behavioural and education strategies) is an effective approach to improve adherence rates. Additionally, an in-depth analysis of the interventions delivered by the community pharmacists in the current project would have provided more insight into what led to change in adherence levels and reduced cholesterol levels.

#### **4.4 Potential factors affecting lipid levels- Lifestyle measures**

In addition to questions about their use of medications the patients were also asked about a number of factors that may have been affected by the study and that in some cases may have contributed to the change in cholesterol levels. Patients in the study reported on their exercise habits and repeated measures ANOVA showed that the change in the amount of exercise did differ between the study groups. Those in the comparison group did not

increase their overall amount of exercise, whereas those in the intervention group increased their amount of exercise significantly between baseline and Time 2 (when many of these subjects had lifestyle counselling from their pharmacists). Even though the average amount of exercise performed by the intervention group dropped back slightly after Time 2, the change in exercise was still significantly greater than for the comparison group. Thus, it is possible that the lifestyle counselling received at baseline (as well as during subsequent interviews, though to a lesser extent) may have contributed to the increased exercise habits of the intervention group and consequent drop in their total cholesterol levels.

There were also small changes in the foods eaten by subjects in both groups. All patients were asked about their consumption of 21 foods, including lipid lowering margarines. Those in the intervention group stated that they consumed more skim milk at Time 2 and began consuming more meat in comparison with the comparison group during the course of the study. A change in food consumption may contribute to the reduced cholesterol levels, however, this effect is not conclusive. Furthermore, a change in only two out of 21 foods may indicate that the intervention delivered by the participating pharmacists did not have a strong impact on the types of food eaten by the patients. It may also be possible that a change in dietary intake in this group of patients required a longer period of time or a different intervention style than was offered as part of this study.

In a final therapeutic outcomes monitoring service model to be disseminated to community pharmacies, it is important to ensure that lifestyle interventions such as dietary and exercise advice should be an essential part of improving long-term patient health outcomes.

#### **4.5 Patient perceptions**

Patients' perceptions about their medication, health professionals, own health and well being were also measured as part of this study. At baseline there were virtually no differences in perceptions between the two study groups, with the exception that patients in the intervention group felt more strongly that health professionals did not seem interested in their condition. However, during the course of the study this difference disappeared and a number of other differences in perceptions in the intervention and comparison groups became apparent. Compared with those in the comparison group, over the course of the study, patients in the intervention group tended to think that they had less trouble remembering to take their pills, they did not let the side effects prevent them from taking their medication, they had less trouble affording their medications, found their medications more convenient to take, felt more comfortable asking their pharmacist questions about their medications and were less likely to think that a medication organiser would be helpful.

Additionally, over the course of the study, and relative to those in the comparison group, patients in the intervention group also came to feel that they understood their health professional's explanations of information about their anti-hyperlipidaemic medication, and that they knew why they were taking their medication. Improvements in patients' perception of pharmacists have also been observed by other researchers (Shibley and Pugh 1997).

In light of the low detection of non-adherence by both the BMQ and MARS questionnaires, the perception findings stand out as being consistently in the direction that would be desired in an intervention aimed at changing patient cognitions in regard to the role of pharmacists in general, and specifically their own use of anti-hyperlipidaemic medication. Each of these results is one that would be wished for in a cognitive pharmaceutical service for increasing patient adherence to medication (not only anti-hyperlipidaemic medication), and increasing the role of pharmacists in patient medication information and use. Kiortsis *et al* (2000) demonstrated that patients' perceptions of the efficacy of their anti-hyperlipidaemic medications in preventing future cardiovascular disease was a strong predictor of adherence to therapy.

The only anomalous finding was the shift towards not thinking that medication organisers were useful amongst the intervention group when compared to the comparison group. This finding, however, may be due to successful use of other strategies to increase adherence that do not require organisers, such as reminders.

All of these congruent findings in regard to patient perceptions suggest that the lowering of cholesterol levels observed may be due to shifts in patient perceptions. The changes in patient perceptions may have also led to improvements in adherence levels (though the reporting of non-adherence was too low to conduct any statistical analysis) as well as the changes in lifestyle (exercise and diet) observed.

Changes in patient perceptions are posited by a number of models of adherence (eg. The Health Beliefs Model, Theory of Planned Behaviour and the Self-Regulatory model) as having an effect on patient adherence to medication regimens (Cummings *et al* 1981, Kelly *et al* 1987 Leventhal, Zimmerman and Gutmann, 1984), and the present study has shown a consistent pattern of clear adherence promoting changes in intervention group patients' perceptions compared to the comparison group. Thus, while the adherence measurements used in this study did not detect the medication adherence changes, the measured changes in patient perceptions and popular models of patient adherence suggest that the intervention group patients are likely to have become more adherent to their medication regimens during

the course of the study, and this effect would have contributed to the reduction of total cholesterol observed in this study.

#### **4.6 Economic analysis**

There were no differences between the two groups' hospital admissions and GP visits during the course of the study and the analysis, therefore, was simply conducted on a cost per patient basis. The costs were slightly lower for pharmacists who were trained individually in the field and the average lipid lowering was slightly greater in pharmacies that were trained in the field. It should be noted however, that although these figures seem, *prima facie*, to argue for training in the pharmacy the sample of two successful field trained intervention pharmacies (almost diametrical opposites in demographics) is far too small to draw any conclusion. Many factors can come into play, such as, location, pharmacist communication style, and busyness of the pharmacy. It is possible that the individual training has more impact on the knowledge and skills gained by the pharmacists, but there is not enough data to draw a conclusion from this study.

#### **4.7 Study limitations**

There were several limitations in the study methods that may potentially impact the results obtained. The first limitation was the recruitment of pharmacies and patients. Recruitment is generally a vexed issue in pharmacy practice research (Ellerby, Williams & Winfield 1993, Liddell, 1996, Rosenbloom 2000), and the present study was not an exception. Initial recruitment of pharmacists meant that the project coordinator had to contact an average of approximately 5.5 pharmacies in order to recruit one pharmacy into the study. However, in the second wave of recruitment that was undertaken to replace those pharmacies which had pulled out of the study, the same coordinator found that it was only necessary to contact, on average, less than 2 pharmacies to recruit one pharmacy into the study. The only difference in selection for contact of the latter group was that they were selected to be in pharmacies that were not geographically close to each other. There was, otherwise no difference in the contact method used, and the only possible reason that may be proposed is that the project coordinator became more experienced with recruiting and was able to more easily influence the pharmacists to take part. It is understood from discussions with other researchers (Mitchell and Saini 2005) that a 'hit rate' of 1 in 2 for enrolling pharmacists in research is an excellent result.

Patient recruitment was the responsibility of the pharmacists in this study and the results achieved by the different pharmacists, the perceptions of the recruitment process and the optimum recruitment process for each pharmacy differed markedly across those who took

part in the study. Common factors that explained pharmacy perceptions and recruitment success were difficult to elucidate. Nearly all pharmacists reported difficulties recruiting patients into the study. However this was not universal. It was apparent that recruiting patients by sending a mail-out that invited their customers to take part in University-sponsored research, was a successful method of patient recruitment.

Recruitment of patients for the study was a major difficulty for the pharmacists, and may have been an underlying reason for pharmacists withdrawing from the study. In addition to those 2 pharmacists who explicitly stated that they pulled out due to the difficulty of recruitment a number expressed frustration to the project coordinator during the recruitment process.

The reasons pharmacists gave in regard to why they were not successful in recruiting patients or did not have success in retaining patients, centred around the time demands on the pharmacist, job mobility of the pharmacists, the length of the questionnaire, the discomfort of the pin-prick cholesterol measurement every 12 weeks and the multi-lingual nature of the pharmacy catchment in south western Sydney. However, pharmacists who retained patients throughout the study commented that their patients were thrilled when they saw their cholesterol lowered, that it was a 'revelation' to the pharmacist that their patients lowered their cholesterol through this type of service, that the pharmacist liked taking part in research, that the pharmacists liked doing 'something out of the ordinary' and in one case that the pharmacist was sad that the study had concluded and there was nothing more 'out of the ordinary' to be done.

A second limitation was the dropout rate of the patients. Of the 142 patients recruited, 97 completed the study. This dropout rate could be a reflection of the study duration, the length of study questionnaire used to collect data, and / or the measurement of blood cholesterol levels. Although a large number of patients did not complete the study, a comparison of the demographics showed a difference in only one characteristic. Thus, the continuing patients were the same as those that dropped out with regard to the demographic characteristics measured in the study. However, the reduction in sample size has an impact on the statistical analysis conducted, in particular on determining the patient profile who responded to the interventions delivered by the pharmacists.

The low recruitment and high drop-out rate had a significant impact on the power of the study to detect changes in adherence, reducing it to 44%. This reduction in power has more than likely reduced the probability of finding a statistically significant difference in the

adherence levels observed. Nevertheless, the study had sufficient power to detect a statistically and clinically significant difference in total cholesterol levels. Thus the lack of difference in adherence levels in the intervention group should be interpreted with caution, and a larger study would be required to determine the impact of the service delivered by community pharmacists on adherence levels.

A third study limitation was that dispensing records were not able to be used to measure adherence rates and triangulate the data with the BMQ. The inability to use the record was that many of the subjects were not tied to one pharmacy or were new customers brought into the pharmacy by the research. Therefore, this method could not be relied upon as an accurate measure of patient adherence (Osterberg and Blaschke 2005).

A further limitation was that the BMQ was difficult to administer and score by the pharmacists, and the outcome did not warrant its use as an outcome measure.

Although the accuracy and precision of Accutrend GC™ have been reported (see Appendix 1 and Section 2.7.2), the data collected can still be affected by the operator. To minimise this impact, all participants were provided with training. In the absence of laboratory lipid test data to validate each of the total blood cholesterol levels collected for the study patients, it is not possible to state that data collection was not affected by the operator.

Finally, due to budgetary constraints it was not possible to gather the blood lipid fractions and to give patients a Framingham risk assessment. This shortcoming would have the effect of lowering patient motivation to lower their blood lipid levels. The risk assessment should be considered for inclusion in future research.

## **5 CONCLUSIONS**

In summary, it is possible to lower the total blood cholesterol levels of pharmacy customers using a low cost Cognitive Pharmaceutical Service, which focuses on adherence to therapy. Although it is possible, or even probable, that this lowering in total blood cholesterol levels occurred due to increased patient adherence to medication regimens, the evidence from this study is indirect and relies on changes in measures of patient perceptions over the course of the study. Having said that, it must also be said that those measures were extremely congruent in suggesting that the perceptions of the intervention group patients changed in directions that would render them more likely to be adherent to medication regimens, and there is no strong evidence that there are other factors that may be affecting patient's blood cholesterol levels differentially eg. exercise.

Pharmacists have an important role to play in counselling patients about lipid lowering therapy, hyperlipidaemia, life style changes as well as evaluating patients' adherence to therapy and monitoring the impact of therapy through measuring total blood cholesterol levels.

Finally, the economic analysis yielded a cost of delivering the service, and suggested that training pharmacists individually in the field may be more effective both in terms of cost and effectiveness. However, it is only a suggestion at this time and would require specific research, or the support of a number of other studies using either or both of the training methods to be able to determine if this is in fact the case.

### **5.1 Outcomes and Recommendations:**

- A potentially remunerable community pharmacy based therapeutic outcomes monitoring service model for hyperlipidaemia (incorporating an adherence promoting service) was developed and evaluated.
- Trained community pharmacists were able to deliver a therapeutic outcomes monitoring service to their patients on anti-hyperlipidaemic medications which resulted in a lowering of their total blood cholesterol levels.
- Improved therapeutic outcomes in terms of total blood cholesterol levels were obtained in the patient group who received the service from the community pharmacists.
- The results gained suggest that the therapeutic outcomes monitoring service outlined in this study may have positive impacts, and warrants further evaluation in community pharmacies.
- The instruments used could not detect enhanced patient adherence to drug therapy and a consequent quality use of medicines by the patients. However, the positive outcomes demonstrated with the clinical data, indirectly show that it was possible that there was an improvement in patient adherence to therapy which could not be detected in this study, possibly due to the sample size.
- If the type of service outlined in this report is instituted or studied further, the length of



the questionnaire and frequency of lipid readings used in this study should be reduced. It is posited that this would have the effect of increasing patient retention, increasing pharmacist satisfaction and reducing the cost of delivering the service.

- If the type of service outlined in this report is instituted or studied further that the instrumentation used should be capable of taking blood lipid fractions and, if possible delivering a Framingham risk assessment. It is thought that the addition of these measures would enhance patient motivation and retention and extend the efficacy of the protocol.



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## APPENDICES

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## 7 APPENDICES

## 1 Literature Review

### 1. Introduction

Cardiovascular disease is a largely preventable disease. However in Australia, it is still responsible for 40% of all deaths <sup>1</sup>. The benefits of lowering cholesterol on reducing cardiovascular risk are well established <sup>2</sup> however poor adherence to lipid-lowering therapy limits the efficacy of existing lipid-lowering medications <sup>3</sup>.

This paper examines adherence in the context of lipid lowering drugs. It also looks at strategies for increasing adherence to these drugs, with a particular focus on the role of the community pharmacist in increasing adherence to lipid lowering drugs.

### 2. Adherence

The concept of adherence in the context of health care has been an area of extensive research over the past thirty years<sup>4</sup>. A commonly used definition of adherence is “*the extent to which a patient’s behaviour (in terms of taking medication, following a diet, modifying habits, or attending clinics) coincides with medical or health advice*” <sup>5</sup>. However this definition was originally used by Haynes and Sackett <sup>5</sup> to describe **compliance** rather than **adherence** and gives an incomplete description of adherence. While adherence and compliance are often use interchangeably, compliance implies that the patient is in a passive role under the authority of health care professionals. In contrast, adherence places the patient in a more active, collaborative role <sup>4</sup> but still refers to patients adhering to their prescribed treatment regimen. This paper will use the term adherence as the preferred term to describe patient’s medication taking behaviour (compliance and adherence to therapy).

Adherence can be a single or a continuous measure. A continuous measure is more commonly used <sup>3</sup>, for example if a patient takes three of the five doses in an antibiotic course, they are 60% adherent. If treatment is discontinued, this equates with zero adherence.

### 3. The Current Situation

A review of the literature on adherence to drug regimens has revealed estimates of adherence from 15% to 93% for long term drug regimens<sup>4</sup>. In another review, Sackett and Snow <sup>9</sup> report adherence rates of approximately 50% for long term preventative therapy. Lipid lowering therapy is a long-term and preventative drug treatment and therefore would be expected to display adherence levels within this range.

The largest study on adherence to lipid lowering drugs was the Helsinki Heart Study<sup>3</sup>. This study looked at primary prevention of cardiovascular disease with gemfibrozil in middle-aged men with dyslipidaemia. Adherence was studied using mean daily capsule counts, semi-annual urine analysis and serum digoxin marker analysis. Good adherence was defined as taking at least 90% of doses. Only 36% of the participants showed good adherence to gemfibrozil according to the capsule count. Furthermore, the control group had only marginally better adherence with 39% classified as good adherers. The results may not give an accurate picture of adherence to lipid lowering therapy today because they exclusively apply to gemfibrozil. Currently statins are the first line treatment for dyslipidaemia. These drugs have very different side effect and dosing profiles to gemfibrozil, two factors which have been found to affect adherence.

A more recent study examined the prescription claim data of 7287 patients in Canada and the USA for lipid-lowering drugs<sup>14</sup>. Participants were all aged over 65 and had filled at least one prescription for lipid-lowering drugs. The primary outcome was persistence which was defined by whether or not patients picked up sufficient repeat prescriptions for lipid-lowering drugs. It was found that patients did not have an adequate supply of their medications to cover 40% of the days in the year. Patients using statins had the best persistence rates (64% of days covered) and those using cholestyramine had the worst persistence (37%). About half of the surviving patients had stopped taking their lipid lowering drugs altogether 5 years after the research commenced.

Wei<sup>15</sup> claims that the patients involved in a study on adherence to statins appeared to demonstrate higher adherence rates than observed in an earlier study<sup>14</sup>, with greater than 80% adherence in 69% of patients. However the findings of the two studies are not directly comparable as different outcomes were used. Some comparison can be drawn as similar methods were employed. The higher rates of adherence found could possibly be explained by the characteristics of the participants – all of whom had experienced their first myocardial infarction between 1990 and 1995. Wei<sup>15</sup> was examining adherence to lipid-lowering drugs as secondary prevention, whereas Avorn<sup>14</sup> investigated lipid-lowering for both primary and secondary prevention. A review of adherence to lipid-lowering drugs<sup>3</sup> found that adherence is higher in secondary prevention groups than primary prevention groups. It was thought that this may be because patients taking lipid-lowering drugs as primary prevention may experience adverse effects from the medication while not perceiving any benefits.

Lipid adherence in an Australian context has been investigated by Simons and colleagues<sup>16</sup>.

This was a prospective study that examined the dispensing data of 610 patients who had been newly prescribed lipid-lowering drugs. The primary outcome measured was the number of patients failing to obtain repeat prescriptions. It was found that 60% of patients apparently discontinued their medication over the 12 month study period. Almost a third of patients discontinued because they were not convinced that the treatment was necessary however significant numbers of patients also discontinued therapy due to a lack of efficacy (32%) or because of experiencing adverse effects (7%). Patients under 50 years old were more likely to discontinue therapy than older patients, and those taking other cardiovascular drugs were more likely to persist with treatment. An interesting finding from a health care provider perspective was that of the patients who experienced poor efficacy only half were switched to a different lipid-lowering agent.

The studies mentioned above have used various types of adherence measures on a dichotomous or continuous scale. Persistence rates have also been used in measuring adherence to therapy limiting the comparison of studies solely on measuring adherence. These studies include investigations of adherence to lipid lowering drugs in both lipid clinic and community settings. A common finding in both settings is the disparity between adherence rates to different classes of lipid lowering drugs, with patients using statins generally displaying higher degrees of adherence than those using older lipid lowering drugs such as gemfibrozil and cholestyramine. A major limitation of these studies is that many use prescription refill data as the main determinant of adherence. It is not known whether patients took their medication once it was bought. Furthermore some studies cannot be generalised to the population of patients taking lipid lowering drugs due to restricted age bracket of the subjects.

#### **4. Strategies to Increase Adherence**

Studies in the literature have highlighted the less than optimum levels of adherence to lipid lowering therapy. An understanding of the causes of non-adherence is required, in order to develop targeted strategies to improve adherence to therapy. Balkrishnan<sup>17</sup> classified reasons for nonadherence into several categories – medication, medical, demographic, economic, health care professional, patient's beliefs and knowledge. This review will focus on medication/medical, patient's beliefs and health care professional related factors as these can be addressed by pharmacists in community practice. Adherence trends related to demographic factors (eg. age, gender, socioeconomic position) will be discussed briefly. However economic factors such as costs of medications and amounts reimbursed to patients for medications are generally controlled at a government or manufacturer level rather than a

pharmacy level and are not within the scope of this review.

There have been conflicting reports on how adherence is affected by demographic factors. Wei<sup>15</sup> found that women were more likely to adhere to statin therapy than men. He did not find an association between socioeconomic level and adherence. This is in contrast with results from Avorn<sup>14</sup> which indicate no difference in adherence between males and females and that a lower socioeconomic status was associated with lower adherence. Avorn<sup>14</sup> also found a decrease in adherence associated with increasing age. Another study showed women were 33% more likely to discontinue lipid-lowering therapy and that age had no consistent effect on adherence<sup>13</sup>. These seemingly contradictory findings may be explained by the sample populations used in the different studies. For example, all patients in the study by Avorn<sup>14</sup> were over 65 years old whereas the sample groups in the studies by Wei<sup>15</sup> and Andrade<sup>13</sup> were not age restricted. It is possible that the effect of age on adherence is confounded by other related factors, such as polypharmacy and cognitive or physical impairment.

Medication regimen related causes of non adherence are the simplest factors for a pharmacist to address as interventions are generally at a clinical or administrative rather than a behavioural level. These can include side effect profiles, dosage regimens, number of medicines the patient is using, efficacy of treatment, cost and dosage form. Changing within and between therapeutic classes can significantly alter dosage regimens and side effect profiles of lipid-lowering drugs. Eriksson<sup>11</sup> compared cholestyramine and pravastatin and found that there was 77% adherence to cholestyramine and 95% and 91% adherence to pravastatin 20mg and 40mg respectively. Comparing the properties of these two agents gives a good indication of why these results were obtained. Cholestyramine was given at doses of 16 grams per day, which should be dissolved in 400-600mL water then administered one hour after or 4-6 hours before other medications according to the manufacturers instructions<sup>18</sup>. This can be contrasted with a single evening dose of pravastatin. Patients with complex drug regimens are less adherent than those on simpler regimens<sup>19</sup>. Of the patients using cholestyramine 56% experienced gastrointestinal adverse effects compared with 12% in both pravastatin groups.

A study of 1028 randomly selected adults over 55 in 1993 found that there was a significant ( $p < 0.01$ ) relationship between an increase in the number of medications taken and poorer compliance<sup>20</sup>. However research completed recently on adherence in patients on long term cardiovascular medicines by found the opposite – that patients on more medications tend to

be more adherent<sup>21</sup>. This supports other studies which found that patients on more medicines were more adherent<sup>22,23</sup>. Billups<sup>22</sup> suggests that the inconsistency may be explained by the Health Belief Model – *“Patients who believe they are ill (which may be the case for those taking several drugs) are likely to take steps necessary to maintain their health (taking drugs as prescribed)”*.

Patient related factors affecting adherence are more difficult to address because modification of patient attitudes is often required and some can not be changed at all (for example physical and cognitive capabilities). Factors that can be modified include patient perceptions about drugs, motivation, and locus of control.

A study by Jackevicius<sup>24</sup> examined adherence to statin therapy in elderly patients, comparing rates of adherence between a group with acute coronary syndromes and a group without. The group with acute coronary syndromes (ie. the secondary prevention group) had a 40.1% adherence rate over the two year study period, compared to 25.4% adherence for the other group (ie. the primary prevention group). The author theorised by the authors that the primary prevention group had lower adherence to statins because they were asymptomatic and perceived no immediate benefit from the medication. Educating patients about the implications of uncontrolled hyperlipidaemia may improve adherence to lipid-lowering drugs because this may help them understand why they are taking these drugs.

A patient's demonstrated locus of control should be evaluated when considering how to improve their adherence. Patients with an internal locus (ie. those who feel they have control over a situation) may respond to opportunities to contribute to discussion on their treatment regimen<sup>25</sup> whereas those with an external locus (ie. feel that the situation is being controlled) may respond better to medication management aids such as blister packs.

Factors affecting adherence related to health care professionals include the patient-practitioner relationship, provision of adequate and appropriate information, monitoring and adjusting treatment as required and involvement of the patient in planning their medication regimen<sup>26</sup>. Culos-Reed<sup>26</sup> emphasises the importance of tailoring adherence interventions to the individual patient and recommends that patient-centred counselling be used to achieve this. Patient-centred counselling is described as practitioners being aware of and acting on patient cues, providing information and solving therapeutic problems in collaboration with the patient.

Increasing patient adherence to lipid lowering medications is an area where pharmacists can

play an important role, due to their accessibility and position in the health care system<sup>27</sup>, as well as their knowledge and skills. Pharmacists can be involved in identifying factors which may affect adherence such as medication regimen, lack of motivation to take medications and lack of understanding of rationale and goals of treatment. Once reasons for non adherence are identified interventions can be initiated by the pharmacist, in collaboration with the patient and/or doctor. Due to the importance of the pharmacist in intervening in the treatment of non adherent patients, it is important that pharmacists have access to tools for identifying non adherence and are aware of how to use them.

## **5. Identifying Non-Adherence**

There is no simple single method for identifying non adherence. The methods used can be broadly categorised into direct and indirect methods<sup>9</sup>. There are advantages and disadvantages to both and not all methods are suitable for use in community practice. Direct methods of assessment are objective measures of adherence to treatment regimen, whereas indirect methods are more subjective and positive results do not always equate with medication taking.

Direct methods involve testing bodily fluids (usually blood or urine) for drugs, metabolites or marker substances. This has the advantage of being an objective measure, however it is not possible to tell whether the patient has been taking the drug consistently or has just taken it prior to the testing. There can also be considerable interpatient pharmacokinetic differences which confound results<sup>22</sup>. Direct methods also are not available for all drugs<sup>28</sup>. These methods may not be practical in a community setting due to the analytical equipment and expertise required.

Indirect methods include self report by the patient, tablet counts, examination of dispensing records, doctor's assessment of patient adherence and clinical outcomes (eg. change in blood pressure, blood sugar levels, lipid levels). The accuracy of some of these measures has been called into question. For example, a review on adherence by Stephenson<sup>28</sup> quotes a figure of 10% sensitivity for doctor's detection of non adherence. Stephenson also reviewed studies comparing patient self reports with pill counts. Pooled results of 4 studies showed a sensitivity of 55% and a specificity averaging 87% for self reports. Other methods such as tablet counts can be time consuming and costly to perform. However a combination of methods can be useful for obtaining an indication of whether or not a patient is adherent<sup>28</sup>.

Most of the studies assessing adherence to lipid lowering therapy mentioned in section 3



used dispensing records to estimate adherence. This method has the advantage of being a fast and efficient method of checking adherence for large populations<sup>22</sup>. In practice, this method could be combined with self report by patients using non judgemental and non threatening questioning<sup>28</sup>. This gives a clearer picture of adherence than using the dispensing record alone because it addresses the possibility that the patients may not take all dispensed medications. It is possible that patients may not be truthful in reporting their adherence however it is possible to identify over half of those who are not complying through the use of careful questions<sup>22</sup>.

The use of surrogate markers (ie. lipid levels) may be useful, however one-off results cannot be used as a measure of adherence. This is because there is often not a clear relationship between adherence to a particular drug and the therapeutic outcome<sup>4</sup>. Many factors other than adherence can influence lipid levels – for example diet, exercise, pharmacokinetics and inappropriate therapeutic agent or dosage. However lipid-level analysis on a regular basis, in combination with self reporting by the patient and questioning about other lipid lowering factors (eg diet and exercise) by the doctor or pharmacist may be of use in assessing and enhancing adherence<sup>28</sup>. This model avoids the pitfalls associated with one-off lipid by examining trends in lipid levels and considering other causative factors.

Lipid level analysis at a community practice level has become more practical due to the introduction of point-of-care devices which analyse lipid content in capillary blood obtained by finger pricks. Currently available point-of-care lipid testing devices include the Accutrend GC<sup>®</sup> analyser and the Cholestech LDX<sup>®</sup> analyser. These tools can be used by pharmacists to assess and enhance adherence to lipid lowering drugs. If desktop lipid analysis is to be carried out as part of adherence determination, it is important that the analyser is accurate and that consistent results can be obtained. Research findings on the accuracy and reliability of desktop lipid analysers have been largely positive. Two studies comparing the results of the Accutrend GC analyser with laboratory results of both capillary and venous blood found that the Accutrend system to be a reliable system for the determination of total cholesterol with high accuracy and precision<sup>29, 30</sup>. Gottschling<sup>30</sup> found that the Accutrend GC results were within 2.5-3.2% of laboratory results and were not affected by triglycerides, urate or haematocrit within normal reference ranges. Del Canizo<sup>29</sup> performed a similar study and found that mean differences between values obtained with the Accutrend GC were actually smaller than those obtained using laboratory methods.

An Australian government report on a similar analyser - the Cholestech LDX analyser,

recommended that “*restricted use of near patient testing, as an alternative to laboratory testing of lipids, should be considered in settings or circumstances where there is adequate training, accreditation and quality assurance*”<sup>31</sup>. It has been found that results from the Cholestech LDX analyser can vary depending on the operator and hence training of operators is recommended<sup>32</sup>. Due to the similarity of the Accutrend GC and Cholestech LDX machines, it could be assumed that adequate training of operators is also essential for Accutrend GC operators. This training includes the use of the device and quality assurance of the measurements by different operators.

There are a variety of methods available for pharmacists to use in assessing adherence to lipid lowering medications. The simplest and least expensive of these are asking the patient about adherence and examining dispensing records. However the results regarding point-of-care lipid analysers suggest that there is scope for the use of such devices in community practice in combination with other adherence assessment methods. The recommendations put forward in the report by the Medical Services Advisory Committee<sup>31</sup> provide useful guidelines for the utilisation of point-of-care lipid analysers in community practice.

## 6. Pharmacist's Role

The ImPACT study<sup>33</sup> had the objective of demonstrating that “*pharmacists, working collaboratively with patients and physicians and having immediate access to objective point-of-care patient data, promote patient persistence and compliance with prescribed dyslipidaemic therapy that enables patients to achieve their National Cholesterol Education Program goals*”. Patients enrolled in the study demonstrated rates of persistence and compliance (93.6% and 90.1%) superior to those found in earlier studies<sup>14-16</sup>.

Many interventions which aid in increasing adherence are already a part of the community pharmacist's job description – reviewing medication regimens, checking dispensing records for interval between repeats, provision of written information and counselling on medication use and appropriate non pharmacological treatments<sup>27</sup>. However there are additional tasks that community pharmacists can also carry out to supplement existing interventions.

Pharmacists are in a good position to explore reasons for non adherence. Many patients are non adherent for what appear to be illogical reasons<sup>16</sup>. Identification of these reasons along with education about the nature of cardiovascular disease and the role of lipid-lowering drugs may improve adherence. Other barriers to adherence may be modifiable once identified. For example patients are unable to cope with a complex medication regimen can be assisted by

medication management aids such as blister packs or dosette boxes.

Providing a point-of-care lipid monitoring service is another task community pharmacists can perform to aid adherence<sup>33</sup>. Such a service can involve patients more in their treatment and give them an increased awareness of their condition and progress which may improve adherence.

It has been suggested that a telephone or postal reminder service to patients may be of use in increasing adherence to lipid-lowering drugs<sup>6</sup>, however a study by Guthrie<sup>34</sup> trialling a telephone and postal reminder service on 10335 patients on pravastatin therapy did not find that these services had any effect on compliance in the study group compared to a control group of 2765 patients receiving usual care

A study by Vivian<sup>35</sup> examined a pharmacist-coordinated hypertension clinic. Under the model used, pharmacists were given prescribing authority for blood pressure drugs in accordance with a defined protocol. At the monthly appointments, pharmacists discussed side effects and lifestyle changes as well as assessing adherence to blood pressure medications. This model had no interventions specific to improving adherence. The intervention group showed a significant decrease in systolic blood pressure compared with the control group (-18.4 compared with -3.98) ( $p=0.01$ ), however there were no differences in adherence observed between or within groups at baseline or the end of the study.

Community pharmacists can play an important role in increasing patient adherence to lipid lowering treatment and improving therapeutic outcomes. This has been indicated by the success of trials such as ImPACT. The interventions used in this study can be adapted for use in community pharmacy.

## **7. What has been done?**

Several studies in recent years have examined the effect of pharmacist-coordinated programs on improving hyperlipidaemia management<sup>33, 36, 37</sup>. In these studies pharmacists were given new responsibilities and roles, for example monitoring lipid levels<sup>33</sup> and adjusting doses in response to lipid levels<sup>37</sup>. All studies showed significant improvements in the percentage of patients reaching the lipid level goals.

The ImPACT study used point-of-care lipid testing in conjunction with interprofessional collaboration and information exchange in an effort to ensure that results and information obtained by pharmacists were acted upon by doctors. This study found that the intervention used resulted in persistence and compliance rates significantly higher than those obtained

previously<sup>13-15</sup>. Limitations of this study were that no control group was used and only patients completing the study were included in the results.

A study by Vallaincourt examined the effect of a pharmacist managed lipid clinic on the percent of patients reaching Canadian lipid level goals in the Canadian defence force<sup>37</sup>. The roles of the pharmacist in this study were to establish an initial treatment plan for each patient and document this in the doctor's notes, reinforce recommendations on diet and exercise, order blood tests, identify problems related to medications, write prescriptions modifying dosage of lipid lowering treatments and refer patients to other health care professionals. It was found that at follow up 94 patients (80%) had reached their LDL goals, compared to 58 (50%) at baseline, and 71 (61%) had reached all lipid goals compared to 39 (33%) at baseline. It was also found that the primary care physicians accepted all 93 recommendations made by pharmacists.

A similar study published by O'Donnell in 2001<sup>36</sup> had similar aims to the study by Vallaincourt but was specific to patients achieving LDL cholesterol goals. The design of the lipid clinic used in this study included a clinical pharmacist and dietician who evaluated current drug therapy and lifestyle of the patients and helped patients to implement recommended changes. The clinic protocol included encouraging patients to continue visiting the clinic until their lipid goals had been met and maintained for 6-12 months. This study reported that 73% of patients in the clinic achieved LDL goals, compared to 10-20% quoted in literature on usual care<sup>38</sup>.

These studies have all demonstrated the value of pharmacists in the management of hyperlipidaemia, however they use attainment of lipid goals as an endpoint and do not directly address the issue of adherence to lipid lowering drugs, although this may have been included as part of the intervention. The effect of a pharmacist managed lipid program on adherence to lipid lowering drugs is an important area of research which can complement the findings from these studies and further increase adherence to lipid lowering drugs.

## **8. Summary**

Adherence has been the focus of a large number of studies in recent years. The term adherence is increasingly being used in the place of compliance because of the more active, collaborative connotations associated with the word. It is often used interchangeably with compliance.

At present, adherence to lipid lowering therapy is consistent with adherence rates for other medications treating chronic conditions. It has been found that lipid lowering drugs are not being utilised effectively, particularly in non clinic situations among patients using these drugs as primary prevention measures against cardiovascular disease.

Strategies to increase adherence generally focus on identifying causes of non adherence and acting to modify these where possible. Pharmacists can be of particular use in identifying and addressing non adherence associated with medications, patient beliefs and health care professionals.

The use of point-of-care lipid testing devices has potential for use as an adjunct to other methods of identifying non adherence and is suitable for use in community pharmacy in accordance with recommendations made by the Medical Services Advisory Committee.

The involvement of pharmacists in lipid clinics and programs to increase patient attainment of lipid goals has been examined in several studies<sup>33, 36, 37</sup> with positive findings. However these studies have not evaluated the impact of pharmacist intervention on adherence to lipid lowering drugs.

The aims of the grant are to develop, implement and evaluate a new cognitive service in community pharmacy for conducting therapeutic outcomes monitoring in consumers with hyperlipidaemia to promote patient adherence to drug therapy and to conduct a cost-effectiveness analysis of the delivery of this service by pharmacists.

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## 2 Pilot Study

### Abstract

**Objective.** To pre-test and assess the feasibility of the data collection tools for a new remunerable cognitive service focussing primarily on monitoring adherence to lipid lowering drugs.

**Method.** A convenience sample of community pharmacists were selected and trained on the use of the data collection tools: SF-12 (quality of life), the Brief Medication Questionnaire (BMQ) <sup>1</sup>, consumer demographics and Barriers to Medication Use (BMU). Pharmacists were asked to document the time taken to complete the forms; ease of completion (from 1 [very easy] to 5 [not easy at all]); problems encountered; as well as the content of their verbal consultation with each consumer and strategies suggested to improve adherence, using a standard data collection sheet.

**Setting.** Four community pharmacies in Sydney.

**Key Findings.** The total mean time taken to complete all forms was 17 minutes. The mean ease of completion score was 1.20 for the demographic questionnaire, the SF-12 and the data sheet, with no problems reported for these instruments. The BMQ and BMU were less easy to complete with mean scores of 1.73 and 2.20 respectively. Problems encountered with the BMQ and BMU were due to awkward wording of the questions and patient difficulty in understanding.

**Conclusions.** It appears that it is feasible to use the forms to collect consumer data and data on the consultation process with consumers. The results have highlighted a need for training to enhance pharmacists' skills in adherence promotion through provision of strategies and counselling.

## Introduction

Cardiovascular disease is one of Australia's major health concerns, accounting for around 40% of all deaths each year<sup>2</sup>. Management of modifiable cardiac risk factors, such as dyslipidaemia, hypertension, smoking and diabetes mellitus, is the most effective means of prevention<sup>3</sup>. There are effective drugs and non drug treatments available to manage cardiac risk factors, however the mortality rate is still unacceptable for a largely preventable disease.

Lipid lowering drugs are one of the most widely prescribed groups of therapeutic agents in Australia<sup>4</sup>. Although the benefits of therapy with these agents on reducing cardiac risk have been proven in a number of studies<sup>5 6 7</sup>, their efficacy is limited by patient adherence. A review of literature on adherence to drug regimens showed estimates of adherence ranging from 15-93% for long term drug regimens<sup>8</sup>. Studies examining adherence specific to lipid lowering drugs have reported rates of 90% of doses taken in 36% of patients<sup>9</sup> and 80% of doses taken in 69% of patients<sup>10</sup>. An Australian study in 1996 found that 40-60% of patients had discontinued treatment with lipid lowering drugs one year after starting<sup>11</sup>.

Factors contributing to non adherence can be classified into those related to the patient's medication regimen (eg. number of medications, side effects), the patient's health beliefs, health care professionals, demographic and socioeconomic factors (eg. cost of medication)<sup>12</sup>. To improve adherence, one or more of these areas can be targeted by health professionals and specific factors for each patient which limit adherence addressed.

Community pharmacists are in an ideal position to identify poor adherence to medications and to positively influence patient adherence. They are often the first place patients go to for health and medication advice and are readily accessible by most of the population<sup>13</sup>.

In Australia, there are currently no widespread community pharmacist-delivered services that monitor and promote adherence to lipid lowering medications. This study forms part of a larger research project which aims to develop, implement and evaluate a new cognitive service to conduct therapeutic outcomes monitoring in consumers to promote adherence to drug therapy. This study aims to collate and pre-test the protocols and instruments for data collection for the project.

## **Methods**

### **Participants**

As the purpose of this study was to pre-test the research instruments, a convenience sample of six community pharmacies was selected. Pharmacists were trained in the use of the data collection instruments. Each pharmacist was asked to recruit 5-10 patients (who met the following inclusion criteria) to pre-test the instruments. The inclusion criteria were: at least 18 years of age, fluent in written and spoken English and taking at least one lipid lowering medication.

### **Data Collection Instruments**

Four questionnaires were administered to patients – the Brief Medication Questionnaire, a modified version of the Barriers to Medication Use Questionnaire, the Short Form-12 Quality of Life Survey and a patient demographic questionnaire.

The Brief Medication Questionnaire (BMQ) which is a validated and reliable tool<sup>1</sup>, assesses patient adherence to medications and problems that patients may have with taking their medications. Patient dispensary records from the three months prior to the study were collected for use in combination with BMQ for evaluating adherence. The dosage and dispensing intervals were used to give an indication of patient adherence.

The Barriers to Medication Use Questionnaire (BMU) modified for this study is not validated but is based on a heart failure specific instrument<sup>14</sup>. This instrument was tested on a sample of 128 subjects and demonstrated modest internal consistency in two of the five barrier domains and weaker internal consistency in the remaining three. The relationships between BMU scores and adherence, and BMU scores and health-related quality of life were examined to test the construct validity. A negative correlation was observed between BMU and adherence, and, although not statistically significant, the author concluded that this provided some evidence for the construct validity of the BMU questionnaire.

For this study, the BMU was modified by removal of the social support barrier domain, as this was specific to heart failure. Several questions in other domains, relating to heart failure or United States health care system were also removed. The modified questionnaire then consisted of four domains - Patient Knowledge, Previous Medication Experience, Communication and Health Care Professionals. There are 22 multiple choice questions and two open ended questions. These ask about what information patients are given regarding their medications and which health care professionals provide it, practical factors affecting

adherence (eg. side effects, cost of medications), how patients receive and understand information about their condition and their relationship with their health care professionals.

The different types of barriers assessed by the BMQ and the BMU warrant the use of both instruments in this study. The BMQ is a general tool which examines that patients' whole medication regimen and assesses barriers which may impair adherence to any of the patients' medications – for example whether the patient can remember to get their repeats on time, whether they can read the print on the medication labels or whether the number of medications they are taking is overwhelming. The BMU is more specific to the medications that the patient is using to lower cholesterol – it assesses patient attitudes towards these medications, knowledge of side effects and drug interactions and non-adherent behaviours specific to lipid lowering drugs (eg. taking extra doses to compensate for fatty meals).

The Short Form-12 Quality of Life Survey (SF-12) was selected for this study. It is another validated and reliable tool which measures the effect of physical and mental health on patients' quality of life. The physical and mental component scores (PCS and MCS) are calculated using a table of empirical values which correspond to each answer given. A score of 50 represents "average" health status for that component and higher scores indicate above average health status.

The patient demographic questionnaire consisted of questions compiled from a previous survey used by researchers in the faculty. It included items on patient gender and age, languages spoken at home, level of education, occupation, employment status and current medical conditions.

In addition to the questionnaires administered to the patients, a pharmacist-specific instrument (the data sheet) was produced to record the strategies used by the pharmacist in response to the information gathered from the patient questionnaires. Strategies were categorised into four groups - the provision of written information, provision of verbal information, other adherence aids provided and recommendations made to other health care professionals.

### **Pre-testing Process**

Pharmacists were asked to administer the four questionnaires to patients and use the information gained from patients in the BMQ and BMU to identify factors which may contribute to poor adherence to lipid lowering drugs. Pharmacists were also asked to provide

strategies to address these barriers.

A list of strategies was provided as a guide for pharmacists to use to address specific barriers. The strategy list was compiled from strategies used in similar studies and other literature related to medication use and adherence <sup>3, 15, 16</sup>. Pharmacists were not constrained by the strategies listed and were encouraged to use their own strategies as well. Pharmacists were not trained on the provision of strategies as the aim of this study was to pre-test the data collection instruments.

Pharmacists used the following indicators for each patient (in an Indicators Questionnaire) in pre-testing:

1. Time taken to use the instruments
2. Ease of use for each instrument
3. Patient receptiveness to any strategies used
4. Problems encountered with the instruments

Pharmacists were asked to record the time taken (in minutes) for each questionnaire. They rated ease of use for each survey on a scale of 1 (very easy) to 5 (not easy at all) for each patient. They were asked to indicate whether they had experienced any problems with each of the instruments. If they replied yes, they were asked to describe the problem. Pharmacists also indicated how receptive the patients were to any strategies used and whether they felt the information recorded on the data sheet accurately described what occurred during counselling.

### **Data Analysis**

Data from all five research instruments and the Indicators Questionnaire were entered into SPSS version 11.5 and descriptive analysis conducted.

The mean summative score was computed for the ease of use scale for each instrument.

## Results

### Pharmacy Characteristics

Six pharmacies were approached to participate in the study. One pharmacy withdrew during the study due to time and financial reasons and another was unable to recruit any patients during the study due to staff shortages. The remaining four pharmacies were located on the North Shore (2), South-Western Sydney and the Northern Suburbs. Of the pharmacists involved, two were pharmacy owners, one was an experienced pharmacist in charge and one was a recent graduate.

Each pharmacy was asked to recruit 5-10 patients. The study period was from September 23, 2003 to October 14, 2003. A total of twenty four patients were recruited in this time.

### Patient Demographics

The average patient age was 69 years (sd=9). Approximately 67%(n=16) were female. A total of 20 (83%) were born in Australia. Most (60%, n=14) were retired.

### Time Taken

The mean time taken for pharmacists to administer the four patient-specific questionnaires and complete the pharmacist-specific data sheet was 17 minutes. The section taking the most time was the barriers to adherence questionnaire (mean 6 minutes) while the data sheet took the least time (1.8minutes) (see Table 1).

**Table 1. Time taken to complete**

Instruments	Time taken			
	Min (min)	Max (min)	Mean (min)	Std. Deviation
Demographics	1	5	2.20	1.37
BMQ	1	15	4.40	3.94
BMU	2	15	6.13	3.40
SF12	1	5	2.00	1.31
Data sheet	1	5	1.80	1.27

## Ease of Use

The mean scores for each section are shown in table 2.

**Table 2. Ease of Use of Tools**

Instrument	Summative Score			
	Minimum	Maximum	Mean	Std. Deviation
Demographic	1	3	1.20	0.56
BMQ	1	5	1.73	1.10
Barriers	1	5	2.20	1.21
SF12	1	3	1.20	0.56
Data sheet	1	3	1.20	0.56

The BMQ had the lowest reported ease of use. Pharmacists indicated that patients had difficulties understanding the questions, in particular those which had with double negatives. One pharmacist reported that the multiple choice options should be reversed with Strongly Agree on the left and Strongly Disagree on the right.

Pharmacists did not report any other problems with completing the five questionnaires. They also appeared to have no problems identifying strategies to aid patient adherence.

## Adherence levels

The mean number of medications taken by patients was 5 (range: 1-13). Patient adherence levels were calculated using the BMQ (Question One) in which patients reported how many doses of their medications they have missed and how many doses they were prescribed. The BMQ was scored in conjunction with dispensary records. Adherence was calculated as the percentage of doses taken. For lipid lowering medications, the adherence range was 85-100% (median 100%). For other medications the adherence range was 71-100% (median 100%).

Additionally, the Regimen Screen, Belief Screen and Recall Screen scores have also been compiled for each patient (Table 3) by the researcher from the BMQ. The Regimen screen score ranges from 0-7 and screens for potential non-adherence. A score of greater than one constitutes a “positive screen” and indicates that the patient may be non adherent to therapy. The Belief screen score range is dependent on how many drugs the patient reported problems with. The Recall screen score range is 0-2. A score greater than one (“positive screen”) for the Belief screen or Recall screen indicates that patients may have barriers to adherence related to their beliefs or in remembering to take their medications.

Patients scored the best for the Recall screen, with 100% recording negative screens. The Belief screen showed the worst results – 13% of patients screened positive to having belief barriers. For the Regimen screen, 8% (n=2) screened positive for potential non adherence to their medication regimens.

**Table 3. BMQ Results.**

<b>Status</b>	<b>Screen</b>		
	<b>Regimen</b> n(relative frequency %)	<b>Belief</b> n(relative frequency %)	<b>Recall</b> n(relative frequency %)
Positive	2(8%)	3(13%)	0(0)
Negative	22(92%)	21(83%)	24(100%)



## Barriers

### Patient Knowledge

The patients' responses to the knowledge section of the BMU have been reported in Table 4. Patients' reported knowledge levels were generally good, with 96% (n=23) of patients strongly agreeing or agreeing with the statement "I know why I am taking each of my medications". Responses indicated a high level of knowledge about the beneficial effects of their medications and awareness of side effects. Most (92%) patients strongly agreed or agreed that they are always given instructions on how to use their medications by their health care professionals. However about a third of patients agreed or strongly agreed that they are never told about drug interactions.

**Table 4. Barriers to Adherence - Patient Knowledge**

	n	Strongly Agree n(%)	Agree n(%)	Neutral n(%)	Disagree n(%)	Strongly Disagree n(%)
I know why I am taking each of my medications	24	18 (75)	5 (21)	1 (profe4)	0 (0)	0 (0)
Before starting a new medication I know all the good things it will do for me.	24	13 (54)	10 (42)	1 (4)	0 (0)	0 (0)
I am fully aware of the side effects of my medications	24	9 (36)	13 (54)	0 (0)	2 (8)	0 (0)
I am always given instructions for how to use my medications	24	12 (50%)	10 (42)	1 (4)	0 (0)	1 (4)
I am never told about drug interactions	24	1 (4)	8 (33)	6 (25)	6 (25)	3 (13)

### Previous Experience

The barriers to adherence most commonly reported by the patients were related to the cost of medications or side effects (Table 5). Only three patients reported using a medication organiser to help them take their medications. All patients disagreed that they never felt any benefit from their medications.

**Table 5. Barriers to Adherence - Previous Experience**

	n	Strongly Agree n(%)	Agree n(%)	Neutral n(%)	Disagree n(%)	Strongly Disagree n(%)
The bad (or "side") effects of my medications prevent me from taking them as prescribed.	24	2 (8)	1 (4)	3 (13)	7 (29)	11 (46)
I cannot afford my medications	24	0 (0)	2 (8)	3 (13)	7 (29)	12 (50)
I always make sacrifices to afford my medications.	24	2 (8)	3 (13)	3 (13)	6 (25)	10 (42)
The times for taking my medications are inconvenient.	24	0 (0)	0 (0)	1 (4)	12 (50)	11 (46)
I never feel any benefit from my medications.	24	0 (0)	0 (0)	0 (0)	12 (50)	12 (50)
A medication organiser helps to remind me about taking my medications.	24	1 (4)	2 (8)	3 (13)	1 (4)	11 (46)
I increase the dose of my medication when I have fatty foods.	24	0 (0)	0 (0)	1 (4)	4 (17)	19 (79)

## Communications

Patients reported that they had good communications with their doctors and pharmacists, with almost agreeing that that they always ask their doctors and pharmacists questions when they did not understand something about their medications (Table 6). Most also agreed that they understand the information provided to them about their medications and in general, in response to their questions.

**Table 6. Barriers to Adherence – Communications**

	n	Strongly Agree n(%)	Agree n(%)	Neutral n(%)	Disagree n(%)	Strongly Disagree n(%)
I always ask my doctor questions when I do not understand something about my medications.	24	16 (67)	7 (29)	0 (0)	1 (4)	0 (0)
I always ask my pharmacist questions when I do not understand something about my medications	24	16 (67)	8 (33)	0 (0)	0 (0)	0 (0)
I never know what to ask my doctor about my medications.	24	0 (0)	1 (4)	1 (4)	9 (38)	13 (54)
I never know what to ask my pharmacist about my medications.	24	0 (0)	1 (4)	0 (0)	9 (38)	14 (58)
I always understand the answers to my questions.	24	11 (46)	12 (50)	0 (0)	1 (4)	0 (0)
My doctor/pharmacist explains information about my medication in a way that I can understand.	24	13 (54)	9 (38)	0 (0)	2 (8.3)	0 (0)

### Health Care Professionals

Patients generally had a high regard for their doctors and pharmacists (Table 7). Most believed that their doctors and pharmacists have adequate knowledge to answer their questions. Most trusted their doctors and pharmacists and disagreed that these people are not interested in what they have to say about their condition. Interestingly, one patient reported they are afraid to tell their doctors and pharmacists about not taking some doses of their medication.

**Table 7. Barriers to Adherence – Health Care Professional**

	n	Strongly Agree n(%)	Agree n(%)	Neutral n(%)	Disagree n(%)	Strongly Disagree n(%)
These people have adequate knowledge to answer my questions.	24	13 (54)	9 (38)	0 (0)	1 (4)	1 (4)
These people do not seem interested in what I have to say about my condition.	24	1 (4)	0 (0)	0 (0)	6 (25)	17 (71)
I am afraid to tell these people that I have missed taking some medications.	24	0 (0)	1 (4)	0 (0)	8 (33)	15 (63)
I trust these people.	24	17 (71)	6 (25)	0 (0)	0 (0)	1 (4)

### Strategies Used

The strategies used by pharmacists reflect the high adherence observed and the small number of barriers reported in this study. Most strategies used by pharmacists involved the provision of written and verbal information as well as verification that patients understood this information. Many patients received more than one strategy – in particular patients receiving written information had this information reinforced in verbal counselling.

### Written Information Provided

Written information was provided to address barriers related to a lack of patient knowledge about their medications or conditions. Consumer Medicine Information (CMI) was the most common written information provided to patients. Some patients received more than one

CMI. In total, twenty CMI were given to thirteen patients. Only one self care fact card was given out.

### Verbal Information Provided

Pharmacists reported providing 71 pieces of verbal information. Most of these were information about medication names (n=16), indication (n=13) and dosing time (n=14). Pharmacists were less likely to provide information on side effects (n=9), drug interactions (n=4) and generic equivalences (n=4).

### Adherence Aids Provided

The most common strategies used to encourage adherence were verification of patient understanding (n=11) and discussion of routines for taking medications (n=9) (Table 8). Pharmacy 1 and 2 accounted for 85% of adherence strategies used.

**Table 8. Adherence Strategies Provided**

	Pharmacy 1 (n=9 patients)	Pharmacy 2 (n=6)	Pharmacy 3 (n=5)	Pharmacy 4 (n=4)	Total
Pill Box	1	2	-	-	3
Blister packs	1	-	-	-	1
Medication alarm	1	-	-	-	1
Repeat reminders	1	2	-	-	3
Generic substitution	1	6	-	1	8
Routine for taking medications	4	1	4	-	9
Medication diary	1	1	-	-	2
Verification of understanding	6	3	-	2	11
Medication chart	1	4	-	-	5
Other	-	1	-	-	1
Total	17	20	4	3	44

### Recommendations made to GP

Pharmacists recorded making five recommendations to GPs as a result of this study. One medication management review was recommended as well as a change in lipid lowering agent, an increase in dose of lipid lowering agent and two substitutions to less expensive brands.

As pharmacists did not have access to accurate cholesterol levels, it would not be expected

that many recommendations be made in relation to dose of lipid lowering drugs. The recommendation of a change of therapeutic agent was warranted because the patient was experiencing side effects to their current medication.

In this study, there was no follow up carried out to determine the outcomes of these recommendations.

### **SF-12 Quality of Life Survey**

SF-12 scores were calculated for twenty three of the patients in this study. The remaining patient's survey was missing data, preventing calculation of scores. Patients had a mean Physical Component Score (PCS) of 45.56 (sd=9.7) and a mean Mental Component Score (MCS) of 58.61 (sd=5.34).

### **Limitations**

The limitations of this study are mainly in regard to the data collected on adherence, barriers and strategies used. These limitations prevent the extrapolation of this data for the purposes of determining adherence trends or barriers to adherence, however the original aim of the study - to pre-test the data collection instruments – is largely independent of the limitations discussed below.

As this was a feasibility study done in a limited time frame, the sample size was small. Originally five pharmacies were recruited however one pharmacy withdrew from the study without collecting any data and another did not withdraw but also collected no data due to staff shortages. An additional pharmacy was recruited later in the study and given the same training and materials as the others, to give a total of four pharmacies in the study.

The pharmacies selected were a convenience rather than a representative sample. A representative sample was not required for this study because the study was testing the feasibility of using the tools in a pharmacy, rather than the effect of an adherence service on clinical outcomes. It was therefore more important to recruit pharmacies that were willing to participate and pre-test the instrument.

The pharmacists reported that they had only approached patients whom they predicted would agree to participate – this may account for the high adherence rates recorded (and hence the nature and number of strategies used).

The pharmacists received their training on-site at the pharmacies while they were on duty. There were interruptions and distractions during training. To overcome this problem, pharmacists were given a flow chart detailing what they had to do and were encouraged to read through it as well as all the forms and the strategy list before recruiting patients. They were also supplied with phone numbers to contact the researchers if they had any problems with using the data collection instruments.

Dispensary records were collected to use in combination with BMQ data for estimating adherence. These are of limited use if patients do not get all their prescriptions at the same pharmacy or if no directions are given on prescriptions. In this study, the majority of patients appeared to obtain most of their medications from the same pharmacy so the dispensary records were of value in estimating adherence.

## **Discussion**

Overall the service was well received by patients and pharmacists. Pharmacists did not report any problems with recruiting patients. Patients were generally receptive to the questionnaires and adherence strategies.

The primary indicators – ease of use and time taken – provided useful information for the future applications of the data collection instruments. The other data collected in this study provided helpful insights into factors that should be considered when developing protocols for delivery of the service.

The mean ease of use scores for each questionnaire indicated that pharmacists were quite comfortable using the instruments. The main problems reported with administration of the questionnaires were related to readability of the questions in the barriers to adherence questionnaire – in particular, double negatives in some of the questions. The questions concerned were not altered from the original questionnaire however those containing double negatives did show low correlations with a validated health-related quality of life scale used in the study <sup>14</sup>. A review of the readability of all questions in the barriers questionnaire should be carried out and the instrument re-tested prior to its use in the larger study.

The time taken to collect data is important information to consider when developing the protocols for the service to be used in the larger study. Delivery of the service needs to be time efficient for the benefit of both the pharmacists and the patients so it is important to ensure that all components can be delivered within an acceptable time frame.

The length of the questionnaires was not reported to be a problem by the pharmacists who administered it to patients however the pharmacist who withdrew from the study said that this was one factor that prevented him from participating. In a study examining a community pharmacy based lipid adherence service in the United States, pharmacists spent 30-60 minutes with the patient for the initial visit and 10-30 minutes in subsequent visits. This service used on-site cholesterol testing but also included comprehensive history taking and goal setting components <sup>17</sup>. The times taken in the follow up visits for the American study would be comparable with those found in this study as the components of the visits are quite similar.

In the larger study, cholesterol levels will be tested during the patient visit. Pharmacists will also need to interpret the results of the barriers questionnaire and BMQ and provide more comprehensive counselling to address adherence issues. Streamlining the data collection process could be considered when planning the service. One option for shortening this process is for patients to self-administer the BMQ prior to their appointment with the pharmacist. The BMQ was designed to be potentially self-administered by patients <sup>1</sup> and may in fact provide a more accurate record as pharmacists will not be in a position to “help” patients remember the names and indications of their medications.

The adherence levels reported in this study were exceptionally high compared to other levels quoted in literature <sup>8-11</sup>. As discussed in Limitations, this is most likely because pharmacists only approached patients they thought would agree to participate in the study. The high levels of adherence may also explain the number and nature of strategies suggested by pharmacists to improve adherence. It should be noted however that adherence to medication is extremely difficult to determine <sup>18</sup>. Asking patients about their adherence can be of some use however it has been found that patients tend to overestimate their adherence even if they admit to missing doses <sup>19</sup>.

In this study, the Brief Medications Questionnaire was used in combination with dispensary records to give an indication of patient adherence. While the information from dispensary records can aid in determining adherence the data obtained is of limited use as many patients get their prescriptions at multiple pharmacies and have incomplete records.

The information and adherence strategies provided by pharmacists reflect the high levels of adherence observed. Pharmacists provided a large amount of verbal information about medications to the patients (a mean of 3 items per patient) however other strategies were



utilised much less. The most commonly used adherence strategies were verification of patient understanding and discussion of routines for taking medications. Most patients in this study did not require adherence aids such as pillboxes, medication alarms and medication diaries. The small number of recommendations made to GPs is likely because pharmacists had no documentation of patients' lipid levels and hence were unable to determine whether their lipid lowering doses were effective. Also patients reported high satisfaction with their medication regimens with all selecting either "well" or "okay" for the BMQ question asking how well each medication worked for them.

Because this study was pre-testing the data collection instruments for the larger study, pharmacists only received training in the use of the instruments. They were not trained in how to identify patient barriers from the barriers questionnaire and BMQ or in the provision of strategies to address non adherence. In the larger study pharmacists will receive training in these areas as they will be providing a full adherence service to patients. In this study, pharmacists were given the responsibility of choosing the patients they wished to recruit. In the larger study, protocols for recruitment of patients will need to be included so that all eligible patients are approached for participation in the study. This will avoid the recruitment bias towards adherent patients observed here.

The SF-12 was included in this study as it will be used in the larger study to determine the effect of the lipid adherence service on health related quality of life. The patients here had lower physical component scores than average, but above average mental component scores. The pharmacists were not aware of the final SF-12 scores for their patients however patient responses to some questions may have influenced the adherence strategies suggested.

### **Summary**

The data collection instruments for the lipid adherence service have been pre-tested in community pharmacies and, on the whole, pharmacists found them easy to use.

The time taken to use the data collection instruments was established. This information will be useful in determining the structure of the service and what time periods will be allocated to other components of the service.

Some problems were encountered with the instruments, in particular comprehension of some questions in the BMU. These problems need to be addressed and the modified instrument

re-tested prior to the use of this instrument in the larger study.

The patients recruited in this study were selected by the pharmacists. This is most likely responsible for the high adherence levels observed. This issue needs to be addressed in the main study with all eligible patients being approached to participate to reduce the bias in the sample.

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## List of Barriers and Strategies:

<b>Factors Related to Medication Regimen</b>	
<b>Barrier</b>	<b>Strategies</b>
Too many medications, complicated medication regimen.	Recommend medication management review. Medication management devices – eg. blister packs, dosette box, medication chart.
Inconvenient dosing times.	Consider change in agent (eg. from simvastatin to atorvastatin to enable morning dosing) Consider changing from gemfibrozil to statins
Unacceptable side effects	Recommend change of therapeutic agent
Insufficient clinical outcomes	<i>Improve adherence</i> Increase dose Review exercise, diet plan Other aids to lower cholesterol – fish oil, omega 3 margarines.
Patient forgets to take medications	Medication management devices – eg. pill boxes, calendars/diaries, alarms Encourage patient to develop a routine that includes taking their medication – eg. keep their tablets next to toothbrush and take one when they clean their teeth before bed/in the morning.
Patient has trouble remembering to pick up repeats/get new prescriptions	Suggest/provide diary to write these dates in, provide last repeat reminders. Reminders from pharmacy (monthly)
Patient can't read instructions on prescription labels.	Arrange for labels in the patient's own language or large font
Patient is confused with different brands of their medications.	Stick to one brand of each drug. Ask patient to bring in all their medications and check for doubling up of therapeutic agents. Medication card with details of prescriptions etc
Medications are too expensive	Arrange for least expensive brand. Explain Safety Net scheme to patient – particularly if they obtain prescriptions from multiple pharmacies. Check that patient is on PBS medications where possible. Recommend patient investigates concession eligibility from Centrelink if appropriate.

<b>Factors Related to Patient Understanding and Knowledge</b>	
<b>Barrier</b>	<b>Strategies</b>
Patient does not understand what their medications are for.	Provide verbal and written information on disease state and medications. Discuss: <ul style="list-style-type: none"> <li>• Dose, indication</li> <li>• Possible side effects</li> <li>• Possible drug interactions</li> <li>• Missed dose information</li> </ul>
Patient takes extra doses of lipid lowering medications to make up for fatty meals.	Review how their medication works (eg. acting on production of cholesterol by the body rather than on ingested cholesterol)
Patient doesn't notice any benefits of taking their medications.	Discuss cholesterol levels – emphasise that although they won't notice any difference in how they feel, lowering cholesterol is very important for preventing heart attacks/angina. <i>Discuss exercise/diet/weight loss – these will also help lower cholesterol and patient <b>will</b> notice a difference in how they feel.</i>
Patient doesn't understand how or when to take their medications.	Review doctor's instructions and CMI. Ask patient to verify what has been discussed. Give clearly written instructions on when to take which medication.
Patient reports that they don't always understand the answers to their questions.	Use verification techniques when explaining information to patients – ask them to verify what has been explained. Use written information (self care cards, CMI) in conjunction with verbal explanations. <i>Consider use of videos if available.</i>

<b>2.1.1 Factors Related to Health Care Professionals</b>	
<b>Barrier</b>	<b>Strategies</b>
Patient doesn't trust their GP's knowledge or judgement.	<i>Talk to GP about these things... (how to do this without getting in trouble from the GP?)</i> <i>Forward copy of patient report to GP...</i>
Patient feels that their GP doesn't tell them enough about their condition	
Patient feels that they are not involved in decisions about their treatment	
Patient does not get any feedback from health care professionals on their progress.	
Patient is afraid to tell health care professionals that they have missed taking some medications.	Reassure patient that health care professionals want to help them and if they are having trouble with their medications, there is assistance available.

### **3 Recruitment aids**

#### **3.1.1 Informational article**

##### **Are you taking cholesterol lowering medications?**

Did you know that most people who take cholesterol lowering medications are not using them properly so that they can get the best out of them? This can mean that some of the money you spend on these medications is wasted and your health may suffer in the long run. In collaboration with community pharmacies, the University of Sydney is conducting a study that aims to help you get the best from your medication and lower your risk of heart disease.

The University is asking local people to participate in the study, which is being undertaken at North Richmond Pharmacy, North Richmond, and Blaxland's Pharmacy, Windsor. If you are eligible for the study you will receive cholesterol check-ups from your pharmacist every 3 months for 9 months, and be part of a study that is aimed at helping you, and eventually all Australians, to get the maximum benefit from their cholesterol lowering medications. There is no cost to you aside from the normal cost of your medications.

When you attend the pharmacy for your free cholesterol check you will be asked to complete a questionnaire. All information collected in this questionnaire will be used solely for research purposes by the University and will be strictly confidential.

People who want to find out more about the program should contact one of the pharmacists below.

**PHARMACIST'S NAMES AND NUMBERS SUPPLIED HERE**

### 3.1.2 Letter to patients

Dear Patient,

As part of this Pharmacy's on-going commitment to providing optimal health service to our patients, the University of Sydney has selected our pharmacy to conduct a study involving patients taking cholesterol-lowering medications.

Our computer records show you are currently taking prescription medication to lower your blood cholesterol levels.

Do you have high cholesterol and want help with getting it down?

Are you over 18?

Can you read and write English?

Would you like some more help to get the best from your cholesterol lowering medication?

If you answered yes to these questions, you are eligible for the study. During the 9 months of the study, you will receive cholesterol check-ups from our pharmacist to help make the most of your medication.

This is a FREE service. All you need to do is come to our pharmacy for four 20 minutes appointments over the next 9 months.

All information collected by the University of Sydney is confidential and your details will not be given to any other organisations.

Please telephone at if you are eligible and interested in participating in the study.

Your co-operation would be much appreciated.

Regards,

Pharmacist



## 3.1.3 Flyer



# The University of Sydney

## WANT HELP WITH YOUR CHOLESTEROL?

**ARE YOU CURRENTLY TAKING A PRESCRIPTION MEDICATION TO LOWER YOUR BLOOD CHOLESTEROL LEVELS?**

**ARE YOU OVER 18? CAN YOU READ AND WRITE ENGLISH?**

**WOULD YOU LIKE SOME MORE HELP TO GET THE BEST FROM YOUR CHOLESTEROL LOWERING MEDICATION?**

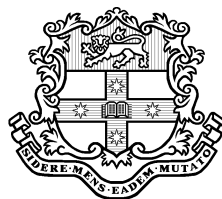
THE UNIVERSITY OF SYDNEY IS CONDUCTING A STUDY AT THIS PHARMACY. IF YOU ARE ELIGIBLE FOR THE STUDY YOU WILL RECEIVE 9 MONTHS OF CHOLESTEROL CHECK-UPS FROM YOUR PHARMACIST TO HELP YOU MAKE THE MOST OF YOUR MEDICATION.

THERE WILL BE NO COST TO YOU BESIDES YOUR NORMAL PAYMENT FOR YOUR MEDICATION. ALL YOU WILL NEED TO DO IS COME TO THIS PHARMACY FOR FOUR 20-MINUTE APPOINTMENTS OVER THE NEXT 9 MONTHS.

ALL INFORMATION COLLECTED BY THE UNIVERSITY OF SYDNEY IS CONFIDENTIAL AND YOUR DETAILS WILL NOT BE GIVEN TO ANY OTHER ORGANISATION.

**PLEASE TELEPHONE OR TALK TO THE PHARMACIST IN THIS PHARMACY FOR MORE INFORMATION.**

## 4 Pharmacist and Consumer Information Sheets and Consent Forms



**The University of Sydney**

**Faculty of Pharmacy**

**NSW 2006 Australia**

*Dr Grenville Rose, Project Coordinator*

**Telephone:** (02) 9036 9551

**Fax:** (02) 9351 4471

**e-mail:** grenville@pharm.usyd.edu.au

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### **Participant Information Sheet- Community Pharmacists (Study Group)**

#### **“A community pharmacist delivered therapeutics outcome monitoring service for hyperlipidaemia”**

Dear Colleague,

You are invited to participate in the above research project. The overall aim of the project is to develop a new remunerable cognitive service in community pharmacy for conducting therapeutic outcomes monitoring in consumers with hyperlipidaemia, and which leads to enhanced medication adherence. With a focus on hyperlipidaemia where adherence to therapy has been shown to be problematic, the service will include problem assessment; use of targeted adherence strategies and follow-up. Dr Parisa Aslani, Dr Ines Krass, Dr Timothy Chen, Ms Paula Whitehead and Dr Grenville Rose from the Faculty of Pharmacy at the University of Sydney are conducting the research. For this study to be successful and of benefit to the pharmacy profession, it is important that as many pharmacists as possible take part. Your pharmacy appeared in a random selection of Sydney community pharmacies, and your participation in this study will be greatly appreciated.

If you agree to participate in this project, you will be asked to recruit 10 consumers (subjects) who meet the following inclusion criteria:

- at least 18 years of age
- able to take part in the study without the help of a translator
- taking an antihyperlipidaemic medication

Additionally, you will be asked to provide a therapeutics outcome monitoring service to the subjects, provide the dispensing records for the subjects, and collect data on subjects' medication adherence and quality of life using standard data collection sheets provided by the researchers. It is anticipated that the entire process of recruiting consumers, providing the service and collecting data will last approximately 30 minutes. Additionally, with your permission, a sample of your interactions with the subjects will be audiotaped for in-depth qualitative analysis of the service provided. You will also be asked to conduct a cholesterol test using the Accutrend GC near patient cholesterol monitor. If you take part in this study you will be supplied with and trained in the use of this equipment

You will receive remuneration for the recruitment of subjects, delivery of the therapeutic outcomes monitoring service and the collection of data. This remuneration is \$100 per subject who completes the study.

You will be provided with training, both off-site (at the University of Sydney) and on-site (at your community pharmacy) prior to and during the research project. The training will focus on providing pharmacists with the knowledge and skills required to deliver a medication adherence service to patients on lipid lowering therapy, and a therapeutic outcomes monitoring service.

All aspects of the research, including results, will be strictly confidential and only the researchers named above will have access to information on participants. A report of the study may be submitted for publication, but individual participants will not be able to be identified in such a report, and only group data will be recorded. All data collected will be stored securely at the University and will be destroyed after seven years.

Participation in this study is entirely voluntary. You are not obliged to participate and, if you do choose to participate, you may withdraw at any time, without penalty or prejudice. If you do withdraw from the study, you may ask to have any information already collected about you destroyed.

Once you have read this information, a researcher will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact the project coordinator:

- Dr Grenville Rose, Project Coordinator, Tel: (02) 9036 9551

This information sheet is for you to keep.

Yours faithfully,

Grenville Rose

<b>Any person with concerns or complaints about the conduct of a research study can contact the Manager of Ethics and Biosafety Administration, University of Sydney, on (02) 9351 4811.</b>
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# The University of Sydney

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If you agree to participate in this project, you will be asked to recruit 10 consumers who meet the following inclusion criteria:

- at least 18 years of age
- able to take part in the study without the help of a translator
- taking an antihyperlipidaemic medication

Additionally, you will be asked to provide the dispensing records for the consumers, and collect data on consumers' medication adherence and quality of life using standard data collection sheets provided by the researchers. It is anticipated that the entire process of recruiting consumers and collecting data will last approximately 10-15 minutes. You will also be asked to conduct a cholesterol test using the Accutrend GC near patient cholesterol monitor. If you take part in this study you will be supplied with and trained in the use of this equipment

You will receive remuneration for the recruitment of subjects and the collection of data. This remuneration is \$25 per subject who completes the study.

All aspects of the research, including results, will be strictly confidential and only the researchers named above will have access to information on participants. A report of the study may be submitted for publication, but individual participants will not be able to be identified in such a report, and only group data will be recorded. All data collected will be stored securely at the University and will be destroyed after seven years.

Participation in this study is entirely voluntary. You are not obliged to participate and, if you do choose to participate, you may withdraw at any time, without penalty or prejudice. If you do withdraw from the study, you may ask to have any information already collected about you destroyed.

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**Participant Information Sheet- Consumers (Study Group)****“A community pharmacist delivered therapeutics outcome monitoring service for hyperlipidaemia”.**

Dear Participant,

You are invited to take part in the above study which aims to investigate how you take your lipid lowering medications. This study is being conducted by Dr Parisa Aslani, Dr Ines Krass, Dr Timothy Chen, Ms Paula Whitehead and Dr Grenville Rose from the Faculty of Pharmacy at the University of Sydney are conducting the research.

In order to take part in this study, you must be:

1. Over the age of 18 years
2. Able to take part in this study without the help of a translator
3. Currently taking one of the medications specified by the pharmacist and which is for lowering your high lipid / cholesterol levels.

If you meet the above criteria and agree to participate in the study, you will receive a counselling service by the pharmacist in the community pharmacy (approximately 30 minutes in duration). During the counselling service the pharmacist will ask questions from you about how you take your lipid lowering medications and any issues you may have about taking the medications, as well as your quality of life. Additionally, the counselling session may be audiotaped, but only with your permission. The pharmacist will first inform you if the session is to be recorded. With your permission, the pharmacist will also provide a copy of your medication history held in the pharmacy dispensary system to the researchers.

You will also have your cholesterol taken by the pharmacist 4 times over the 12 months (at four separate occasions). This procedure will involve a small pin prick on the finger and will be conducted according to standard infection control procedures, the same as at your doctor or hospital. You will feel the pin prick as a small sharp pain at the end of your finger and one drop of blood will be taken from the finger for each test. Some people might feel faint during the procedure, but a trained pharmacist will be in continual attendance during the cholesterol test.

As part of the study, you will be requested to attend the pharmacy after the initial visit, at three monthly intervals for a total of four visits. During these visits the pharmacist will have brief counselling sessions with you (approximately 10 minutes in duration).

All aspects of the study, including results, will be strictly confidential and only the investigators named above will have access to information on participants. A report of the study may be submitted for publication, but individual participants will not be identifiable in such a report and only group data will be reported. Participation in this study is entirely voluntary: you are not obliged to participate and - if you do participate - you can withdraw at any time without penalty or prejudice.

If you would like to know more at any stage, please feel free to contact any the project coordinator.

- Dr Grenville Rose, Tel: (02) 9036 9551

Thank you for your time and participation. This information sheet is for you to keep.

Yours faithfully,

Dr Grenville Rose

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In order to take part in this study, you must be:

1. Over the age of 18 years
2. Able to take part in this study without the help of a translator
3. Currently taking one of the medications specified by the pharmacist and which is for lowering your high lipid / cholesterol levels.

If you meet the above criteria and agree to participate in the study, you will receive a counselling service by the pharmacist in the community pharmacy (approximately 15 minutes in duration). During the counselling service the pharmacist will ask questions from you about how you take your lipid lowering medications and any issues you may have about taking the medications, as well as your quality of life. With your permission, the pharmacist will also provide a copy of your medication history held in the pharmacy dispensary system to the researchers.

You will also have your cholesterol taken by the pharmacist 4 times over the 12 months (at four separate occasions). This procedure will involve a small pin prick on the finger and will be conducted according to standard infection control procedures, the same as at your doctor or hospital. You will feel the pin prick as a small sharp pain at the end of your finger and one drop of blood will be taken from the finger for each test. Some people might feel faint during the procedure, but a trained pharmacist will be in continual attendance during the cholesterol test.

As part of the study, you will be requested to attend the pharmacy after the initial visit, at three monthly intervals for a total of four visits. During these visits the pharmacist will have brief counselling sessions with you (approximately 10 minutes in duration).

All aspects of the study, including results, will be strictly confidential and only the investigators named above will have access to information on participants. A report of the study may be submitted for publication, but individual participants will not be identifiable in such a report and only group data will be reported. Participation in this study is entirely voluntary: you are not obliged to participate and - if you do participate - you can withdraw at any time without penalty or prejudice.



If you would like to know more at any stage, please feel free to contact the project coordinator.

- Dr Grenville Rose, Tel: (02) 9036 9551

Thank you for your time and participation. This information sheet is for you to keep.

Yours faithfully,

Dr Grenville Rose

<b>Any person with concerns or complaints about the conduct of a research study can contact the Manager of Ethics and Biosafety Administration, University of Sydney, on (02) 9351 4811.</b>
--



# The University of Sydney

Faculty of Pharmacy

NSW 2006 Australia

*Dr Grenville Rose, Project Coordinator*

*Telephone: (02) 9036 9551*

*Fax: (02) 9351 4471*

*e-mail: grenville@pharm.usyd.edu.au*

## Informed Consent Form- Community Pharmacists

**“A community pharmacist delivered therapeutics outcome monitoring service for hyperlipidaemia”.**

I, .....(please print your name)

of .....(your address)

have read and understood the “Pharmacist Information Sheet” on the above research study and have discussed it with one of the researchers, Dr Grenville Rose. I am aware of the procedures involved in the study and understand what is expected of me. Specifically, I give consent to the audiotape recording of the counselling sessions with consumers participating in the above study.

I freely choose to participate in this study and understand that I can withdraw at any time without penalty or prejudice. I also understand that the research study is strictly confidential and that only group data will be published and used in future research. No personal details will be revealed at any time during or after the study.

**Signature:**.....

**Name (please print):** .....

**Date:** .....

**Signature of witness:** .....

**Name of witness (please print):**.....

**Date:** .....

**Any person with concerns or complaints about the conduct of a research study can contact the Manager of Ethics and Biosafety Administration, University of Sydney, on (02) 9351 4811.**



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Faculty of Pharmacy

NSW 2006 Australia

*Dr Grenville Rose, Project Coordinator*

**Telephone:** (02) 9036 9551

**Fax:** (02) 9351 4471

**e-mail:** grenville@pharm.usyd.edu.au

## Informed Consent Form- Consumers

### **"A community pharmacist delivered therapeutics outcome monitoring service for hyperlipidaemia".**

I, .....(please print your name)

of .....(your address)

have read and understood the "Participant Information Sheet" on the above research study and have discussed it with one of the researchers, Dr Grenville Rose. I am aware of the procedures involved in the study and understand what is expected of me. Specifically, I give consent to the following:

1. Release of pharmacy dispensary medication history by my community pharmacist(s) to the researchers.
2. Audiotape recording of the counselling session with the pharmacist participating in the above study.
3. Pin prick cholesterol test by the pharmacist using the Accutrend GC cholesterol monitor

I freely choose to participate in this study and understand that I can withdraw at any time without penalty or prejudice. I also understand that the research study is strictly confidential and that only group data will be published and used in future research. No personal details will be revealed at any time during or after the study.

**Signature:**.....

**Name (please print):**.....

**Date:**.....

**Signature of witness:** .....

**Name of witness (please print):**.....

**Date:**.....

**Any person with concerns or complaints about the conduct of a research study can contact the Manager of Ethics and Biosafety Administration, University of Sydney, on (02) 9351 4811.**

## 5 Training Material

### Presentation 1

*A community pharmacist delivered  
therapeutics outcome monitoring service  
for hyperlipidaemia*

*Dr Parisa Aslani*  
*Associate Professor Ines Krass*  
*Dr Tim Chen*  
*Ms Paula Whitehead*

*Dr Grenville Rose*



## **Aim**

- ♦ To evaluate the impact of a community pharmacist delivered therapeutic outcomes monitoring service in consumers with hyperlipidaemia, which is aimed at promoting patient adherence to drug therapy

## Groups

### ♦ Control

- ♦ Recruit patients
- ♦ Collect patient data over 9 months (at four time intervals)
- ♦ Routine counselling practice

### ♦ Study

- ♦ Recruit patients
- ♦ Collect patient data over 9 months (at four time intervals)
- ♦ Increased patient consultation

## Data Collected

- ♦ Blood cholesterol levels
- ♦ Patient adherence levels- use of questionnaire
- ♦ Practice at data collection



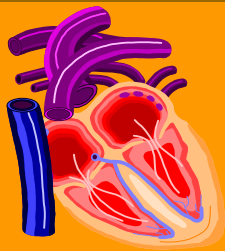
## Program for the Day

### ♦ Morning:

- ♦ Overview of CV risk factors
- ♦ Hyperlipidaemia and Coronary Heart Disease
- ♦ Use of Accutrend GC
- ♦ Administering patient questionnaires

## Presentation 2

# **Lipids and Ischaemic Heart Disease (IHD)**



**Associate Professor  
Ines Krass**

## **Learning Objectives**

***After study of this topic you should be able to:***

1. Describe the processes involved in cholesterol homeostasis.
2. Explain the processes in atherosclerotic plaque formation and rupture.
3. Differentiate between the different types of hyperlipidaemias.
4. Identify risk factors for the development of coronary heart disease (CHD).
5. Explain the principles of dietary management of hyperlipidaemias.
6. Discuss the pharmacologic management of hyperlipidaemias with resins, statins, probucol, fibrates and nicotinic acid.
7. Identify the major ADRs and drug interactions of lipid-lowering drugs.
8. Counsel a patient on the use of lipid-lowering medications.

## Scenario 1:

Mr. Williams a local plumber and a regular customer presents you with a prescription for **Zocor** tablets. He tells you he has just been to the doctor who told him his cholesterol is too high and has told him to start on these tablets because he may develop heart disease. He's not too keen on taking medication and wonders if high cholesterol means he's going to have a heart attack.. How might you respond?

## ***What is Ischaemic Heart Disease?***

- **Ischaemia** deficiency in the supply of blood to a particular part of the body.
- **Ischaemic Heart Disease (IHD)** due to coronary heart disease (CHD) ie narrowing of the coronary arteries.

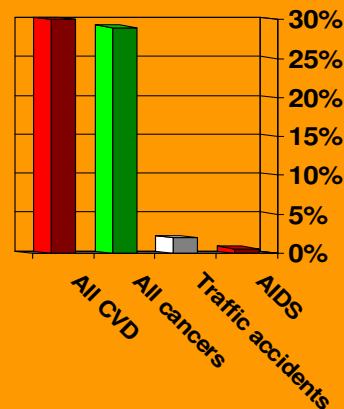
### **Two major complications**

- 1) angina pectoris
- 2) acute myocardial infarction (AMI)



## Epidemiology

- A leading cause of death in Australia
- 21% of all deaths in Australia in 2000 due to IHD
- Males at much greater risk than females < 65 yrs.



## Pathogenesis

- atherosclerosis
- coronary artery spasm
- coronary thrombosis

### Atherosclerosis

- arteriosclerosis due to the formation of atheromatous plaque.
- atheroma begins with a fatty streak and develops into a fibrous plaque
- this plaque narrows the lumen of the artery and acts as a focus for the development of thrombosis.

# Hyperlipidaemias

## Main lipids

- cholesterol
- triglycerides
- phospholipids

## Role of Cholesterol

- synthesis of bile acids, steroid hormones, cell membranes.
- sources: 40% dietary, 60% endogenous production.

# Role of triglycerides

- composed of free fatty acids, used as an energy source.
- sources: diet, conversion of carbohydrates in the liver.

## Lipid transport lipoproteins

5 types

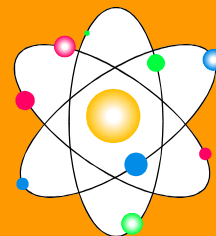
- 1) **chylomicrons** -  
TG + dietary CH
- 2) **VLDL** - mainly  
TG + 10-15% CH
- 3) **IDL** - CH + TG
- 4) **LDL** - 60-70% CH
- 5) **HDL** - 20-30% CH

### Aetiology

- **Genetic**,  
inherited defects in lipid metabolism)
- **Other diseases** (eg diabetes, hypothyroidism)
- **Lifestyle**  
(dietary)
- **Medications** (thiazides, loop diuretics,  $\beta$  blockers without ISA)

## Main types of Hyperlipidaemias

- hypercholesterolaemia in which cholesterol is raised
- mixed (combined) hyperlipidaemia in which levels of both cholesterol and triglycerides are raised
- predominant hypertriglyceridaemia in which triglycerides are raised



## Epidemiology

- The 1999–00 Australian Diabetes, Obesity and Lifestyle Study (AusDiab) found that over six million Australian adults (aged 25 years and over) had cholesterol levels higher than 5.5 mmol/L.
- Total blood CH > 5.5 mmol/L - greatly increased risk of developing CHD.
- Levels above 6.5 mmol/L are considered to indicate extremely high risk
- Around 50% of both men and women (aged 25 years and over) had blood cholesterol levels above 5.5 mmol/

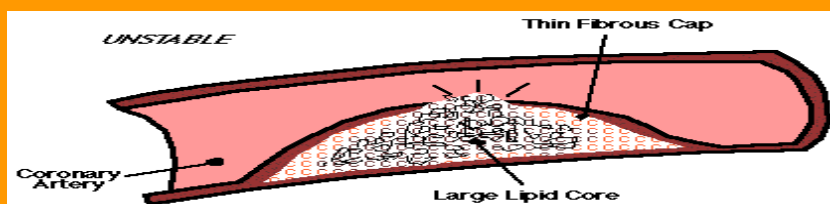
## Proposed mechanism for the development of atherosclerosis

- Damage to the endothelial lining of the artery.
- Monocytes enter damaged epithelium and become macrophages.
- Oxidative changes take place in the LDL which damage them and make them targets for phagocytosis.
- Macrophages and smooth muscle of the damaged vessel take up cholesterol from LDL and TG from VLDL to form atheroma.
- Fibrosis begins, plaque grows and begins to obstruct blood flow
- Platelets attach to atheroma danger of thrombosis-release of PDGF; hypertrophy of smooth muscle; atheroma to enlarge
- Thrombosis and embolism

## Reasons for thrombosis

- Damage to the endothelium causes a fall in prostacyclin levels hence thromboxane  $A_2$  levels predominate (can be inhibited by daily aspirin).
- The rough surface of the atheroma can promote the formation of fibrin.
- The hard atheroma can fracture and this can stimulate coagulation of the blood.
- Thrombus can block the blood vessel where it is formed or break off and form an embolus which will travel and block a narrower or smaller blood vessel.

## Arterial spasm



- ***A sudden contraction of an artery can occur in the peripheral or coronary arteries.***
- This spasm can occur in relatively normal vessels or be superimposed on atherosclerosis
- Can cause variant angina, MI, arrhythmia.

## Other risk factors in IHD

- male sex
- family history of premature CHD (in 1st degree rel <55 yrs)
- diabetes
- hypertension
- obesity(BMI>25)
- smoking
- personal history of vascular disease
- alcohol consumption
- hyperlipidaemias

### The Multiple Risk Intervention Trial (MRFIT)

- 300,000 men aged 35-57 years followed up for 12 years.
- Trial showed a strong association between **smoking, high BP, high cholesterol levels** and **mortality from CHD**.

## Rationale for lowering lipid levels

### Secondary Prevention Trials

- focus on the benefits of lipid lowering therapy in patients with established disease (i.e. angina or myocardial infarction).

### Primary Prevention Trials

- investigated the value of lipid-lowering in patients without established CHD

## Major cholesterol-lowering trials

Trial	Drug	Number of patients	Baseline CH (mmol/L)	Follow-up (years)	CHD mortality	
					Intervention	Placebo
Primary Prevention						
LRC-CPPT	Cholestyramine	3806	>6.8	7.4	1.6%	2.0%
WOSCOPS	Pravastatin	6596	>6.5	4.9	1.3%	1.9%*
AFCAPS /TexCAPS	Lovostatin	5608	4.6-6.8	5.2	0.6%	0.9%
Secondary Prevention						
4S	Simvastatin	3617	5.5-8.0	5.4	5.0%	8.5%#
CARE	Pravastatin	3583	<6.2	5.0	4.6%	5.7%
LIPID	Pravastatin	7498	4.0-7.0	6.0	6.4%	8.3%■

\*p<0.05; ■ p<0.01; #p<0.001. Adapted from Lipid Management Guidelines \*

## By how much and how quickly does reduction in serum CH lower risk of IHD?

- The combined evidence shows conclusively that lowering a person's serum cholesterol concentration results in substantial protection from IHD
- The benefits of serum cholesterol reduction are related to age; a 10% reduction in serum cholesterol concentration produces a reduction in ischaemic heart disease of
  - 50% at age 40,
  - 40% at age 50,
  - 30% at age 60, and
  - 20% at age 70
- The benefit can be realised quickly - the greater part after two years and the full benefit after five years

M R Law, N J Wald, S G Thompson *BMJ* 1994;308:367-372 (5 February)

## Management

- The aim is to achieve ideal body weight (BMI between 20-25 Kg/m<sup>2</sup>) by reducing caloric intake and increasing energy output through exercise.
- The emphasis of the diet should be on fat modification.
  - replace a proportion of saturated fatty acids with n-6 polyunsaturated fatty acids to achieve a ratio of polyunsaturated to saturated fatty acids of greater than 1;
  - include in the diet a daily intake of at least 1g of n-3 fatty acids from fish and fish oil;
  - replace saturated fatty acids with carbohydrate, polyunsaturated or mono-unsaturated fatty acids
  - diet high in complex carbohydrates and soluble fibres (fruits, cereals and vegetables)
- Moderate alcohol intake
- Smoking cessation
- Exercise -30 minutes on most days of the week (e.g. brisk walking, low pace swimming)

## Guidelines for treatment of dyslipidaemia

The criteria which classify an individual to be at high risk of CHD include the following:

- known CHD
- peripheral vascular disease
- diabetes mellitus
- hypercholesterolaemia
- chronic renal disease
- LDL-C > 4.0 mmol/L or TC > 6.0 mmol/L

**plus any 2 or more** other risk factors including

HDL < 1 mmol/L, family history, hypertension, BMI\* > 25 Kg/m<sup>2</sup>, smoking, impaired glucose tolerance, microalbuminuria and aged >45.



## Lipid targets for high risk patients

Total cholesterol (TC)	$\leq 4$ mmol/L	
Triglycerides (TG) fasting	$\leq 2$ mmol/L	
LDL-Cholesterol (LDL-C)	$\leq 2.5$ mmol/L	
HDL cholesterol (HDL-C)	$\geq 1.00$ mmol/L	

## Pharmacological intervention

### Predominant LDL elevation (hypercholesterolaemia)

#### First line HMG Co-A reductase

#### inhibitors: (Statins)

- LDL lowering potency on a mg per mg basis:  $>$  *atorvastatin*  $>$  *simvastatin*  $>$  *pravastatin*  $>$  *fluvastatin*
- They inhibit 3-hydroxy 3-methylglutaryl-coenzyme A reductase
- CH synthesis  $\downarrow$  and hepatocyte LDL receptors  $\uparrow$ .  
Uptake of LDL is increased and serum CH  $\downarrow$ .  
Triglycerides also  $\downarrow$  and HDL  $\uparrow$ .
- Generally well tolerated.

## Statins (cont)

### ADRS

- **GI effects** (constipation, diarrhoea and flatulence)
- **myopathy** (muscle weakness) rare (0.5%)  
concurrent use with azole antifungals, nicotinic acid, gemfibrozil, erythromycin and cyclosporin - ↑ incidence to 30%
- **abnormal liver enzymes** (2%)
- **lens opacities** (rare)

### Counselling

- Take dose at night
- Seek medical advice if muscle pain, fever, tenderness or weakness occur
- Avoid alcohol and grapefruit juice

### Monitoring

- Monitor lipid levels after 4-8 weeks
- Baseline LFTs eg transaminase and every 3 months (> 3x normal – cease statin)
- Measure creatine kinase (CK) if myositis occurs

## Ion exchange resins

- form a non-absorbable complex with bile acids and block entero-hepatic circulation.
  - they may also ↑ LDL catabolism in the liver by producing an ↑ in LDL receptors resulting in a ↓ in LDL-C of 15 - 20%.
  - Cholestyramine (*Questran*) - 4g - 8g 2-3 x a day.
  - Colestipol (*Colestid*) - 5g - 10g 2-3 x a day.
- ADRS**
- not well tolerated, constipation, bloating, abdominal pain, gas, nausea.
  - may interfere with absorption of fat soluble vitamins.
- Drug Interactions**
- ↓ absorption of digoxin, warfarin, thiazides, antibiotics, thyroid

## Other Second Line Therapies

### Nicotinic acid

- ↓ the release of VLDL, LDL by the liver. Increases HDL levels
- synergistic effects with resins.

**ADRS** Flushing, can decline with long term use) pruritis, gout, hyperglycaemia.

- Therapy is initiated slowly.
- Usual dose: up to 2-3g tds.

### Probucol (*Lurselle*)

- ↓ synthesis of LDL and HDL, not a first line therapy.
- May be used with resins. Dose: 500mg bd

**ADR** Diarrhoea.

## Other second line therapies

### Oestrogen

- ↓ LDL-C and ↑ HDL-C
- may exert its effects at the level of the artery wall
- oral oestrogen reduces TG but transdermal may not particularly useful in post menopausal women who have had a hysterectomy
- if LDL-C > 8 mmol/L should use a statin.
- protection against CHD is modest and can be offset by an increased risk of thrombembolism

## Mixed Hyperlipidaemia

### High fasting TG with high LDL-C

- If TG < 4 mmol/L use a statin in addition to diet
- TG > 4 mmol/L use **Gemfibrozil 600 mg bd.**
- ↓ VLDL due to stimulation of lipoprotein lipase. HDL levels rise.


### ADRS

- Gastrointestinal, (Take with meals), rash, eczema
- Report any muscle pain weakness or tenderness
- abnormal liver function tests. Rare effect: myopathy
- Requires close supervision if given with statins.

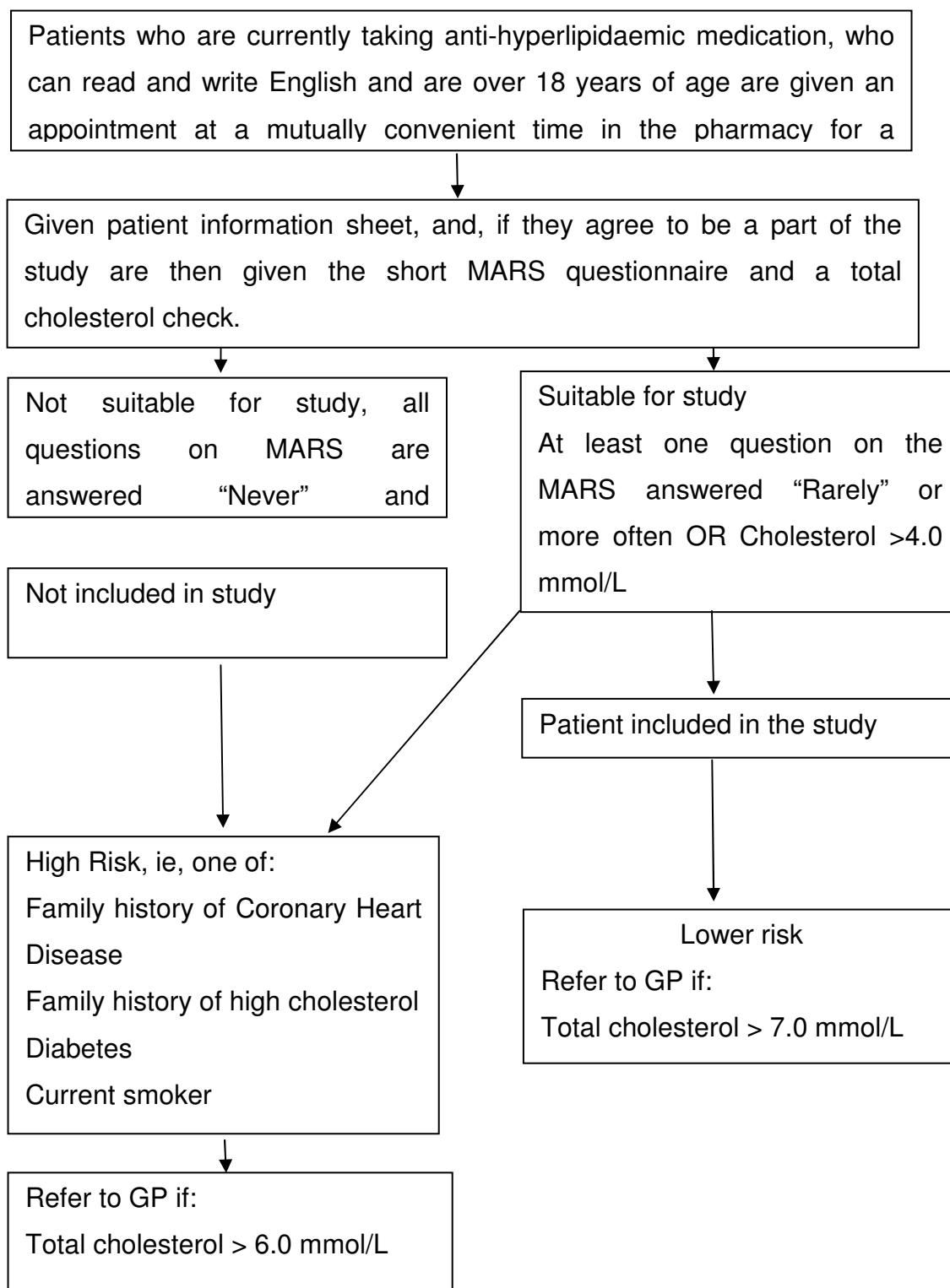
## Hypertriglyceridaemia: (TG > 4.0 mmol/L)

- Gemfibrozil 600 mg bd
- Nicotinic acid
- Fish Oils: rich in omega 3-fatty acids.

## Plant sterols or stanols

- **Reduce serum total and LDL-CH**
- **Available in margarine or spreads**
- **Effectiveness in foods other than spreads is not established**
- **reduce the absorption of dietary and biliary CH**
- **25gm/day-  10% reduction**

## Presentation 3




## Presentation 4




## *Compliance, Adherence and Concordance*

*Dr Parisa Aslani*



## Outline

- Compliance or Adherence
- Concordance
- Differences between compliance and concordance
- Factors contributing to non-compliance
- Impact of non-compliance
- Measures of compliance



## Compliance or Adherence

*The extent to which a person's behaviour (in terms of taking medication, following diets or implementing other lifestyle changes) coincides with medical or health advice"*

(Haynes, 1979)

## Non-Compliant Patient

- Irrational in decision making (medications)
- No choice in therapy
- No relationship with health care professional





## Categories of Non-Compliance

- Primary
- Secondary
- Intentional
- Non-intentional



## Sub-Categories

- Underdoser
- Overdoser
- Drug holiday taker
- Previsit compliant
- Random compliers
- Time dependent
- Complying when symptoms present

## Concordance

*"is based on the notion that the work of the prescriber (or pharmacist) and patient in the consultation is a negotiation between equals and that therefore the aim is a therapeutic alliance between them"*

(Marinker 1997)

## Concordance

*"The concept of concordance suggests frank exchange of information, negotiation, and a spirit of cooperation"*

(Mullen 1997)

## Differences

- Two different concepts
- One-way vs two-way
- Decision making process
- Non-compliance: patient
- Non-concordance: partnership
- Compliance is an outcome of concordance

## Importance of Concordance

- Improved health professional-patient communication
- Improved adherence
- Increased satisfaction
- Improved patient health status /outcome

## Factors Influencing Concordance

- Patient
  - perception of illness and drug therapy
  - health beliefs
  - perceptions of health professional
- Health professional
  - information provided
  - communication skills
- Health problem
  - impact of illness and therapy

## Rates of Compliance

- 1/3 of prescriptions written are never dispensed.
- 20-80% of patients adhere to therapy.
- 50-90% adherence rate to chronic regimens.
- 20-60% of elderly adhere to therapy.
- Adherence to short term therapy better than long term.
- Adherence is greatly reduced in the first 10 days.

•  
•

### Rates of Compliance- lipid lowering therapy

- Recent Australian study: 50% discontinued their lipid lowering therapy within 6 months of starting
- 40-60% discontinuation rates 1 year after commencement of therapy

•  
•

### Implications of Non-compliance

- Drug failure
- Increased cholesterol levels
- Increased cardiovascular events eg stroke
- Increased mortality and morbidity
- Increased financial costs

## Factors Influencing Compliance

- Treatment / Medication
  - Chronic disease
  - Chronic medication use
  - Concurrent medications
  - Complexity of regimen (d, bd vs tds, qid)
  - Adverse drug reactions
  - Drug interactions
  - Benefits of therapy (vs risks)

## Factors Influencing Compliance

- Patient characteristics
  - Sociodemographics- little impact (Gordillo 1999, Friedland & Williams 1999)
  - Forgetfulness, too many visits
  - Change in routine, inconvenience
  - Patient beliefs and knowledge
  - Privacy (21% missed doses- Gwadz *et al.* 1999)
  - Inability to take medication

## Measures of Compliance

- Defining compliance in relation to clinical outcome
- Self-report
- Dispensing Records
- Biological markers
- Direct observation
- Other measures

## Self-Report

- Diary
- Self-completion questionnaire
- Structured Interview
- Over-reporting of adherence
- Admittance to non-compliance is valid
- Missed doses over a short time frame
- Easy, inexpensive, insight into non-adherence

## Dispensing Records

- Hospital / community pharmacy
- No data on actual taking of medication and correct dosage interval

## Biological Markers

- Drug levels (urine, blood, saliva)
- Cholesterol levels (LDL, HDL, TG)
- Drug pharmacokinetics
- Efficacy of drug
- Sensitivity to non-adherence
- Long term changes and Repeated measures



## Other Measures

- Pill counts
- Direct Observation
- Adverse Drug Reactions
- MEMS caps
- Pill counts- overestimate
- Direct observation- Hawthorne effect
- ADRs- similar for some drugs

## Implementation Strategies

- Communication and counselling skills
- Encourage, empower to ask questions
- Provide information
- Include in decision making
- Ask about compliance
- Address problems
- Consider outcomes
- Short-term implications

## Implementation Strategies

- Fear about taking medication
- Unwillingness to accept illness
- Perceived stigma attached to illness
- Risks vs benefits
- Fear of loss of control to illness or GP
- ADRs
- Inconvenient regimen
- Costs
- Lack of confidence in clinician's decision

## Components of Intervention

- Consultation in a semi-private area
- Establishing rapport
- Communication
- Objective of consultation
- Patient adherence / beliefs / barriers
- Addressing barriers
- Monitoring therapy
- Follow-up
- Referral to GP

## On-site Training: Project Overview

- Hyperlipidaemia is a major factor in Coronary Heart Disease (CHD)
- There is good evidence that lowering cholesterol with medications reduces overall mortality.
- However, 40% - 60% of people discontinue medication after 1 year. This percentage rises over time

## Project Overview

- Non-adherence to medication can lead to;
  - increased mortality and increased hospitalisation for the patient
  - Increased costs for both the patient and the health system.

## Project Overview

- Main reasons for non-adherence are;
  - Medication regime complexity
  - Patient understanding of the disease and therapy
  - Patient/Health professional relationship

## Project Overview

- Types of strategies to increase adherence include;
  - Provision of clear and direct messages about the importance of adherence
  - inclusion of patients in the decision making about treatment and goals
  - using behavioural strategies
  - assessing adherence at each visit
  - the use of reminder systems

## Project Overview

- Pharmacist interventions have been shown to increase adherence.
- However, few studies have addressed combining communication and behavioural strategies.
- No Australian studies have addressed these issues.

## Project Overview

- The current project aims to develop, and trial a community pharmacist delivered service
- The service will be evaluated in both clinical and economic terms
- This is a crucial step towards establishing a remunerable pharmacy delivered adherence service.

## Presentation 6

## On-site Training: Screening

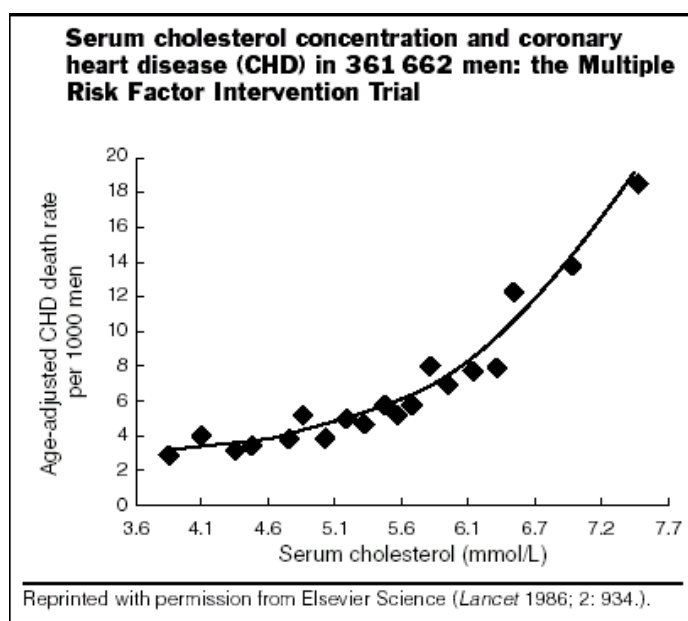
- Screening is a health service in which members of a defined population, who do not necessarily perceive themselves as at risk of disease, are asked a question or offered a test which will identify individuals who require further treatment.

## Case Selection

- Targeted groups are identified and then invited to attend for testing and possible further treatment.

## The place of Dyslipidaemia in Coronary Heart Disease (CHD)

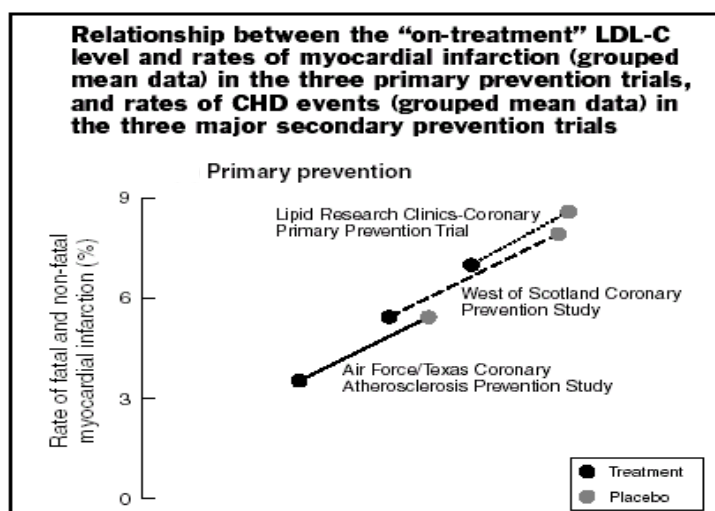
- Multiple Risk Factor Intervention Trial and Framingham studies both show positive relationship between elevated cholesterol and CHD (prospective studies).
- However, most patients with CHD do not have markedly high cholesterol levels.



MJA 5<sup>th</sup> November 2001 Volume 175, Supplement

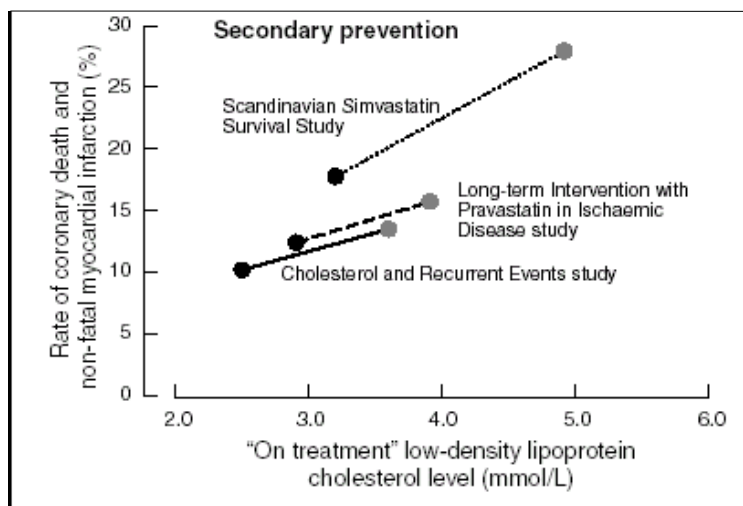
## Intervention studies

- Large scale double Blind studies conducted over more than 4 years and with death or Myocardial infarction and the end points.
- All primary prevention studies found a reduction in risk of CHD. (one was non-significant at 5% probability )
- Secondary prevention studies also show a reduced risk of CHD and total mortality.



MJA 5<sup>th</sup> November 2001 Volume 175, Supplement





MJA 5<sup>th</sup> November 2001 Volume 175, Supplement

## Cardiovascular disease

- The health and economic burden of cardiovascular disease (CVD) exceeds that of any other disease.
- CVD was the leading cause of death in Australia in 2000, ahead of all cancers and other groups of causes of death, accounting for 49,741 deaths or 39% of all deaths.
- During 1990 – 2000, death rates from CVD fell by 4.2% per year for males and 4.0% per year for females.
- Coronary heart disease (CHD) is the largest single cause of death in Australia.

National Heart Foundation-2003

## Cardiovascular disease

- **CHD death rates climbed steadily from 1940 to 1968 and since then have declined steadily. During 1996 – 2000 death rates declined annually by 6.3% in males and 5.6% in females.**
- **Among Australians having a heart attack, over four in ten will die within a year but over half of all heart attack deaths will occur before the person reaches the hospital.**
- **People with a history of CHD account for 5% of the population but 31% of coronary events.**
- **Stroke is the second largest cause of death for both males and females in Australia.**

National Heart Foundation-2003

## Cardiovascular diseases

- **Death rates for CVD as a whole, including both CHD and stroke have declined due to:**
  - **reduction in prevalence of some risk factors (high blood pressure, tobacco smoking and saturated fat intake)**
  - **improvements in disease management including counselling, drug use, emergency care, medical**
  - **and surgical treatment and follow up care.**

## Trends in Risk Factors

- In 1995, over 10 million adult Australians (about 80% of the adult population) had at least one of the following cardiovascular risk factors: tobacco smoking, physical inactivity, high blood pressure, or overweight. Four in five men and three in four women had at least one of these risk factors.
- In 1999-2000, 29% or 3.6 million Australians aged 25 years and over had high blood pressure (140/90mm Hg) or were on medication for that condition.
- In 1999-2000, over six million Australians aged 25 years and over (that's 50% of the population) had total blood cholesterol levels higher than 5.5 mmol/L.

## Trends in Risk Factors

- In 1999-2000, an estimated 7.5 million Australians aged 25 yrs and over were overweight or obese (60%) and of these 2.6 million (21% of the population aged 25 years and over) were obese.<sup>4</sup>
- In 2001, one in five Australians aged 14 yrs and over smoked regularly (3.1 million adults).<sup>4</sup>
- More than 5.8 million adult Australians (43% of the population) did not undertake physical activity at the levels recommended to achieve a health benefit in 1999.<sup>4</sup>
- People who are physically inactive are nearly twice as likely to have a fatal or non-fatal coronary event than those who do moderate levels of activity.<sup>1</sup>

## Trends in Risk Factors

- There is strong and consistent evidence that people who experience depression or are socially isolated or do not have quality social support are at greater risk of developing CHD. These three factors can have as great an effect on a person's risk of coronary heart disease as other, better-known risk factors.
- The CHD risk is directly related to the severity of depression: a one to two fold increase in CHD for minor depression and three to five fold increase for major depression.
- In addition, social isolation and lack of quality social support are independent risk factors for CHD onset and prognosis: the risks are increased two to three fold and three to five fold, respectively.

## Case selection using Accutrend GC

- Clients must currently be taking cholesterol lowering medication
- Be over 18
- Read and write English at high school level
- Must have total cholesterol level higher than 4.0 mmol/L

## Recruitment

- When a suitable subject is identified;
  - Give the patient information and consent form, the form may need explanation
  - If informed consent is given the patient should be given the demographic form to complete
  - The questionnaire should then be administered with pharmacist guidance
  - Final 'sealed section' must be completed without pharmacist intervention.

## Measuring cholesterol

- Use finger pricking device and lancets provided by the researchers
- Lancet and platform should be discarded after each use to prevent cross-infection
- Leave finger pricking device empty after use
- Apply patients blood directly to the strip which is located on a flat surface

Pharmaceutical Society of Australia Document PG 0797c

## Measuring Cholesterol cont'd

- Keep a sharps container at point of use
- Wear fresh gloves for each person tested
- Wash hands immediately if contamination occurs
- Wipe finger pricking device in sodium hypochlorite (10,000 parts/million) if device becomes contaminated with blood

Pharmaceutical Society of Australia Document PG 0797c

## Using the Accutrend GC

- Researcher to demonstrate use

## Administering the Questionnaires

- The questionnaire is in two parts
  - 1. Assisted completion, you may assist the client in completing this part of the questionnaire
  - 2. 'Sealed section' to reduce response bias answers to this section will be seen by the researchers only
- Do not lead the client, allow each person to find their own answers.

## Administering the Questionnaires

- If it becomes clear during the first interview that the client is not capable of completing the questionnaire discontinue and thank them for their time.
- Please read the questionnaires yourselves prior to administration, if you have any questions contact Grenville.

**6 Questionnaires and Data Sheets**

- **Please read the instructions in the questionnaire and complete all sections.**
- **If you are unsure about any of the questions please ask your pharmacist for help.**
- **There are no right or wrong answers, and the only bad answer is one that doesn't tell us how you are actually using your medication or how you feel about using your medication. The reason we are asking these questions is that we want to know the problems people are having when they are using their medication so that we can help people get better results from taking them.**



**1. Please list below all of the medications you took IN THE PAST WEEK. For each medication you list, please answer each of the questions below.**

a. Medication name and strength	b. How many days did you take it this week?	b. How many times a day did you take it?	d. How many pills/injections did you take each time?	e. How many times did you miss taking a pill/injection?	f. For what reasons were you taking it?	g. How well does the medication work for you? 1 = well 2 = okay 3 = not well

**2. Do any of your medications bother you in any way?**

(please place a tick in the appropriate box)

YES	€	NO	€
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**2a. If yes, please name the medication and mark below how much it bothers you, otherwise please go to question 3.**

*Please place a tick below a lot, some, or a little, to show how much the medication bothers you*

Medication Name	A lot	Some	A little	In what way does it bother you?
1.				
2.				
3.				
4.				
5				

3. Below is a list of problems that people sometimes have with their anti-cholesterol medications. Please show, by placing a tick in the appropriate box, how hard it is for you to do each of the following:

	Very hard	Somewhat hard	Not hard at all	Comment (Which medicine)
a. Open or close the medicine bottle.	€	€	€	
b. Read the print on the bottle.	€	€	€	
c. Remember to take all the pills/injections	€	€	€	
d. Get your repeats on time	€	€	€	
e. Take so many medicines at the same time.	€	€	€	

4. The next part of the questionnaire is asking about your thoughts and feelings towards your ANTI-CHOLESTEROL medications. Please show whether you agree or disagree with a statement by placing a tick in the appropriate box.

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
a. I know exactly why I am taking each one of my anti-cholesterol medications.	€	€	€	€	€
b. Before starting a new medication, I know all the good things it will do for me.	€	€	€	€	€
c. I am fully aware of all the bad (or "side") effects that may happen from my anti-cholesterol medications.	€	€	€	€	€
d. I am always given clear instructions on how to take my anti-cholesterol medications.	€	€	€	€	€
e. I am never told about how different drugs I take might affect each other (interact)	€	€	€	€	€

**5. Please think about your anti-cholesterol medications and place a tick in the box that best describes your opinion of the following statements.**

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
a. The bad (or "side") effects of my anti-cholesterol medications prevent me from taking them as prescribed.	€	€	€	€	€
b. I cannot afford my anti-cholesterol medications	€	€	€	€	€
c. I always have to make sacrifices to afford my anti-cholesterol medications.	€	€	€	€	€
d. The times for taking my anti-cholesterol medications are inconvenient.	€	€	€	€	€
e. I never feel any benefit from my anti-cholesterol medications.	€	€	€	€	€
f. A medication organiser helps to remind me about taking my anti-cholesterol medications.	€	€	€	€	€
g. I increase the dose of my anti-cholesterol medication when I have fatty foods.	€	€	€	€	€

**6. Please think about your anti-cholesterol medications and place a tick in the box that best describes your opinion of the following statements.**

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
a. I always ask my doctor questions when I do not understand something about my anti-cholesterol medications.	€	€	€	€	€
b. I always ask my pharmacist questions when I do not understand something about my anti-cholesterol medications.	€	€	€	€	€
c. I'd like to ask questions but I never know what to ask my doctor about my anti-cholesterol medications.	€	€	€	€	€
d. I'd like to ask questions but I never know what to ask my pharmacist about my anti-cholesterol medications.	€	€	€	€	€
e. I always understand the answers to my questions.	€	€	€	€	€
f. My doctor/pharmacist explains information about my anti-cholesterol medication in a way that I can understand.	€	€	€	€	€

**7. Is there anything that makes it hard for you to take your cholesterol medication in the way that your doctor wants you to?**

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**8. Is there anything you have done that makes it easier for you to take your medications?**

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**Please complete the rest of the questions by yourself and place these sheets in the envelope marked RESEARCHERS. You do not have to show this part of the questionnaire to the pharmacist unless you want to.**

**9. Please show whether you agree or disagree with each statement ABOUT YOUR HEALTH CARE PROFESSIONALS by placing a tick in the appropriate box.**

	<b>Strongly Agree</b>	<b>Agree</b>	<b>Neutral</b>	<b>Disagree</b>	<b>Strongly Disagree</b>
a. These people have enough knowledge to answer my questions.	€	€	€	€	€
b. These people do not seem interested in what I have to say about my illness.	€	€	€	€	€
c. I am afraid to tell these people that I have missed taking some of my medications.	€	€	€	€	€
d. I trust these people.	€	€	€	€	€

**10. In general, would you say your health is: (please tick the appropriate box)**

<b>Excellent</b>	<b>Very Good</b>	<b>Good</b>	<b>Fair</b>	<b>Poor</b>
€	€	€	€	€

**11. How much of the time during the past 4 weeks...**

	<b>All of the time</b>	<b>Most of the time</b>	<b>A Good Bit of the Time</b>	<b>Some of the time</b>	<b>A little of the time</b>	<b>None of the time</b>
<b>a.</b> Have you felt calm and peaceful?	€	€	€	€	€	€
<b>b</b> Did you have a lot of energy?	€	€	€	€	€	€
<b>c.</b> Have you felt downhearted and blue?	€	€	€	€	€	€

**12. DURING THE LAST MONTH how many hours of exercise (eg. brisk walking, a sporting activity) do you think you have done each week?**

<b>None</b>	<b>1-2 hrs</b>	<b>2-5hrs</b>	<b>5-10 hrs</b>	<b>More than 10 hrs</b>
€	€	€	€	€

13. Please show, with a tick in the appropriate box, how often you have eaten each of the following foods during the past month.

Food	Every day	2-3 times per week	Once a week	Less than once a week	Never
Skim or low fat milk	€	€	€	€	€
Full cream milk	€	€	€	€	€
Full fat ice cream	€	€	€	€	€
Low fat ice cream	€	€	€	€	€
Full fat soy milk	€	€	€	€	€
Low fat soy milk	€	€	€	€	€
Nuts (eg. Peanuts, cashews)	€	€	€	€	€
White bread	€	€	€	€	€
Wholemeal/grain bread	€	€	€	€	€
Fruit	€	€	€	€	€
Vegetables	€	€	€	€	€
Meat	€	€	€	€	€
Fish	€	€	€	€	€
Peanut butter	€	€	€	€	€
Lite Peanut butter	€	€	€	€	€
Nutella	€	€	€	€	€
Breakfast cereal (flakes/flakes and fruit)	€	€	€	€	€
Porridge/Muesli	€	€	€	€	€
Butter	€	€	€	€	€
Margarine	€	€	€	€	€
Cholesterol lowering spread (eg. Logicol)	€	€	€	€	€

<b>QUESTIONS ABOUT USING YOUR MEDICINES</b>
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- Many people find a way of using their medicines which suits them
- This may differ from the instructions on the label or from what their doctor has said
- We would like to ask you a few questions about how you use your medicines

Here are some ways in which people have said that they are using their medicines
--

Your own way of using your medicines	Always	Often	Sometimes	Rarely	Never
a. I forget to take them					
b. I alter the dose					
c. I stop taking them for a while					
d. I decide to miss out a dose					
e. I take less than instructed					

Below are some questions on your use of medical services before you became involved in this cholesterol study with your pharmacist. If you would complete this survey as accurately as you can it would be of great assistance to the study.

**Q1. Have you had any admissions into hospital between May 2003 and May 2004?**

Yes.....<sup>1</sup> No.....<sup>2</sup> **If no go to Q3**

**Q2. If yes, how many times were you admitted ? \_\_\_\_\_**

	<b>What were you admitted for?</b> Please list each admission separately	<b>When were you admitted?</b> (approximate date)	<b>What hospital were you admitted to?</b>	<b>How many days did you stay in hospital?</b>
<b>1</b>				
<b>2</b>				
<b>3</b>				

**Q3. Have you had any visits to the hospital emergency department between April 2003 and April 2004?**

Yes.....<sup>1</sup> No.....<sup>2</sup> **If no go to Q6**

**Q4. If yes, how many visits did you have? \_\_\_\_\_**

<b>Q5.</b>	<b>What did you visit for?</b> Please list each visit separately	<b>How long were you there?</b> (approximate number of hours)
<b>1</b>		
<b>2</b>		
<b>3</b>		



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**Q6. Have you had any visits to your GP between April 2003 and April 2004 for your cholesterol or for conditions related to your cholesterol?**

Yes.....<sup>1</sup> No.....<sup>2</sup> **If no go to Q8**

**Q7. If yes, how many visits did you have? \_\_\_\_\_**

**Q8. Have you missed any work days between April 2003 and April 2004 because of your cholesterol or conditions related to your cholesterol?**

Yes.....<sup>1</sup> No.....<sup>2</sup>

**Q9. If yes, how many work days have you missed? \_\_\_\_\_**

Below are some questions about your use of medical services since the last time you completed a questionnaire for this study. If you would complete this survey as accurately as you can it would be of great assistance to the study.

**Q10. Have you had any admissions into hospital in the last three months?**

Yes.....<sup>1</sup> No.....<sup>2</sup> **If no go to Q12**

**Q11. If yes, how many times were you admitted ? \_\_\_\_\_**

	<b>What were you admitted for?</b> Please list each admission separately	<b>When were you admitted?</b> (approximate date)	<b>What hospital were you admitted to?</b>	<b>How many days did you stay in hospital?</b>
<b>1</b>				
<b>2</b>				
<b>3</b>				

**Q12. Have you had any visits to the hospital emergency department in the last three months**

Yes.....<sup>1</sup> No.....<sup>2</sup> **If no go to Q15**

**Q13. If yes, how many visits did you have? \_\_\_\_\_**

<b>Q14.</b>	<b>What did you visit for?</b> Please list each visit separately	<b>How long were you there?</b> (approximate number of hours)
<b>1</b>		
<b>2</b>		
<b>3</b>		

---

**Q15. Have you had any visits to your GP in the last three months for your cholesterol or for conditions related to your cholesterol?**

Yes.....<sup>1</sup>                      No.....<sup>2</sup> **If no go to Q17**

**Q16. If yes, how many visits did you have? \_\_\_\_\_**

**Q17. Have you missed any work days in the last three months because of your cholesterol or conditions related to your cholesterol?**

Yes.....<sup>1</sup>                      No.....<sup>2</sup>

**Q18. If yes, how many work days have you missed? \_\_\_\_\_**

**THANK YOU FOR TAKING THE TIME TO COMPLETE THIS SURVEY**

## 7 Comparison of demographics of continuing and withdrawing patients

### Completion status \* Gender Crosstabulation

	Male	Female	Total
<b>Withdrew</b>	22	23	45
<b>Completed</b>	62	35	97
<b>Total</b>	84	58	142

### Chi-Square Tests of Gender Crosstabulation

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.873(b)	1	.090		
Continuity Correction(a)	2.285	1	.131		
Likelihood Ratio	2.850	1	.091		
Fisher's Exact Test				.101	.066
Linear-by-Linear Association	2.853	1	.091		
N of Valid Cases	142				

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 18.38.

### Completion status by country of birth crosstabulation

	Australia	Overseas	Total
<b>Withdrew</b>	21	24	45
<b>Completed</b>	62	35	97
<b>Total</b>	83	59	142

### Chi-Square tests of country of birth crosstabulation

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.767(b)	1	.052		
Continuity Correction(a)	3.090	1	.079		
Likelihood Ratio	3.740	1	.053		
Fisher's Exact Test				.067	.040
Linear-by-Linear Association	3.740	1	.053		
N of Valid Cases	142				

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 18.70.

### Completion status by language spoken at home crosstabulation

	English	Other	Total
<b>Withdrew</b>	36	8	44
<b>Completed</b>	83	12	95
<b>Total</b>	119	20	139

**Chi-Square tests of main language spoken at home crosstabulation**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.752(b)	1	.386		
Continuity Correction(a)	.369	1	.544		
Likelihood Ratio	.728	1	.394		
Fisher's Exact Test				.439	.267
Linear-by-Linear Association	.747	1	.388		
N of Valid Cases	139				

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 6.33.

**Completion status by other languages spoken at home crosstabulation**

	English	Other	None	Total
<b>Withdrew</b>	13	6	25	44
<b>Completed</b>	27	10	50	87
<b>Total</b>	40	16	75	131

**Chi-Square tests of other languages spoken at home crosstabulation**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.133(a)	2	.936
Likelihood Ratio	.131	2	.936
Linear-by-Linear Association	.003	1	.960
N of Valid Cases	131		

a 0 cells (.0%) have expected count less than 5. The minimum expected count is 5.37.

**Completion status by highest education level achieved crosstabulation**

	None	Primary school	School certificate (year 10)	Higher school certificate (Year 12)	Trade or other cert	Tertiary (diploma, bachelor or higher)	Total
<b>Withdrew</b>	0	6	13	6	10	10	45
<b>Completed</b>	1	16	29	14	24	11	95
<b>Total</b>	1	22	42	20	34	21	140

**Chi-Square tests of completion status by highest level of education achieved crosstabulation**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	3.205(a)	5	.668	.703		
Likelihood Ratio	3.376	5	.642	.720		
Fisher's Exact Test	3.107			.716		
Linear-by-Linear Association	1.499(b)	1	.221	.231	.124	.025
N of Valid Cases	140					

a 2 cells (16.7%) have expected count less than 5. The minimum expected count is .32.

b The standardized statistic is -1.224.

**Completion status by occupation crosstabulation**

	Man- ager	Prof.	Trade	Clerical workers	Prod and trans	Service	Labour	Home	Stud- ent	Other	Tot
<b>Withdrew</b>	4	9	8	5	2	4	1	5	3	1	42
<b>Completed</b>	4	15	18	7	8	7	4	18	2	6	89
<b>Total</b>	8	24	26	12	10	11	5	23	5	7	131

**Chi-Square tests of occupation crosstabulation**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	7.064(a)	9	.631	.651		
Likelihood Ratio	7.128	9	.624	.695		
Fisher's Exact Test	6.905			.661		
Linear-by-Linear Association	1.666(b)	1	.197	.201	.105	.012
N of Valid Cases	131					

a 10 cells (50.0%) have expected count less than 5. The minimum expected count is 1.60.

b The standardized statistic is 1.291.

**Completion status by job status crosstabulation**

	Full time	Part time	Retired	Unable to work during health reasons	Unemployed	Total
<b>Withdrew</b>	14	3	24	3	0	44
<b>Completed</b>	25	15	27	8	2	77
<b>Total</b>	39	18	51	11	2	121

**Chi-Square tests of job status crosstabulation**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	7.078(a)	4	.132	.123		
Likelihood Ratio	8.071	4	.089	.106		
Fisher's Exact Test	6.545			.139		
Linear-by-Linear Association	.065(b)	1	.798	.861	.433	.068
N of Valid Cases	121					

a 3 cells (30.0%) have expected count less than 5. The minimum expected count is .73.

b The standardized statistic is -.256.

**Completion status by others in the family with hear related health problems crosstabulation**

	Cholesterol	Heart disease	Total
<b>Withdrew</b>	7	23	30
<b>Completed</b>	28	41	69
<b>Total</b>	35	64	99

**Chi-Square tests of others in the family with hear related health problems crosstabulation**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	2.721(b)	1	.099	.114	.076	
Continuity Correction(a)	2.019	1	.155			
Likelihood Ratio	2.836	1	.092	.114	.076	
Fisher's Exact Test				.114	.076	
Linear-by-Linear Association	2.694(c)	1	.101	.114	.076	.048
N of Valid Cases	99					

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 10.61.

c The standardized statistic is -1.641.

**Completion status by diabetic status crosstabulation**

	Yes	No	Total
<b>Withdrew</b>	3	42	45
<b>Completed</b>	24	73	97
<b>Total</b>	27	115	142

**Chi-Square tests of diabetic status crosstabulation**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	6.522(b)	1	.011	.011	.007	
Continuity Correction(a)	5.401	1	.020			
Likelihood Ratio	7.561	1	.006	.011	.007	
Fisher's Exact Test				.011	.007	
Linear-by-Linear Association	6.476(c)	1	.011	.011	.007	.006
N of Valid Cases	142					

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 8.56.

c The standardized statistic is -2.545.

**Completion status by “have you previously had heart disease?” status**

	Yes	No	Total
<b>Withdrew</b>	12	33	45
<b>Completed</b>	38	58	96
<b>Total</b>	50	91	141

**Chi-Square tests of “have you previously had heart disease” crosstabulation**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	2.234(b)	1	.135	.186	.095	
Continuity Correction(a)	1.705	1	.192			
Likelihood Ratio	2.292	1	.130	.186	.095	
Fisher's Exact Test				.186	.095	
Linear-by-Linear Association	2.218(c)	1	.136	.186	.095	.050
N of Valid Cases	141					

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 15.96.

c The standardized statistic is -1.489.

**Crosstabulation of completion status by cigarette smoker status.**

	Yes	No	Total
<b>Withdrew</b>	5	40	45
<b>Completed</b>	22	74	96
<b>Total</b>	27	114	141

**Chi-Square tests of cigarette smoker status**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	2.758(b)	1	.097	.112	.073	
Continuity Correction(a)	2.048	1	.152			
Likelihood Ratio	2.980	1	.084	.112	.073	
Fisher's Exact Test				.112	.073	
Linear-by-Linear Association	2.739(c)	1	.098	.112	.073	.048
N of Valid Cases	141					

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 8.62.

c The standardized statistic is -1.655.



## 8 Comparison of demographics of comparison and intervention group patients- INTERVENTION VERSUS COMPARISON GROUP DEMOGRAPHICS

### Gender \* Condition Crosstabulation

		Condition		Total
		Intervention	Control	
Gender	Male	33	29	62
	Female	16	19	35
Total		49	48	97

### Gender \* Condition Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.505(b)	1	.477		
Continuity Correction(a)	.249	1	.618		
Likelihood Ratio	.505	1	.477		
Fisher's Exact Test				.530	.309
Linear-by-Linear Association	.500	1	.480		
N of Valid Cases	97				

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 17.32.

### Country of birth \* Condition Crosstabulation

		Condition		Total
		Intervention	Control	
Country of birth	Australia	29	33	62
	Overseas	20	15	35
Total		49	48	97

### Country of birth \* condition Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.962(b)	1	.327		
Continuity Correction(a)	.592	1	.442		
Likelihood Ratio	.965	1	.326		
Fisher's Exact Test				.399	.221
Linear-by-Linear Association	.952	1	.329		
N of Valid Cases	97				

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 17.32.

**Main language spoken at home \* Condition Crosstabulation**

		Condition		Total
		Intervention	Control	
Main language spoken at home	English	44	39	83
	Other	5	7	12
Total		49	46	95

**Main language spoken at home \* condition Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.540(b)	1	.462		
Continuity Correction(a)	.182	1	.670		
Likelihood Ratio	.542	1	.462		
Fisher's Exact Test				.545	.335
Linear-by-Linear Association	.535	1	.465		
N of Valid Cases	95				

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 5.81.

**Other languages spoken at home \* Condition Crosstabulation**

		Condition		Total
		Intervention	Control	
Other languages spoken at home	English	16	11	27
	Other	7	3	10
	None	19	31	50
Total		42	45	87

**Other languages spoken at home \* condition Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	5.309(a)	2	.070	.075		
Likelihood Ratio	5.382	2	.068	.075		
Fisher's Exact Test	5.204			.078		
Linear-by-Linear Association	3.665(b)	1	.056	.059	.036	.015
N of Valid Cases	87					

a 1 cells (16.7%) have expected count less than 5. The minimum expected count is 4.83.

b The standardized statistic is 1.915.

**Highest level of education \* Condition Crosstabulation**

		Condition		Total
		Intervention	Control	
Highest level of education	None	1	0	1
	Primary school	7	9	16
	School certificate (year 10)	13	16	29
	Higher school certificate (Year 12)	10	4	14
	Trade or other cert	9	15	24
	Tertiary (diploma, bachelor or higher)	7	4	11
Total		47	48	95

**Highest level of education \* Condition Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	6.440(a)	5	.266	.252		
Likelihood Ratio	6.939	5	.225	.255		
Fisher's Exact Test	6.280			.257		
Linear-by-Linear Association	.086(b)	1	.769	.818	.415	.059
N of Valid Cases	95					

a 2 cells (16.7%) have expected count less than 5. The minimum expected count is .49.

b The standardized statistic is -.294.

**Occupation \* Condition Crosstabulation**

		Condition		Total
		Intervention	Control	
Occupation	Managers	2	2	4
	Professional	6	9	15
	Tradespersons and related	9	9	18
	Clerical workers	6	1	7
	Production and transport	4	4	8
	Sales and service	6	1	7
	Labourers and related	2	2	4
	Homemaker	10	8	18
	Student	0	2	2
	Other	1	5	6
Total		46	43	89

**Occupation \* Condition Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	12.545(a)	9	.184	.180		
Likelihood Ratio	14.334	9	.111	.185		
Fisher's Exact Test	12.027			.189		
Linear-by-Linear Association	.263(b)	1	.608	.612	.318	.027
N of Valid Cases	89					

a 14 cells (70.0%) have expected count less than 5. The minimum expected count is .97.

b The standardized statistic is .513.

**Jobstatus \* Condition Crosstabulation**

		Condition		Total
		Intervention	Control	
Jobstatus	Full time	15	10	25
	Part time	9	6	15
	Retired	8	19	27
	Unable to work during health reasons	4	4	8
	Unemployed	1	1	2
Total		37	40	77

**Jobstatus \* Condition Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	5.974(a)	4	.201	.192		
Likelihood Ratio	6.108	4	.191	.246		
Fisher's Exact Test	6.230			.161		
Linear-by-Linear Association	2.374(b)	1	.123	.127	.075	.025
N of Valid Cases	77					

a 4 cells (40.0%) have expected count less than 5. The minimum expected count is .96.

b The standardized statistic is 1.541.

**Others in family have heart disease or high cholesterol \* Condition Crosstabulation**

		Condition		Total
		Intervention	Control	
Others in family have heart disease or high cholesterol	Cholesterol	16	12	28
	Heart disease	18	23	41
Total		34	35	69

**Others in family have heart disease or high cholesterol \* Condition Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	1.167(b)	1	.280	.332	.202	
Continuity Correction(a)	.697	1	.404			
Likelihood Ratio	1.170	1	.279	.332	.202	
Fisher's Exact Test				.332	.202	
Linear-by-Linear Association	1.150(c)	1	.284	.332	.202	.110
N of Valid Cases	69					

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 13.80.

c The standardized statistic is 1.072.

**Do you have diabetes \* Condition Crosstabulation**

		Condition		Total
		Intervention	Control	
Do you have diabetes	Yes	15	9	24
	No	34	39	73
Total		49	48	97

**Do you have diabetes \* Condition Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	1.832(b)	1	.176	.240	.132	
Continuity Correction(a)	1.251	1	.263			
Likelihood Ratio	1.848	1	.174	.240	.132	
Fisher's Exact Test				.240	.132	
Linear-by-Linear Association	1.813(c)	1	.178	.240	.132	.076
N of Valid Cases	97					

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 11.88.

c The standardized statistic is 1.347.

**Have you previously had heart disease \* Condition Crosstabulation**

		Condition		Total
		Intervention	Control	
Have you previously had heart disease	Yes	20	18	38
	No	28	30	58
Total		48	48	96

**Have you previously had heart disease \* Condition Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	.174(b)	1	.676	.835	.417	
Continuity Correction(a)	.044	1	.835			
Likelihood Ratio	.174	1	.676	.835	.417	
Fisher's Exact Test				.835	.417	
Linear-by-Linear Association	.172(c)	1	.678	.835	.417	.152
N of Valid Cases	96					

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 19.00.

c The standardized statistic is .415.

**Do you smoke cigarettes \* Condition Crosstabulation**

		Condition		Total
		Intervention	Control	
Do you smoke cigarettes	Yes	14	8	22
	No	35	39	74
Total		49	47	96

**Do you smoke cigarettes \* Condition Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	1.812(b)	1	.178	.227	.135	
Continuity Correction(a)	1.217	1	.270			
Likelihood Ratio	1.832	1	.176	.227	.135	
Fisher's Exact Test				.227	.135	
Linear-by-Linear Association	1.793(c)	1	.181	.227	.135	.080
N of Valid Cases	96					

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 10.77.

c The standardized statistic is 1.339.

## 9 Independent samples t test of study group baseline cholesterol scores and repeated measures ANOVA

### Tests of Within-Subjects Effects

F	Sig.	t	df	Sig. (2-tailed)
1.060624	0.304731	2.015405	150	0.045648

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.950	2	1.475	5.975	.003
	Greenhouse-Geisser	2.950	1.913	1.542	5.975	.004
	Huynh-Feldt	2.950	1.970	1.498	5.975	.003
	Lower-bound	2.950	1.000	2.950	5.975	.016
TIME INTERVAL *	Sphericity Assumed	3.045	2	1.523	6.168	.003
INTERVENTION GROUP	Greenhouse-Geisser	3.045	1.913	1.592	6.168	.003
	Huynh-Feldt	3.045	1.970	1.546	6.168	.003
	Lower-bound	3.045	1.000	3.045	6.168	.015
	Sphericity Assumed	48.383	196	.247		
Error (TIME INTERVAL)	Greenhouse-Geisser	48.383	187.446	.258		
	Huynh-Feldt	48.383	193.039	.251		
	Lower-bound	48.383	98.000	.494		
	Sphericity Assumed	48.383	98.000	.494		

### Tests of Within-Subjects Contrasts

Source	FACTOR1	Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Linear	2.947	1	2.947	13.858	.000
	Quadratic	.003	1	.003	.010	.922
TIME INTERVAL * INTERVENTION GROUP	Linear	2.606	1	2.606	12.254	.001
	Quadratic	.439	1	.439	1.562	.214
Error (TIME INTERVAL)	Linear	20.842	98	.213		
	Quadratic	27.541	98	.281		

## 10 Repeated measures ANOVA of MARS

### Your own way of using your medicines: ..... I forget to take them

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.181	2	1.090	2.685	.071
	Greenhouse-Geisser	2.181	1.802	1.210	2.685	.077
	Huynh-Feldt	2.181	1.857	1.174	2.685	.075
	Lower-bound	2.181	1.000	2.181	2.685	.105
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.659	2	.330	.811	.446
	Greenhouse-Geisser	.659	1.802	.366	.811	.435
	Huynh-Feldt	.659	1.857	.355	.811	.438
	Lower-bound	.659	1.000	.659	.811	.370
Error(TIME INTERVAL)	Sphericity Assumed	73.116	180	.406		
	Greenhouse-Geisser	73.116	162.176	.451		
	Huynh-Feldt	73.116	167.126	.437		
	Lower-bound	73.116	90.000	.812		

### Your own way of using your medicines: ..... I alter the dose

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.708	2	1.354	4.258	.016
	Greenhouse-Geisser	2.708	1.856	1.459	4.258	.018
	Huynh-Feldt	2.708	1.916	1.413	4.258	.017
	Lower-bound	2.708	1.000	2.708	4.258	.042
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	2.341	2	1.171	3.682	.027
	Greenhouse-Geisser	2.341	1.856	1.261	3.682	.030
	Huynh-Feldt	2.341	1.916	1.222	3.682	.029
	Lower-bound	2.341	1.000	2.341	3.682	.058
Error(TIME INTERVAL)	Sphericity Assumed	56.596	178	.318		
	Greenhouse-Geisser	56.596	165.220	.343		
	Huynh-Feldt	56.596	170.489	.332		
	Lower-bound	56.596	89.000	.636		



**Your own way of using your medicines: ..... I stop taking them for a while**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.407	2	.203	.494	.611
	Greenhouse-Geisser	.407	1.872	.217	.494	.599
	Huynh-Feldt	.407	1.933	.210	.494	.605
	Lower-bound	.407	1.000	.407	.494	.484
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	1.022	2	.511	1.241	.292
	Greenhouse-Geisser	1.022	1.872	.546	1.241	.290
	Huynh-Feldt	1.022	1.933	.529	1.241	.291
	Lower-bound	1.022	1.000	1.022	1.241	.268
Error(TIME INTERVAL)	Sphericity Assumed	73.286	178	.412		
	Greenhouse-Geisser	73.286	166.633	.440		
	Huynh-Feldt	73.286	171.995	.426		
	Lower-bound	73.286	89.000	.823		

**Your own way of using your medicines: ..... I decide to miss out a dose**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.917	2	.458	1.506	.225
	Greenhouse-Geisser	.917	1.887	.486	1.506	.225
	Huynh-Feldt	.917	1.948	.471	1.506	.225
	Lower-bound	.917	1.000	.917	1.506	.223
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	1.005	2	.502	1.651	.195
	Greenhouse-Geisser	1.005	1.887	.532	1.651	.196
	Huynh-Feldt	1.005	1.948	.516	1.651	.196
	Lower-bound	1.005	1.000	1.005	1.651	.202
Error(TIME INTERVAL)	Sphericity Assumed	54.175	178	.304		
	Greenhouse-Geisser	54.175	167.953	.323		
	Huynh-Feldt	54.175	173.404	.312		
	Lower-bound	54.175	89.000	.609		

**Your own way of using your medicines: ..... I take less than instructed**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.422	2	1.211	4.356	.014
	Greenhouse-Geisser	2.422	1.415	1.711	4.356	.026
	Huynh-Feldt	2.422	1.448	1.673	4.356	.025
	Lower-bound	2.422	1.000	2.422	4.356	.040
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.972	2	.486	1.748	.177
	Greenhouse-Geisser	.972	1.415	.687	1.748	.187
	Huynh-Feldt	.972	1.448	.671	1.748	.186
	Lower-bound	.972	1.000	.972	1.748	.190
Error(TIME INTERVAL)	Sphericity Assumed	49.490	178	.278		
	Greenhouse-Geisser	49.490	125.971	.393		
	Huynh-Feldt	49.490	128.851	.384		
	Lower-bound	49.490	89.000	.556		

## 11 Repeated measures ANOVA of exercise and the food questionnaire

**DURING THE LAST MONTH how many hours of exercise (eg. brisk walking, a sporting activity) do you think you have done each week?**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	5.084	2	2.542	1.830	.164
	Greenhouse-Geisser	5.084	1.825	2.786	1.830	.167
	Huynh-Feldt	5.084	1.885	2.697	1.830	.166
	Lower-bound	5.084	1.000	5.084	1.830	.180
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	10.619	2	5.309	3.822	.024
	Greenhouse-Geisser	10.619	1.825	5.820	3.822	.028
	Huynh-Feldt	10.619	1.885	5.633	3.822	.026
	Lower-bound	10.619	1.000	10.619	3.822	.054
Error(TIME INTERVAL)	Sphericity Assumed	233.373	168	1.389		
	Greenhouse-Geisser	233.373	153.265	1.523		
	Huynh-Feldt	233.373	158.354	1.474		
	Lower-bound	233.373	84.000	2.778		

### Skim or low fat milk

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	14.514	2	7.257	3.947	.021
	Greenhouse-Geisser	14.514	1.863	7.791	3.947	.024
	Huynh-Feldt	14.514	1.927	7.532	3.947	.023
	Lower-bound	14.514	1.000	14.514	3.947	.050
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	16.098	2	8.049	4.378	.014
	Greenhouse-Geisser	16.098	1.863	8.642	4.378	.016
	Huynh-Feldt	16.098	1.927	8.354	4.378	.015
	Lower-bound	16.098	1.000	16.098	4.378	.039
Error(TIME INTERVAL)	Sphericity Assumed	305.172	166	1.838		
	Greenhouse-Geisser	305.172	154.618	1.974		
	Huynh-Feldt	305.172	159.934	1.908		
	Lower-bound	305.172	83.000	3.677		

**Full cream milk**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	3.968	2	1.984	1.047	.353
	Greenhouse-Geisser	3.968	1.860	2.133	1.047	.349
	Huynh-Feldt	3.968	1.921	2.065	1.047	.351
	Lower-bound	3.968	1.000	3.968	1.047	.309
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	4.448	2	2.224	1.174	.312
	Greenhouse-Geisser	4.448	1.860	2.391	1.174	.309
	Huynh-Feldt	4.448	1.921	2.315	1.174	.310
	Lower-bound	4.448	1.000	4.448	1.174	.282
Error(TIME INTERVAL)	Sphericity Assumed	329.710	174	1.895		
	Greenhouse-Geisser	329.710	161.854	2.037		
	Huynh-Feldt	329.710	167.149	1.973		
	Lower-bound	329.710	87.000	3.790		

**Full fat ice cream**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.874	2	1.437	1.646	.196
	Greenhouse-Geisser	2.874	1.932	1.487	1.646	.197
	Huynh-Feldt	2.874	2.000	1.437	1.646	.196
	Lower-bound	2.874	1.000	2.874	1.646	.203
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	1.849	2	.925	1.059	.349
	Greenhouse-Geisser	1.849	1.932	.957	1.059	.347
	Huynh-Feldt	1.849	2.000	.925	1.059	.349
	Lower-bound	1.849	1.000	1.849	1.059	.306
Error(TIME INTERVAL)	Sphericity Assumed	139.655	160	.873		
	Greenhouse-Geisser	139.655	154.591	.903		
	Huynh-Feldt	139.655	160.000	.873		
	Lower-bound	139.655	80.000	1.746		

**Low fat ice cream**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.015	2	.007	.010	.990
	Greenhouse-Geisser	.015	1.897	.008	.010	.988
	Huynh-Feldt	.015	1.966	.007	.010	.990
	Lower-bound	.015	1.000	.015	.010	.922
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.400	2	.200	.268	.765
	Greenhouse-Geisser	.400	1.897	.211	.268	.754
	Huynh-Feldt	.400	1.966	.204	.268	.761
	Lower-bound	.400	1.000	.400	.268	.606
Error(TIME INTERVAL)	Sphericity Assumed	120.925	162	.746		
	Greenhouse-Geisser	120.925	153.695	.787		
	Huynh-Feldt	120.925	159.220	.759		
	Lower-bound	120.925	81.000	1.493		

**Full fat soy milk**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.438	2	.219	1.793	.170
	Greenhouse-Geisser	.438	1.208	.362	1.793	.183
	Huynh-Feldt	.438	1.232	.355	1.793	.183
	Lower-bound	.438	1.000	.438	1.793	.184
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.047	2	.024	.194	.824
	Greenhouse-Geisser	.047	1.208	.039	.194	.707
	Huynh-Feldt	.047	1.232	.039	.194	.712
	Lower-bound	.047	1.000	.047	.194	.661
Error(TIME INTERVAL)	Sphericity Assumed	19.530	160	.122		
	Greenhouse-Geisser	19.530	96.660	.202		
	Huynh-Feldt	19.530	98.565	.198		
	Lower-bound	19.530	80.000	.244		

**Low fat soy milk**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	1.755	2	.878	2.726	.068
	Greenhouse-Geisser	1.755	1.490	1.178	2.726	.085
	Huynh-Feldt	1.755	1.530	1.147	2.726	.083
	Lower-bound	1.755	1.000	1.755	2.726	.103
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.181	2	.090	.281	.755
	Greenhouse-Geisser	.181	1.490	.121	.281	.689
	Huynh-Feldt	.181	1.530	.118	.281	.696
	Lower-bound	.181	1.000	.181	.281	.598
Error(TIME INTERVAL)	Sphericity Assumed	52.148	162	.322		
	Greenhouse-Geisser	52.148	120.673	.432		
	Huynh-Feldt	52.148	123.932	.421		
	Lower-bound	52.148	81.000	.644		

**Nuts (eg. Peanuts, cashews)**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	1.596	2	.798	.942	.392
	Greenhouse-Geisser	1.596	1.883	.848	.942	.387
	Huynh-Feldt	1.596	1.946	.820	.942	.390
	Lower-bound	1.596	1.000	1.596	.942	.335
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	1.914	2	.957	1.129	.326
	Greenhouse-Geisser	1.914	1.883	1.017	1.129	.323
	Huynh-Feldt	1.914	1.946	.984	1.129	.325
	Lower-bound	1.914	1.000	1.914	1.129	.291
Error(TIME INTERVAL)	Sphericity Assumed	145.775	172	.848		
	Greenhouse-Geisser	145.775	161.910	.900		
	Huynh-Feldt	145.775	167.339	.871		
	Lower-bound	145.775	86.000	1.695		

**White bread**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	4.566	2	2.283	1.622	.201
	Greenhouse-Geisser	4.566	1.912	2.388	1.622	.202
	Huynh-Feldt	4.566	1.980	2.306	1.622	.201
	Lower-bound	4.566	1.000	4.566	1.622	.206
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	6.966	2	3.483	2.474	.087
	Greenhouse-Geisser	6.966	1.912	3.643	2.474	.090
	Huynh-Feldt	6.966	1.980	3.519	2.474	.088
	Lower-bound	6.966	1.000	6.966	2.474	.120
Error(TIME INTERVAL)	Sphericity Assumed	233.693	166	1.408		
	Greenhouse-Geisser	233.693	158.708	1.472		
	Huynh-Feldt	233.693	164.317	1.422		
	Lower-bound	233.693	83.000	2.816		

**Wholemeal/grain bread**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	4.399	2	2.199	1.699	.186
	Greenhouse-Geisser	4.399	1.952	2.253	1.699	.187
	Huynh-Feldt	4.399	2.000	2.199	1.699	.186
	Lower-bound	4.399	1.000	4.399	1.699	.196
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	2.166	2	1.083	.836	.435
	Greenhouse-Geisser	2.166	1.952	1.109	.836	.433
	Huynh-Feldt	2.166	2.000	1.083	.836	.435
	Lower-bound	2.166	1.000	2.166	.836	.363
Error(TIME INTERVAL)	Sphericity Assumed	217.501	168	1.295		
	Greenhouse-Geisser	217.501	163.984	1.326		
	Huynh-Feldt	217.501	168.000	1.295		
	Lower-bound	217.501	84.000	2.589		

**Fruit**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.481	2	.241	.329	.720
	Greenhouse-Geisser	.481	1.976	.244	.329	.717
	Huynh-Feldt	.481	2.000	.241	.329	.720
	Lower-bound	.481	1.000	.481	.329	.567
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	1.800	2	.900	1.232	.294
	Greenhouse-Geisser	1.800	1.976	.911	1.232	.294
	Huynh-Feldt	1.800	2.000	.900	1.232	.294
	Lower-bound	1.800	1.000	1.800	1.232	.270
Error(TIME INTERVAL)	Sphericity Assumed	131.540	180	.731		
	Greenhouse-Geisser	131.540	177.818	.740		
	Huynh-Feldt	131.540	180.000	.731		
	Lower-bound	131.540	90.000	1.462		

**Vegetables**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.010	2	.005	.020	.981
	Greenhouse-Geisser	.010	1.689	.006	.020	.967
	Huynh-Feldt	.010	1.738	.006	.020	.970
	Lower-bound	.010	1.000	.010	.020	.889
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.203	2	.101	.395	.674
	Greenhouse-Geisser	.203	1.689	.120	.395	.639
	Huynh-Feldt	.203	1.738	.117	.395	.645
	Lower-bound	.203	1.000	.203	.395	.531
Error(TIME INTERVAL)	Sphericity Assumed	45.123	176	.256		
	Greenhouse-Geisser	45.123	148.648	.304		
	Huynh-Feldt	45.123	152.962	.295		
	Lower-bound	45.123	88.000	.513		

**Meat**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.205	2	.102	.287	.751
	Greenhouse-Geisser	.205	1.963	.104	.287	.747
	Huynh-Feldt	.205	2.000	.102	.287	.751
	Lower-bound	.205	1.000	.205	.287	.594
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	2.383	2	1.191	3.338	.038
	Greenhouse-Geisser	2.383	1.963	1.214	3.338	.039
	Huynh-Feldt	2.383	2.000	1.191	3.338	.038
	Lower-bound	2.383	1.000	2.383	3.338	.071
Error(TIME INTERVAL)	Sphericity Assumed	62.810	176	.357		
	Greenhouse-Geisser	62.810	172.731	.364		
	Huynh-Feldt	62.810	176.000	.357		
	Lower-bound	62.810	88.000	.714		

**Fish**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.790	2	1.395	2.025	.135
	Greenhouse-Geisser	2.790	2.000	1.395	2.025	.135
	Huynh-Feldt	2.790	2.000	1.395	2.025	.135
	Lower-bound	2.790	1.000	2.790	2.025	.158
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	1.517	2	.759	1.101	.335
	Greenhouse-Geisser	1.517	2.000	.759	1.101	.335
	Huynh-Feldt	1.517	2.000	.759	1.101	.335
	Lower-bound	1.517	1.000	1.517	1.101	.297
Error(TIME INTERVAL)	Sphericity Assumed	118.513	172	.689		
	Greenhouse-Geisser	118.513	171.997	.689		
	Huynh-Feldt	118.513	172.000	.689		
	Lower-bound	118.513	86.000	1.378		

**Peanut butter**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	1.691	2	.846	1.053	.351
	Greenhouse-Geisser	1.691	1.934	.875	1.053	.349
	Huynh-Feldt	1.691	2.000	.846	1.053	.351
	Lower-bound	1.691	1.000	1.691	1.053	.308
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.468	2	.234	.291	.748
	Greenhouse-Geisser	.468	1.934	.242	.291	.740
	Huynh-Feldt	.468	2.000	.234	.291	.748
	Lower-bound	.468	1.000	.468	.291	.591
Error(TIME INTERVAL)	Sphericity Assumed	133.305	166	.803		
	Greenhouse-Geisser	133.305	160.496	.831		
	Huynh-Feldt	133.305	166.000	.803		
	Lower-bound	133.305	83.000	1.606		

**Lite Peanut butter**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.572	2	.286	1.199	.304
	Greenhouse-Geisser	.572	1.536	.372	1.199	.296
	Huynh-Feldt	.572	1.579	.362	1.199	.297
	Lower-bound	.572	1.000	.572	1.199	.277
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.090	2	.045	.189	.828
	Greenhouse-Geisser	.090	1.536	.059	.189	.769
	Huynh-Feldt	.090	1.579	.057	.189	.776
	Lower-bound	.090	1.000	.090	.189	.665
Error(TIME INTERVAL)	Sphericity Assumed	38.633	162	.238		
	Greenhouse-Geisser	38.633	124.440	.310		
	Huynh-Feldt	38.633	127.939	.302		
	Lower-bound	38.633	81.000	.477		

**Nutella**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.151	2	.076	.525	.593
	Greenhouse-Geisser	.151	1.748	.087	.525	.569
	Huynh-Feldt	.151	1.806	.084	.525	.574
	Lower-bound	.151	1.000	.151	.525	.471
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.119	2	.059	.412	.663
	Greenhouse-Geisser	.119	1.748	.068	.412	.635
	Huynh-Feldt	.119	1.806	.066	.412	.642
	Lower-bound	.119	1.000	.119	.412	.523
Error(TIME INTERVAL)	Sphericity Assumed	23.084	160	.144		
	Greenhouse-Geisser	23.084	139.864	.165		
	Huynh-Feldt	23.084	144.519	.160		
	Lower-bound	23.084	80.000	.289		

**Breakfast cereal (flakes/flakes and fruit)**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	4.493	2	2.247	1.139	.322
	Greenhouse-Geisser	4.493	1.921	2.339	1.139	.321
	Huynh-Feldt	4.493	1.988	2.260	1.139	.322
	Lower-bound	4.493	1.000	4.493	1.139	.289
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	9.021	2	4.510	2.287	.105
	Greenhouse-Geisser	9.021	1.921	4.696	2.287	.107
	Huynh-Feldt	9.021	1.988	4.537	2.287	.105
	Lower-bound	9.021	1.000	9.021	2.287	.134
Error(TIME INTERVAL)	Sphericity Assumed	331.251	168	1.972		
	Greenhouse-Geisser	331.251	161.347	2.053		
	Huynh-Feldt	331.251	167.007	1.983		
	Lower-bound	331.251	84.000	3.943		

**Porridge/Muesli**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	1.988	2	.994	.630	.534
	Greenhouse-Geisser	1.988	1.947	1.021	.630	.530
	Huynh-Feldt	1.988	2.000	.994	.630	.534
	Lower-bound	1.988	1.000	1.988	.630	.430
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.905	2	.453	.287	.751
	Greenhouse-Geisser	.905	1.947	.465	.287	.745
	Huynh-Feldt	.905	2.000	.453	.287	.751
	Lower-bound	.905	1.000	.905	.287	.594
Error(TIME INTERVAL)	Sphericity Assumed	261.965	166	1.578		
	Greenhouse-Geisser	261.965	161.609	1.621		
	Huynh-Feldt	261.965	166.000	1.578		
	Lower-bound	261.965	83.000	3.156		

**Butter**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	1.196	2	.598	.426	.654
	Greenhouse-Geisser	1.196	1.963	.609	.426	.650
	Huynh-Feldt	1.196	2.000	.598	.426	.654
	Lower-bound	1.196	1.000	1.196	.426	.516
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.136	2	.068	.048	.953
	Greenhouse-Geisser	.136	1.963	.069	.048	.951
	Huynh-Feldt	.136	2.000	.068	.048	.953
	Lower-bound	.136	1.000	.136	.048	.826
Error(TIME INTERVAL)	Sphericity Assumed	227.374	162	1.404		
	Greenhouse-Geisser	227.374	158.990	1.430		
	Huynh-Feldt	227.374	162.000	1.404		
	Lower-bound	227.374	81.000	2.807		



**Margarine**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	5.420	2	2.710	1.524	.221
	Greenhouse-Geisser	5.420	1.922	2.820	1.524	.222
	Huynh-Feldt	5.420	1.989	2.725	1.524	.221
	Lower-bound	5.420	1.000	5.420	1.524	.220
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	5.466	2	2.733	1.537	.218
	Greenhouse-Geisser	5.466	1.922	2.844	1.537	.219
	Huynh-Feldt	5.466	1.989	2.748	1.537	.218
	Lower-bound	5.466	1.000	5.466	1.537	.219
Error(TIME INTERVAL)	Sphericity Assumed	302.297	170	1.778		
	Greenhouse-Geisser	302.297	163.371	1.850		
	Huynh-Feldt	302.297	169.037	1.788		
	Lower-bound	302.297	85.000	3.556		

**Cholesterol lowering spread (eg. Logicol)**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.624	2	1.312	.909	.405
	Greenhouse-Geisser	2.624	1.823	1.439	.909	.397
	Huynh-Feldt	2.624	1.883	1.393	.909	.400
	Lower-bound	2.624	1.000	2.624	.909	.343
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	5.446	2	2.723	1.886	.155
	Greenhouse-Geisser	5.446	1.823	2.987	1.886	.159
	Huynh-Feldt	5.446	1.883	2.891	1.886	.158
	Lower-bound	5.446	1.000	5.446	1.886	.173
Error(TIME INTERVAL)	Sphericity Assumed	242.539	168	1.444		
	Greenhouse-Geisser	242.539	153.130	1.584		
	Huynh-Feldt	242.539	158.210	1.533		
	Lower-bound	242.539	84.000	2.887		

## 12 Repeated measures ANOVA of perceptions of health (Shortened SF12 questionnaire)

In general, would you say your health is: (Excellent to poor, 1-5)

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	1.001	2	.501	1.101	.335
	Greenhouse-Geisser	1.001	1.912	.524	1.101	.333
	Huynh-Feldt	1.001	1.976	.507	1.101	.334
	Lower-bound	1.001	1.000	1.001	1.101	.297
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	3.223	2	1.612	3.543	.031
	Greenhouse-Geisser	3.223	1.912	1.686	3.543	.033
	Huynh-Feldt	3.223	1.976	1.632	3.543	.032
	Lower-bound	3.223	1.000	3.223	3.543	.063
Error(TIME INTERVAL)	Sphericity Assumed	80.058	176	.455		
	Greenhouse-Geisser	80.058	168.253	.476		
	Huynh-Feldt	80.058	173.854	.460		
	Lower-bound	80.058	88.000	.910		

How much of the time during the past 4 weeks...Have you felt calm and peaceful?

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	4.162	2	2.081	2.465	.088
	Greenhouse-Geisser	4.162	1.826	2.279	2.465	.093
	Huynh-Feldt	4.162	1.884	2.210	2.465	.091
	Lower-bound	4.162	1.000	4.162	2.465	.120
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	1.745	2	.872	1.033	.358
	Greenhouse-Geisser	1.745	1.826	.955	1.033	.353
	Huynh-Feldt	1.745	1.884	.926	1.033	.355
	Lower-bound	1.745	1.000	1.745	1.033	.312
Error(TIME INTERVAL)	Sphericity Assumed	150.248	178	.844		
	Greenhouse-Geisser	150.248	162.554	.924		
	Huynh-Feldt	150.248	167.647	.896		
	Lower-bound	150.248	89.000	1.688		

**How much of the time during the past 4 weeks...Did you have a lot of energy?**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	5.088	2	2.544	2.081	.128
	Greenhouse-Geisser	5.088	1.881	2.704	2.081	.131
	Huynh-Feldt	5.088	1.941	2.621	2.081	.129
	Lower-bound	5.088	1.000	5.088	2.081	.153
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	2.740	2	1.370	1.121	.328
	Greenhouse-Geisser	2.740	1.881	1.456	1.121	.326
	Huynh-Feldt	2.740	1.941	1.411	1.121	.327
	Lower-bound	2.740	1.000	2.740	1.121	.293
Error(TIME INTERVAL)	Sphericity Assumed	220.021	180	1.222		
	Greenhouse-Geisser	220.021	169.312	1.300		
	Huynh-Feldt	220.021	174.727	1.259		
	Lower-bound	220.021	90.000	2.445		

**How much of the time during the past 4 weeks... Have you felt downhearted and blue**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	1.129	2	.564	.609	.545
	Greenhouse-Geisser	1.129	1.985	.569	.609	.544
	Huynh-Feldt	1.129	2.000	.564	.609	.545
	Lower-bound	1.129	1.000	1.129	.609	.437
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	6.303	2	3.151	3.400	.036
	Greenhouse-Geisser	6.303	1.985	3.176	3.400	.036
	Huynh-Feldt	6.303	2.000	3.151	3.400	.036
	Lower-bound	6.303	1.000	6.303	3.400	.068
Error(TIME INTERVAL)	Sphericity Assumed	166.850	180	.927		
	Greenhouse-Geisser	166.850	178.626	.934		
	Huynh-Feldt	166.850	180.000	.927		
	Lower-bound	166.850	90.000	1.854		

### 13 Repeated measures ANOVA of perceptions about health care professionals (BMU)

#### These people (doctors/pharmacists) have enough knowledge to answer my questions

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.247	2	.124	.409	.665
	Greenhouse-Geisser	.247	1.990	.124	.409	.664
	Huynh-Feldt	.247	2.000	.124	.409	.665
	Lower-bound	.247	1.000	.247	.409	.524
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.890	2	.445	1.472	.232
	Greenhouse-Geisser	.890	1.990	.447	1.472	.232
	Huynh-Feldt	.890	2.000	.445	1.472	.232
	Lower-bound	.890	1.000	.890	1.472	.228
Error(TIME INTERVAL)	Sphericity Assumed	52.589	174	.302		
	Greenhouse-Geisser	52.589	173.107	.304		
	Huynh-Feldt	52.589	174.000	.302		
	Lower-bound	52.589	87.000	.604		

#### These people do not seem interested in what I have to say about my illness

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	4.849	2	2.425	2.673	.072
	Greenhouse-Geisser	4.849	1.685	2.878	2.673	.082
	Huynh-Feldt	4.849	1.733	2.797	2.673	.080
	Lower-bound	4.849	1.000	4.849	2.673	.106
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	4.983	2	2.491	2.747	.067
	Greenhouse-Geisser	4.983	1.685	2.958	2.747	.077
	Huynh-Feldt	4.983	1.733	2.874	2.747	.075
	Lower-bound	4.983	1.000	4.983	2.747	.101
Error(TIME INTERVAL)	Sphericity Assumed	159.617	176	.907		
	Greenhouse-Geisser	159.617	148.253	1.077		
	Huynh-Feldt	159.617	152.543	1.046		
	Lower-bound	159.617	88.000	1.814		

**I am afraid to tell these people that I have missed taking some of my medications**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.150	2	.075	.118	.888
	Greenhouse-Geisser	.150	1.833	.082	.118	.872
	Huynh-Feldt	.150	1.890	.079	.118	.878
	Lower-bound	.150	1.000	.150	.118	.732
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	2.729	2	1.364	2.158	.119
	Greenhouse-Geisser	2.729	1.833	1.489	2.158	.123
	Huynh-Feldt	2.729	1.890	1.444	2.158	.122
	Lower-bound	2.729	1.000	2.729	2.158	.145
Error(TIME INTERVAL)	Sphericity Assumed	112.539	178	.632		
	Greenhouse-Geisser	112.539	163.097	.690		
	Huynh-Feldt	112.539	168.226	.669		
	Lower-bound	112.539	89.000	1.264		

**I trust these people**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.108	2	.054	.109	.897
	Greenhouse-Geisser	.108	1.967	.055	.109	.894
	Huynh-Feldt	.108	2.000	.054	.109	.897
	Lower-bound	.108	1.000	.108	.109	.742
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.908	2	.454	.912	.404
	Greenhouse-Geisser	.908	1.967	.462	.912	.402
	Huynh-Feldt	.908	2.000	.454	.912	.404
	Lower-bound	.908	1.000	.908	.912	.342
Error(TIME INTERVAL)	Sphericity Assumed	87.618	176	.498		
	Greenhouse-Geisser	87.618	173.117	.506		
	Huynh-Feldt	87.618	176.000	.498		
	Lower-bound	87.618	88.000	.996		

## 14 Repeated measures ANOVA of problems associated with medication taking

### Difficulty opening or closing the medicine bottle

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.048	2	.024	1.004	.368
	Greenhouse-Geisser	.048	1.440	.034	1.004	.347
	Huynh-Feldt	.048	1.472	.033	1.004	.348
	Lower-bound	.048	1.000	.048	1.004	.319
TIME INTERVAL * INTERVENTION GROUP	Sphericity Assumed	.133	2	.066	2.750	.067
	Greenhouse-Geisser	.133	1.440	.092	2.750	.085
	Huynh-Feldt	.133	1.472	.090	2.750	.083
	Lower-bound	.133	1.000	.133	2.750	.101
Error (TIME INTERVAL)	Sphericity Assumed	4.485	186	.024		
	Greenhouse-Geisser	4.485	133.896	.033		
	Huynh-Feldt	4.485	136.895	.033		
	Lower-bound	4.485	93.000	.048		

### Difficulty reading the print on the bottle

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.133	2	.067	1.079	.342
	Greenhouse-Geisser	.133	1.823	.073	1.079	.337
	Huynh-Feldt	.133	1.876	.071	1.079	.339
	Lower-bound	.133	1.000	.133	1.079	.302
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.133	2	.067	1.079	.342
	Greenhouse-Geisser	.133	1.823	.073	1.079	.337
	Huynh-Feldt	.133	1.876	.071	1.079	.339
	Lower-bound	.133	1.000	.133	1.079	.302
Error(TIME INTERVAL)	Sphericity Assumed	11.736	190	.062		
	Greenhouse-Geisser	11.736	173.151	.068		
	Huynh-Feldt	11.736	178.215	.066		
	Lower-bound	11.736	95.000	.124		

**Difficulty remembering to take all the pills/injections**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.892	2	.446	5.591	.004
	Greenhouse-Geisser	.892	1.831	.487	5.591	.006
	Huynh-Feldt	.892	1.885	.473	5.591	.005
	Lower-bound	.892	1.000	.892	5.591	.020
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.809	2	.404	5.068	.007
	Greenhouse-Geisser	.809	1.831	.442	5.068	.009
	Huynh-Feldt	.809	1.885	.429	5.068	.008
	Lower-bound	.809	1.000	.809	5.068	.027
Error(TIME INTERVAL)	Sphericity Assumed	14.997	188	.080		
	Greenhouse-Geisser	14.997	172.114	.087		
	Huynh-Feldt	14.997	177.228	.085		
	Lower-bound	14.997	94.000	.160		

**Difficulty remembering to get your repeats on time**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.211	2	.105	.705	.496
	Greenhouse-Geisser	.211	1.991	.106	.705	.495
	Huynh-Feldt	.211	2.000	.105	.705	.496
	Lower-bound	.211	1.000	.211	.705	.403
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.388	2	.194	1.295	.276
	Greenhouse-Geisser	.388	1.991	.195	1.295	.276
	Huynh-Feldt	.388	2.000	.194	1.295	.276
	Lower-bound	.388	1.000	.388	1.295	.258
Error(TIME INTERVAL)	Sphericity Assumed	28.735	192	.150		
	Greenhouse-Geisser	28.735	191.163	.150		
	Huynh-Feldt	28.735	192.000	.150		
	Lower-bound	28.735	96.000	.299		

**Difficulty taking so many medicines at the same time.**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.213	2	.107	1.411	.247
	Greenhouse-Geisser	.213	1.568	.136	1.411	.246
	Huynh-Feldt	.213	1.607	.133	1.411	.247
	Lower-bound	.213	1.000	.213	1.411	.238
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.396	2	.198	2.618	.076
	Greenhouse-Geisser	.396	1.568	.252	2.618	.089
	Huynh-Feldt	.396	1.607	.246	2.618	.088
	Lower-bound	.396	1.000	.396	2.618	.109
Error(TIME INTERVAL)	Sphericity Assumed	14.053	186	.076		
	Greenhouse-Geisser	14.053	145.809	.096		
	Huynh-Feldt	14.053	149.465	.094		
	Lower-bound	14.053	93.000	.151		

## 15 Repeated measures ANOVA of patient knowledge section of BMU

### I know exactly why I am taking each one of my anti-cholesterol medications.

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	1.627	2	.813	3.857	.023
	Greenhouse-Geisser	1.627	1.997	.815	3.857	.023
	Huynh-Feldt	1.627	2.000	.813	3.857	.023
	Lower-bound	1.627	1.000	1.627	3.857	.052
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	1.040	2	.520	2.466	.088
	Greenhouse-Geisser	1.040	1.997	.521	2.466	.088
	Huynh-Feldt	1.040	2.000	.520	2.466	.088
	Lower-bound	1.040	1.000	1.040	2.466	.120
Error(TIME INTERVAL)	Sphericity Assumed	41.333	196	.211		
	Greenhouse-Geisser	41.333	195.699	.211		
	Huynh-Feldt	41.333	196.000	.211		
	Lower-bound	41.333	98.000	.422		

### Before starting a new medication, I know all the good things it will do for me.

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.687	2	1.343	2.244	.109
	Greenhouse-Geisser	2.687	1.986	1.352	2.244	.109
	Huynh-Feldt	2.687	2.000	1.343	2.244	.109
	Lower-bound	2.687	1.000	2.687	2.244	.137
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.647	2	.323	.540	.584
	Greenhouse-Geisser	.647	1.986	.326	.540	.582
	Huynh-Feldt	.647	2.000	.323	.540	.584
	Lower-bound	.647	1.000	.647	.540	.464
Error(TIME INTERVAL)	Sphericity Assumed	117.333	196	.599		
	Greenhouse-Geisser	117.333	194.676	.603		
	Huynh-Feldt	117.333	196.000	.599		
	Lower-bound	117.333	98.000	1.197		



**I am fully aware of all the bad (or “side”) effects that may happen from my anti-cholesterol medications.**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	4.160	2	2.080	2.200	.114
	Greenhouse-Geisser	4.160	1.953	2.130	2.200	.115
	Huynh-Feldt	4.160	2.000	2.080	2.200	.114
	Lower-bound	4.160	1.000	4.160	2.200	.141
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.507	2	.253	.268	.765
	Greenhouse-Geisser	.507	1.953	.259	.268	.760
	Huynh-Feldt	.507	2.000	.253	.268	.765
	Lower-bound	.507	1.000	.507	.268	.606
Error(TIME INTERVAL)	Sphericity Assumed	185.333	196	.946		
	Greenhouse-Geisser	185.333	191.391	.968		
	Huynh-Feldt	185.333	196.000	.946		
	Lower-bound	185.333	98.000	1.891		

**I am always given clear instructions on how to take my anti-cholesterol medications.**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	1.040	2	.520	1.234	.293
	Greenhouse-Geisser	1.040	1.932	.538	1.234	.293
	Huynh-Feldt	1.040	1.991	.522	1.234	.293
	Lower-bound	1.040	1.000	1.040	1.234	.269
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	1.040	2	.520	1.234	.293
	Greenhouse-Geisser	1.040	1.932	.538	1.234	.293
	Huynh-Feldt	1.040	1.991	.522	1.234	.293
	Lower-bound	1.040	1.000	1.040	1.234	.269
Error(TIME INTERVAL)	Sphericity Assumed	82.587	196	.421		
	Greenhouse-Geisser	82.587	189.384	.436		
	Huynh-Feldt	82.587	195.096	.423		
	Lower-bound	82.587	98.000	.843		

**I am never told about how different drugs I take might affect each other (interact)**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.388	2	1.194	.856	.426
	Greenhouse-Geisser	2.388	1.872	1.275	.856	.420
	Huynh-Feldt	2.388	1.929	1.238	.856	.423
	Lower-bound	2.388	1.000	2.388	.856	.357
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	2.915	2	1.458	1.046	.353
	Greenhouse-Geisser	2.915	1.872	1.557	1.046	.350
	Huynh-Feldt	2.915	1.929	1.511	1.046	.352
	Lower-bound	2.915	1.000	2.915	1.046	.309
Error(TIME INTERVAL)	Sphericity Assumed	262.085	188	1.394		
	Greenhouse-Geisser	262.085	175.999	1.489		
	Huynh-Feldt	262.085	181.356	1.445		
	Lower-bound	262.085	94.000	2.788		

## 16 Repeated measures ANOVA of previous experience section of BMU

**The bad (or “side”) effects of my anti-cholesterol medications prevent me from taking them as prescribed.**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	1.632	2	.816	1.389	.252
	Greenhouse-Geisser	1.632	1.934	.844	1.389	.252
	Huynh-Feldt	1.632	2.000	.816	1.389	.252
	Lower-bound	1.632	1.000	1.632	1.389	.242
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	6.756	2	3.378	5.751	.004
	Greenhouse-Geisser	6.756	1.934	3.494	5.751	.004
	Huynh-Feldt	6.756	2.000	3.378	5.751	.004
	Lower-bound	6.756	1.000	6.756	5.751	.019
Error(TIME INTERVAL)	Sphericity Assumed	102.203	174	.587		
	Greenhouse-Geisser	102.203	168.236	.607		
	Huynh-Feldt	102.203	173.970	.587		
	Lower-bound	102.203	87.000	1.175		

### I cannot afford my anti-cholesterol medications

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.340	2	.170	.280	.756
	Greenhouse-Geisser	.340	1.961	.174	.280	.752
	Huynh-Feldt	.340	2.000	.170	.280	.756
	Lower-bound	.340	1.000	.340	.280	.598
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	10.021	2	5.010	8.241	.000
	Greenhouse-Geisser	10.021	1.961	5.111	8.241	.000
	Huynh-Feldt	10.021	2.000	5.010	8.241	.000
	Lower-bound	10.021	1.000	10.021	8.241	.005
Error(TIME INTERVAL)	Sphericity Assumed	114.306	188	.608		
	Greenhouse-Geisser	114.306	184.313	.620		
	Huynh-Feldt	114.306	188.000	.608		
	Lower-bound	114.306	94.000	1.216		

**I always have to make sacrifices to afford my anti-cholesterol medications**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.877	2	.439	.865	.423
	Greenhouse-Geisser	.877	1.991	.441	.865	.422
	Huynh-Feldt	.877	2.000	.439	.865	.423
	Lower-bound	.877	1.000	.877	.865	.355
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	8.753	2	4.377	8.632	.000
	Greenhouse-Geisser	8.753	1.991	4.398	8.632	.000
	Huynh-Feldt	8.753	2.000	4.377	8.632	.000
	Lower-bound	8.753	1.000	8.753	8.632	.004
Error(TIME INTERVAL)	Sphericity Assumed	96.332	190	.507		
	Greenhouse-Geisser	96.332	189.101	.509		
	Huynh-Feldt	96.332	190.000	.507		
	Lower-bound	96.332	95.000	1.014		

**The times for taking my anti-cholesterol medications are inconvenient**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.890	2	.445	.895	.410
	Greenhouse-Geisser	.890	1.688	.527	.895	.395
	Huynh-Feldt	.890	1.733	.514	.895	.398
	Lower-bound	.890	1.000	.890	.895	.347
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	3.997	2	1.998	4.018	.020
	Greenhouse-Geisser	3.997	1.688	2.367	4.018	.026
	Huynh-Feldt	3.997	1.733	2.306	4.018	.025
	Lower-bound	3.997	1.000	3.997	4.018	.048
Error(TIME INTERVAL)	Sphericity Assumed	94.484	190	.497		
	Greenhouse-Geisser	94.484	160.377	.589		
	Huynh-Feldt	94.484	164.679	.574		
	Lower-bound	94.484	95.000	.995		

**I never feel any benefit from my anti-cholesterol medications.**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	4.148	2	2.074	2.736	.067
	Greenhouse-Geisser	4.148	1.947	2.130	2.736	.069
	Huynh-Feldt	4.148	2.000	2.074	2.736	.067
	Lower-bound	4.148	1.000	4.148	2.736	.102
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.318	2	.159	.210	.811
	Greenhouse-Geisser	.318	1.947	.164	.210	.805
	Huynh-Feldt	.318	2.000	.159	.210	.811
	Lower-bound	.318	1.000	.318	.210	.648
Error(TIME INTERVAL)	Sphericity Assumed	139.504	184	.758		
	Greenhouse-Geisser	139.504	179.160	.779		
	Huynh-Feldt	139.504	184.000	.758		
	Lower-bound	139.504	92.000	1.516		

**A medication organiser helps to remind me about taking my anti-cholesterol medications**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	1.861	2	.930	.796	.453
	Greenhouse-Geisser	1.861	1.949	.955	.796	.450
	Huynh-Feldt	1.861	2.000	.930	.796	.453
	Lower-bound	1.861	1.000	1.861	.796	.375
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	8.630	2	4.315	3.692	.027
	Greenhouse-Geisser	8.630	1.949	4.427	3.692	.028
	Huynh-Feldt	8.630	2.000	4.315	3.692	.027
	Lower-bound	8.630	1.000	8.630	3.692	.058
Error(TIME INTERVAL)	Sphericity Assumed	208.007	178	1.169		
	Greenhouse-Geisser	208.007	173.488	1.199		
	Huynh-Feldt	208.007	178.000	1.169		
	Lower-bound	208.007	89.000	2.337		

**I increase the dose of my anti-cholesterol medication when I have fatty foods**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.899	2	.450	.802	.450
	Greenhouse-Geisser	.899	1.904	.472	.802	.445
	Huynh-Feldt	.899	1.962	.458	.802	.448
	Lower-bound	.899	1.000	.899	.802	.373
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	1.889	2	.944	1.684	.188
	Greenhouse-Geisser	1.889	1.904	.992	1.684	.190
	Huynh-Feldt	1.889	1.962	.963	1.684	.189
	Lower-bound	1.889	1.000	1.889	1.684	.197
Error(TIME INTERVAL)	Sphericity Assumed	106.530	190	.561		
	Greenhouse-Geisser	106.530	180.859	.589		
	Huynh-Feldt	106.530	186.402	.572		
	Lower-bound	106.530	95.000	1.121		

## 17 Repeated measures ANOVA of communication section of BMU

**I always ask my doctor questions when I do not understand something about my anti-cholesterol medications**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.687	2	1.343	2.208	.113
	Greenhouse-Geisser	2.687	1.718	1.564	2.208	.121
	Huynh-Feldt	2.687	1.764	1.523	2.208	.119
	Lower-bound	2.687	1.000	2.687	2.208	.140
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	1.407	2	.703	1.156	.317
	Greenhouse-Geisser	1.407	1.718	.819	1.156	.311
	Huynh-Feldt	1.407	1.764	.797	1.156	.312
	Lower-bound	1.407	1.000	1.407	1.156	.285
Error(TIME INTERVAL)	Sphericity Assumed	119.240	196	.608		
	Greenhouse-Geisser	119.240	168.394	.708		
	Huynh-Feldt	119.240	172.862	.690		
	Lower-bound	119.240	98.000	1.217		

**I always ask my pharmacist questions when I do not understand something about my anti-cholesterol medications**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.714	2	1.357	2.650	.073
	Greenhouse-Geisser	2.714	1.942	1.398	2.650	.075
	Huynh-Feldt	2.714	2.000	1.357	2.650	.073
	Lower-bound	2.714	1.000	2.714	2.650	.107
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	.293	2	.146	.286	.752
	Greenhouse-Geisser	.293	1.942	.151	.286	.745
	Huynh-Feldt	.293	2.000	.146	.286	.752
	Lower-bound	.293	1.000	.293	.286	.594
Error(TIME INTERVAL)	Sphericity Assumed	98.327	192	.512		
	Greenhouse-Geisser	98.327	186.387	.528		
	Huynh-Feldt	98.327	192.000	.512		
	Lower-bound	98.327	96.000	1.024		

**I'd like to ask questions but I never know what to ask my doctor about my anti-cholesterol medications.**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	3.020	2	1.510	1.513	.223
	Greenhouse-Geisser	3.020	1.986	1.521	1.513	.223
	Huynh-Feldt	3.020	2.000	1.510	1.513	.223
	Lower-bound	3.020	1.000	3.020	1.513	.222
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	5.333	2	2.667	2.672	.072
	Greenhouse-Geisser	5.333	1.986	2.685	2.672	.072
	Huynh-Feldt	5.333	2.000	2.667	2.672	.072
	Lower-bound	5.333	1.000	5.333	2.672	.105
Error(TIME INTERVAL)	Sphericity Assumed	191.646	192	.998		
	Greenhouse-Geisser	191.646	190.699	1.005		
	Huynh-Feldt	191.646	192.000	.998		
	Lower-bound	191.646	96.000	1.996		

**I'd like to ask questions but I never know what to ask my pharmacist about my anti-cholesterol medications.**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	3.512	2	1.756	2.339	.099
	Greenhouse-Geisser	3.512	1.980	1.774	2.339	.100
	Huynh-Feldt	3.512	2.000	1.756	2.339	.099
	Lower-bound	3.512	1.000	3.512	2.339	.129
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	8.502	2	4.251	5.662	.004
	Greenhouse-Geisser	8.502	1.980	4.293	5.662	.004
	Huynh-Feldt	8.502	2.000	4.251	5.662	.004
	Lower-bound	8.502	1.000	8.502	5.662	.019
Error(TIME INTERVAL)	Sphericity Assumed	142.653	190	.751		
	Greenhouse-Geisser	142.653	188.123	.758		
	Huynh-Feldt	142.653	190.000	.751		
	Lower-bound	142.653	95.000	1.502		

**I always understand the answers to my questions**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	2.518	2	1.259	2.124	.122
	Greenhouse-Geisser	2.518	1.996	1.262	2.124	.122
	Huynh-Feldt	2.518	2.000	1.259	2.124	.122
	Lower-bound	2.518	1.000	2.518	2.124	.148
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	4.417	2	2.209	3.725	.026
	Greenhouse-Geisser	4.417	1.996	2.213	3.725	.026
	Huynh-Feldt	4.417	2.000	2.209	3.725	.026
	Lower-bound	4.417	1.000	4.417	3.725	.057
Error(TIME INTERVAL)	Sphericity Assumed	115.030	194	.593		
	Greenhouse-Geisser	115.030	193.608	.594		
	Huynh-Feldt	115.030	194.000	.593		
	Lower-bound	115.030	97.000	1.186		

**My doctor/pharmacist explains information about my anti-cholesterol medication in a way that I can understand**

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME INTERVAL	Sphericity Assumed	.179	2	.090	.198	.821
	Greenhouse-Geisser	.179	1.962	.091	.198	.817
	Huynh-Feldt	.179	2.000	.090	.198	.821
	Lower-bound	.179	1.000	.179	.198	.658
TIME INTERVAL * STUDY GROUP	Sphericity Assumed	2.442	2	1.221	2.691	.070
	Greenhouse-Geisser	2.442	1.962	1.244	2.691	.071
	Huynh-Feldt	2.442	2.000	1.221	2.691	.070
	Lower-bound	2.442	1.000	2.442	2.691	.104
Error(TIME INTERVAL)	Sphericity Assumed	88.036	194	.454		
	Greenhouse-Geisser	88.036	190.335	.463		
	Huynh-Feldt	88.036	194.000	.454		
	Lower-bound	88.036	97.000	.908		