Psychological adjustment to the onset of Rheumatoid Arthritis: a longitudinal evaluation of perceptions of and adherence to medication

Lyndsay Dawn Hughes

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Dedication

This thesis is dedicated to my family.

To Mum and Dad. Without the sacrifices that you have made and the desire you have created within me to always learn and improve myself, I would not and could not be where I am today. I am truly grateful for all that you have given me. Without you I would not be the person I am.

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Abstract

Rheumatoid arthritis (RA) is a chronic, progressive autoimmune disease causing inflammation of the synovium resulting in severe pain, joint disfigurement and disability as well as malaise, fatigue and a depressed immune system. Treatment consists of three broad phases; firstly, following diagnosis treatment is focussed on rapid reduction of pain and inflammation. Secondly, maintenance of quiescence is sought through medication. Finally, if disease activity remains high despite medication, escalation to anti-TNF α therapy is required to prevent permanent joint damage and disability. The primary course of treatment is prescription of disease modifying anti-rheumatic drugs (DMARDs) within 3 months of onset of symptoms. However, DMARDs can take 8-12 weeks to exhibit a noticeable benefit whereas unpleasant side effects can occur shortly after initiation. Also, DMARDs do not alleviate pain; therefore it is difficult for patients to attribute recovery to this medication. For these reasons, although it is imperative for future health and functioning to take DMARDs as prescribed, non-adherence is common at 30-50%.

Non-adherence to treatment can be intentional, where a decision is made not to conform to the prescription, or unintentional which is often due to forgetting. To measure intentional non-adherence, a validated measure of adherence for rheumatoid arthritis was reduced through exploratory factor analysis from 19 items to 5 items by removing items that did not add to the explained variance of adherence. The CQR5 explained 53% of the variance in adherence and was shown to have a good fit to the data through confirmatory factor analysis. A discriminant function equation was generated that correctly identifies 88.5% of patients as high or low adherers and has high clinical utility due to the brevity for patients and unidimensionality for easy interpretation. The CQR5 was used throughout the programme of research to measure intentional non-adherence along with a separate measure of unintentional non-adherence.

Four commonly used social cognition models of illness were measured in 227 RA patients to determine which had the best utility for predicting non-adherence to DMARDs. Patients were recruited to represent the three stages of illness including newly diagnosed, established on DMARD therapy and established with concurrent anti-TNF α therapy. Logistic regression analysis showed that the Self Regulatory Model best predicted intentional non-adherence as patients with perceptions of worse consequences of RA and longer disease duration were more likely to be highly adherent to DMARDs in cross-sectional analysis. In contrast, the Theory of Planned Behaviour better predicted

patients who self-reported forgetting their DMARDs with patients with more confidence in being able to take their medications (Perceived Behavioural Control) being less likely to forget.

171 patients were successfully followed-up six months after baseline recruitment. The longitudinal results showed that the social cognition models differed for patients at different stages of the illness suggesting that their experience of living with rheumatoid arthritis influenced perceptions of their illness and medications. Newly diagnosed patients scored lower on factors measuring perceptions of disease chronicity and seriousness whereas patients that had escalated to anti-TNF α therapy scored higher on these factors. The newly diagnosed patients also showed more variability in the social cognition scores whereas the more established patients demonstrated stable models of illness. This supports Leventhal's (1992) theory that illness representations will be regulated through integration of knowledge and experience of an illness.

Structural equation modelling was used to establish the best predictors of intentional non-adherence at six month follow-up. In support of research in other chronic illnesses (Horne & Weinman, 2002; Niklas, Dunbar & Wild, 2010), the effect of perceptions of the consequences and chronicity of the illness on adherence are mediated by perceptions of the necessity of the medication. In addition, the impact of the emotional reaction to the illness on adherence to DMARDs is mediated by concerns about the medication. In addition, this study incorporated factors from the Theory of Planned Behaviour to explain medication adherence and found that the influence of friends and family impacts on the patient's confidence to follow the prescription accurately which in turn as an effect on adherence to DMARDs. This large longitudinal study found that by combining factors from a number of social cognition models, it is possible to explain and predict intentional non-adherence and provides some evidence for best ways to intervene to improve adherence and prognosis.

To provide a more comprehensive and clinically useful picture of non-adherence, a Cost of Illness study was carried which found that patients self-reporting low adherence to DMARDs also had significantly higher costs for this medication. This was caused by an increased incidence of Leflunamide prescribing for patients who often forget their medication and was maintained longitudinally. This association has not been previously reported in the literature and provides some evidence that non-adherence to DMARDs is having a concrete effect on the clinical management of patients.

Finally, an SMS text message based reminder service designed to remind patients who self-report forgetting their medications was tested through a simulation study for the cost and likely benefit in

health related quality of life using the health economic analysis of the longitudinal study and the results of a survey establishing the feasibility of implementing such a service in the rheumatology clinic. A sensitivity analysis testing the number of messages sent and the cost per message found that a reminder service for the sample of patients in this programme of research would cost between £1387.00 and £142.27 per year. This would equate to a cost per Quality Adjusted Life Year (QALY) gain of between £2889.58 and £296.40 by enabling patients to adhere more rigorously to their DMARD regimen.

This programme of research is the first to test four commonly used social cognition models to predict adherence to DMARDs in a large, multi-centre longitudinal study of rheumatoid arthritis patients. Perceptions of the likely duration and consequences of the illness, as measured by the Illness Perceptions Questionnaire and the necessity of medications (measured by the Beliefs about Medications Questionnaire) along with self-efficacy (measured by the Theory of Planned Behaviour) explained 24% of the variance in intentional adherence over six months. The results show the importance of considering intentional and unintentional non-adherence separately as they appear to have different underlying mechanisms as well as patients in different phases of the illness as their experience influences their social cognition models of illness. A simple SMS based reminder service could act as a cue to action to reduce unintentional non-adherence whereas addressing issues surrounding maladaptive perceptions about the illness and the treatment could improve intentional non-adherence which has the potential to improve the prognosis and quality of life for patients as well as safe costs for the NHS.

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List of Abbreviations

ACR	American College of Rheumatology
ANOVA	Analysis of variance
BMQ	Beliefs about Medications Questionnaire
BSR	British Society for Rheumatology
CFA	Confirmatory factor analysis
CFI	Comparative fit index
COI	Cost of illness
CQR5	5 item Compliance Questionnaire for Rheumatology
CQR19	19 item Compliance Questionnaire for Rheumatology
CRP	C-Reactive Protein
CUA	Cost-utility analysis
DAS28	Disease Activity Score 28
DMARDs	Disease modifying anti-rheumatic drugs
DNA	Did not attend (outpatient appointment)
EFA	Exploratory factor analysis
eMEMs	Electronic medication event monitoring
EQ5D	EuroQol 5 Dimension quality of life questionnaire
ERAN	Early Rheumatoid Arthritis Network
ERAS	Early Rheumatoid Arthritis Study
ESR	Erythrocyte Sedimentation Rate

EULAR	European League Against Rheumatism
HAQ	Health Assessment Questionnaire
HBM	Health Belief Model
HCQ	Hydroxychloroquine (a DMARD)
HRQoL	Health related quality of life
ICT	Information and Communication Technology
IPQ	Illness Perceptions Questionnaire
IPQ-R	Revised Illness Perceptions Questionnaire
KMO	Kaiser-Meyer-Olkin
LFM	Leflunamide (a DMARD)
MSA	Measure of sampling adequacy
MTX	Methotrexate (a DMARD)
NAO	National Audit Office
NCP	Non-centrality parameter
NFI	Normed fit index
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NOAR	Norfolk Arthritis Register
NRAS	National Rheumatoid Arthritis Society
NSAIDs	Non-steroidal anti-rheumatic drugs
ONS	Office for National Statistics
OR	Odds Ratio

PAS	Patient administration system
QALY	Quality adjusted life year
QoL	Quality of life
RA	Rheumatoid arthritis
RAM	Reported Adherence to Medication Questionnaire
RCT	Randomised controlled trial
REC	Research Ethics Committee
RMR	Root mean square residual
RMSEA	Root mean square error of approximation
RR	Risk ratio
SEM	Structural equation modelling
SMS	Short Message Service
SRM	Self Regulatory Model
SSZ	Sulfasalazine (a DMARD)
TNF α	Tumour Necrosis Factor alpha
TPB	Theory of Planned Behaviour
TTO	Time Trade Off
VAS	Visual analogue scale
WHO	World Health Organisation

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Chapter 1

Introduction to Rheumatoid Arthritis

1.1: What is Rheumatoid Arthritis?

Rheumatoid Arthritis (RA) is a chronic autoimmune disease which results in inflammation in the synovial membrane of the joints caused by white blood cells which release cytokines resulting in pain, swelling and stiffness. Continued inflammation leads to irreversible damage to the joints through erosion of the cartilage and bone (Neidel, Schulze & Lindschau, 1995). The disease commonly affects the small joints of hands and feet symmetrically (Hameed & Akil, 2010). The National Institute for Health and Clinical Excellence (NICE, 2009) report the incidence rate as 12,000 people per year being diagnosed in the UK, however, as RA is chronic, the cumulative effect results in approximately 400,000 people currently living with the condition in the UK. The average age of onset is 55-64 years (Symmons, 2005) although it can occur at any age and approximately three times as many women as men are affected (Lawrence et al., 1989).

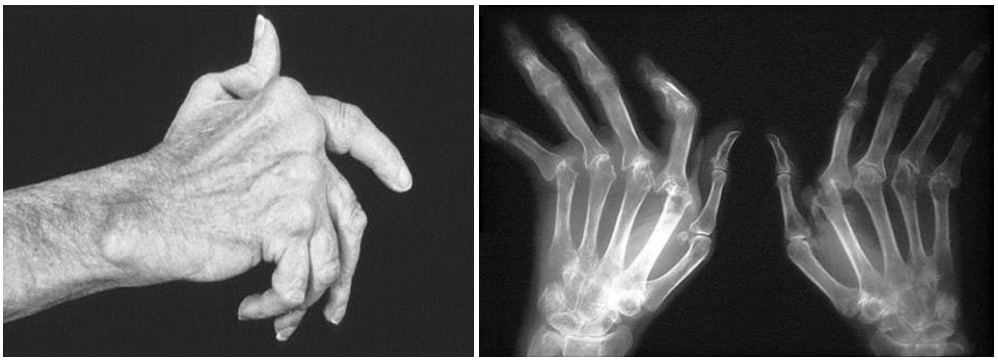


Figure 1.1: Physical and radiological effects of joint erosion in rheumatoid arthritis

The pain and stiffness of joints can lead to loss of mobility; however other symptoms include fatigue, malaise and other extra-articular problems such as skin ulcers, dry eyes and anaemia. Combined, these symptoms can lead to severe disability which generally worsens as the disease progresses. Approximately 70% of patients experience unpredictable “flares” characterised by intense active disease followed by periods of quiescence (Weinblatt & Maier, 1989) with 10-15% of patients displaying progressively disabling disease despite therapy (Young, 1992). As RA is incurable,

treatment is focused upon prevention of joint damage and function loss as well as pain management.

1.2: Aetiology of Rheumatoid Arthritis

The cause of RA is not yet established, however the mechanism behind the inflammation is well known. The key effecter cell appears to be the T-cell which orchestrates the immune response through a host of cytokines. The key cytokines implicated in RA are Tumour Necrosis Factor-alpha and Interleukin 1 (Hameed & Akil, 2010).

There has been recent research indicating that there is a genetic component to RA. Historically, this has been demonstrated through incidence, family and twin studies. For example, there is a much higher incidence of RA in Native American populations at 5.3% for Pima Indians (del Puente, Knowler, Pettit & Bennett, 1989) and 6.8% for Chippewa Indians (Harvey, Lotze, Stevens, Lambert & Jacobson, 1981) compared to Caucasian populations at 0.8-1% (Symmons, 2005). There is also a much *lower* incidence in Africa (Brighton, de la Harpe, van Staden, Badenhorst & Myers, 1988; Silman et al., 1993) and South East Asia (Dans, Tankeh Torres, Amanter & Penserga, 1997; Shichikawa et al., 1999). Although some of this difference may be due to environmental factors, differences in prevalence have been observed in non-indigenous racial groups that have immigrated to Europe and North America supporting the view that there is some genetic component (Silman & Pearson, 2002).

Few studies have looked at the familial risk of RA; however the Norfolk Arthritis Register in England found that there is evidence of a small familial risk of developing RA (Jones, Silman, Whiting, Barrett & Symmons, 1996). Twin studies have consistently shown a fourfold increased concordance in monozygotic twins compared with same-sexed dizygotic twins (MacGregor et al., 2000). Again, the effect of environmental factors is difficult to determine in twin studies, however MacGregor et al. suggest that 50-60% of the occurrence of RA in the twins is explained by shared genetic effects.

A review by Silman & Pearson (2002) suggests that there is some evidence that infectious agents may trigger RA, as the occurrence of RA has reduced in the past 30 years during which time many infectious agents have been eradicated whereas genetic populations have remained stable. However, there are difficulties studying this because RA could be the final pathway from a number of infectious agents which are often also found in the non-RA population. The likelihood is that an individual has a genetic predisposition for RA and a triggering agent (either infectious or not) causes onset of symptoms (Hameed & Akil, 2010).

1.3: Diagnosis of Rheumatoid Arthritis

Traditionally, diagnosis of rheumatoid arthritis can only reliably be made following clinical examination which incorporates serological and radiographic results as there is not yet a set of diagnostic tests that are sensitive or specific enough to definitively classify RA (Hameed & Akil, 2010). NICE (2009) referral guidelines stipulate that any person with suspected persistent synovitis of undetermined cause should be referred to a specialist and that this should be urgent if more than one joint is affected and/or there has been more than 3 months delay from onset of symptoms to seeking medical advice. The emphasis on emergency referral within 3 months of symptom onset reflects evidence that persistent joint damage can occur during the first few months which is irreversible (Brook & Corbett, 1977; Conoghan et al., 2010).

The American College of Rheumatology (ACR; formally the American Rheumatism Association) proposed a set of classification criteria for RA in 1956 (Bennett, Cobb, Jacox, Jessar & Ropes, 1956), however these were heavily criticised for a lack of sensitivity and specificity, particularly for early presentation of rheumatoid arthritis. In response to this, the ACR and the European League Against Rheumatism (EULAR) jointly proposed revised criteria with the aim of improving diagnosis of early RA (Aletaha et al., 2010). The criteria are reproduced in Table 1.1 and should be used for patients who have at least one joint with synovitis (swelling) which is unexplained by another disease.

Once a diagnosis of rheumatoid arthritis has been made, treatment should focus primarily on reduction of the swelling and associated pain and stiffness and long-term control of the autoimmune process to prevent further joint damage. Self-management and psychological adaptation strategies can then be addressed.

Table 1.1: The 2010 ACR/EULAR classification criteria for rheumatoid arthritis (adapted from Aletaha et al., 2010)

Category		Score
A – Joint involvements	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	>10 joints (at least 1 small joint)	5
B – Serology (at least 1 test result is needed for classification)	Negative RF *and* negative ACPA	0
	Low-positive RF *or* low-positive ACPA	2
	High-positive RF *or* high positive ACPA	3
C – Acute phase reactants (at least 1 test result is needed for classification)	Normal CRP *and* normal ESR	0
	Abnormal CRP *or* abnormal ESR	1
D – Duration of symptoms	<6 weeks	0
	≥6 weeks	1
Classification criteria for RA (score based algorithm: add score of categories A-D; a score of ≥6/10 is needed for classification of a patient as having definite RA)		

1.4: Assessment of disease severity

In order to effectively treat and manage rheumatoid arthritis, NICE (2009) guidelines recommend regular measurement of blood inflammatory markers as well as disease activity using a composite score such as the Disease Activity Score 28 (DAS28; see section 1.4.2 for more details). This is essential to inform the decision to increase treatment to control the disease as well as monitoring the effects of decreasing treatment once remission has been established. Regular monitoring of DAS28 score is also a necessary component of escalation of treatment (see section 1.6.4).

1.4.1: Inflammatory blood markers

There are two commonly used inflammatory blood markers which assess levels of inflammation in rheumatoid arthritis patients and therefore are used as a proxy for disease activity:

Erythrocyte Sedimentation Rate (ESR) is a non-specific test of chronic or acute inflammation which can be associated with infections, cancers and autoimmune diseases. As it is non-specific, it must be used in conjunction with other clinical indicators for diagnosis of rheumatoid arthritis; however it can be a useful way of monitoring disease activity as it is inexpensive and can be carried out alongside other blood monitoring tests. Slightly elevated results can occur for benign reasons such as; older age, menstruation, pregnancy and some medications. The test measures the rate at which

erythrocytes (red blood cells) sediment in the laboratory which is measured in millimetres per hour (mm/hr). Normal results for men aged over 50 are <20mm/hr and for women aged over 50; <30mm/hr, however as ESR rates are expected to be elevated in autoimmune disease such as RA, it is useful to track changes *within* an individual to monitor periods of flare and quiescence.

C-Reactive Protein (CRP) is another non-specific measure of inflammation that can be used to assess infection, and more chronic inflammation seen in RA. It is often used to monitor patients' response to therapy and assess disease activity. CRP is more reactive than ESR with changes occurring more quickly at the beginning and end of the inflammatory process and so can be more useful when assessing the effects of fast-acting anti-inflammatory drugs such as corticosteroids (see section 1.6 for more information on RA medication). CRP is produced by the liver in response to general inflammation and the laboratory test assesses the levels of this protein in the blood. Normally, levels of C-reactive protein are not detectable in the blood, although they can be slightly elevated in the latter half of pregnancy or as a response to oral contraceptive. It is possible for patients with rheumatoid arthritis to have undetectable levels of CRP, despite active disease although generally levels above 10mg/dL are considered to be very high and indicative of active disease. As with ESR, CRP is most useful to assess changes of inflammation *within* individuals to be used as a proxy for disease activity.

1.4.2: Disease activity (DAS28)

The Disease Activity Score (DAS28) is a combined index that incorporates subjective assessments of global health and tender joints with objective measurements of inflammation (via ESR or CRP) and physician assessments of swollen joints. During assessment, a trained clinician will evaluate whether 28 specific joints are swollen or tender. These joints include the knee, shoulder, elbow, wrist, Proximal Interphalangeal and Metacarpophalangeal (finger joints) on both sides of the patient's body. Patients are also required to self report their global health on a 100mm visual analogue scale (VAS) and will have some input into the clinician's judgment of which of the 28 joints are tender to touch. The DAS28 is a validated composite score based on a formula with standardized weights to combine the swollen joint count, tender joint count, ESR *or* CRP and the patient's global assessment of health (Prevoo et al., 1996).

The DAS28 has been extensively validated for use in clinical trials (Van Riel & Schumacher, 2001) and correspond well with EULAR response criteria for Disease Modifying Anti-Rheumatic therapy (van Gestel, Haagsma & van Riel, 1998). Scores can range from 0 to 9.4 and usually have a Gaussian

distribution in RA populations. Cut off values have been identified to be used in relation with the British Society for Rheumatology's (BSR) recommendations (Ding et al., 2010) with remission set at <2.6, low activity; 2.6-3.2, moderate activity; 3.2-5.1 and high disease activity at >5.1 (Fransen & van Riel, 2005). A change of 1.2 points (twice the measurement error) within an individual patient is considered to be significant (van Gestel et al., 1998).

1.4.3: Functional disability (HAQ)

The Health Assessment Questionnaire (HAQ; Fries, Spitz, Kraines & Holman, 1980) is the most commonly used measure to assess functional disability in arthritis patients. It has been cited over 400 times and is usually used as an outcome measure for clinical trials in rheumatoid arthritis (Felson et al., 1993). Patients are asked to self report their ability to perform eight functions over the past week including; dressing, arising, eating, walking, hygiene, reach, grip, and common activities (Bruce & Fries, 2003; Fries, Spitz & Young, 1982) with response options of *(without ANY difficulty-with SOME difficulty-with MUCH difficulty-UNABLE to do)*. The total score (max=24) is divided by the number of items completed (max=8) resulting in scores ranging between 0 and 3 with higher values indicating greater disability. Patients are also asked to indicate if they need either an aid to perform an activity (e.g. a walking stick) or help from someone else for each of the eight functions. Scores are weighted more heavily if a patient requires help or an aid.

The HAQ has been shown to have good reliability and validity across many applications and in different patient populations and has been significantly correlated with a wide variety of health status measures, including self-report measures, biochemical and clinical studies, assessment of morbidity, evaluation of health care resource utilization and cost estimations (Ramey, Fries & Singh, 1996). A review by Bruce & Fries (2003) demonstrated that the HAQ is a useful and well accepted measure with excellent clinical utility that has the ability to sensitively detect changes in functional disability in rheumatoid arthritis patients.

1.5: Prognosis

As rheumatoid arthritis is incurable, patients are faced with progressive disability (Young, 1992) as well as an increased risk of co-morbidity and mortality. It has been shown that life expectancy can be shortened by up to seven years for men and three years for women with RA (Chan, Wilson & Cronstein, 2010). One reason for this is the increased incidence of cardiovascular disease, particularly for women as those with seropositive inflammatory polyarthritis have been shown to have a twofold increased risk in death due to cardiovascular disease (Goodson et al., 2002). This

could be due to high levels of C-Reactive Protein which have been linked to increased risk of cardiovascular death in RA when compared to controls with osteoarthritis who were matched for potential risk factors (Kitas, Banks & Bacon, 2001; Kitas & Erb, 2003). However, there are other areas of concern as Symmons, Jones, Scott & Prior (1998) found an increased mortality ratio of 2.7 (2.4:3.0) with an increased number of deaths from respiratory causes and cancers in addition to cardiovascular disease. Although the increased risk of mortality in RA has been known for some time, the exact mechanisms are not fully understood as yet and therefore as well as the need to control inflammation to reduce the burden of the RA itself, it is important for treatment to also consider other co-morbidities that may result from the pathology itself or the treating medications.

1.6: Treatment for Rheumatoid Arthritis

For the majority of patients, treatment will be commenced following diagnosis by a rheumatologist in secondary care (Lard, Huizinga, Hazes & Vliet Vlieland, 2001) which will likely be as a result of active disease and the accompanying symptoms (Watkins, Shifren, Park & Morrell, 1999). Therefore, treatment forms two strategies; firstly, reduction of symptoms to improve quality of life for patients and secondly, to prevent further joint damage and preserve function. A number of different treatments are given to relieve symptoms (Matteson, 2000) which are described in more detail below.

1.6.1: Corticosteroids

Corticosteroids (e.g. Prednisolone) are useful to stimulate quick remission (NICE, 2009) and can be given orally, intra-muscularly or intravenously. They are frequently prescribed during a flare of disease to quickly reduce pain and swelling and can be used in the longer term to reduce disease progression. However long-term use is not advised as they can cause serious side effects such as osteoporosis, hypertension, diabetes, cataracts and weight gain (Erb et al., 2002) and can suppress the hypothalamus-pituitary-adrenal axis (NICE, 2009).

1.6.2: Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) have, in the past, been used prolifically to relieve pain in rheumatoid arthritis (Brooks & Day, 1991). They have a rapid onset of action and are usually at least in part effective at reducing inflammation (Young, 2008). However, more recent guidelines by NICE (2009) recommend that oral NSAIDs should be used at the lowest effective dose and for the shortest possible period of time. This is due to their potential for toxicity and contraindications with

co-morbidity because of interactions with other drugs such as diuretics and ACE-inhibitors (Young, 2008).

1.6.3: Disease Modifying Anti-Rheumatic Drugs (DMARDs)

Rheumatoid arthritis responds well to traditional Disease Modifying Anti-Rheumatic Drugs (DMARDs; Park et al., 1999; Young, 2008), such as Methotrexate, which are considered to be the foundation of RA treatment to prevent accelerated disease progression and to maintain function (ten Wolde et al., 1996). There is increasing evidence that the early use of DMARDs produces better outcomes, particularly in the short term (van der Heide et al., 1996) and therefore, NICE (2009) guidelines stipulate that DMARDs should be offered to all patients newly diagnosed with RA ideally within three months of the onset of symptoms. It is therefore important that these medications are taken as directed by a medical professional for a sustained period of time in order to maintain disease suppression (Nikiphorou & Young, 2010). However, DMARDs can take months to start to exhibit noticeable benefits and often have undesirable side effects such as skin rash, ulcers, and gastrointestinal problems including nausea, vomiting and diarrhoea (Young, 2008). Although DMARDs are the mainstay of RA treatment, the lack of immediate benefit and the presence of side effects and inconveniences such as blood monitoring can lead to non-adherence by patients reducing the efficacy of these medications. The most commonly prescribed DMARDs are described in more detail below.

Methotrexate (MTX) is the anchor DMARD and the gold standard against which new therapies are compared. It is administered weekly either orally or subcutaneously on the same day every week. Common side effects include bone marrow suppression and gastrointestinal problems (eg nausea, vomiting). Folic acid is frequently prescribed alongside MTX to combat nausea. Although MTX is the most commonly prescribed DMARD in the UK, it can be contraindicated for a number of reasons including; pregnancy, high alcohol intake and impaired liver function. Monitoring blood tests are required every 6-8 weeks to check for abnormal renal and hepatic function and MTX should not be used if regular monitoring is not achieved.

Sulfasalazine (SSZ) was the first drug developed specifically for RA. It is taken orally, typically twice daily. Common side effects include; headache, skin rash, nausea and diarrhoea. There is also the potential for serious side effects such as toxicity, drug-induced hepatitis and cytopenia. As with Methotrexate, regular blood monitoring tests are needed to check for hepatic and haemotological problems.

Hydroxychloroquine (HCQ) is an anti-malaria drug with proven efficacy in early and mild rheumatoid arthritis. It is taken daily by tablet. Side effects are less common and severe than other DMARDs, however, evidence of radiological joint protection is minimal and so it is often used as combination therapy with other DMARDs. Following initial blood tests checking for normal renal and hepatic function, regular blood monitoring is not required for HCQ *per se*, however as it is usually used in combination with MTX or SSZ, regular checks will still be needed. Hydroxychloroquine can damage the retina and so yearly ophthalmological tests are recommended.

Leflunamide (LFM) is the newest DMARD and has been shown to be as efficacious as MTX, although it is more expensive. It may be useful in patients who have not responded to MTX, although it can be used in conjunction. LFM is taken orally once daily. Similar side effects to other DMARDs are possible including nausea, skin rash, hair loss and more seriously, a lowered blood count and life-threatening liver disease. For this reason, regular blood monitoring is required. Leflunamide also has a long wash out period of 2 years required before conception and so is not recommended for men or women who are planning to have children.

1.6.4: Anti-TNF α agents (biologics)

It has been shown that Tumour Necrosis Factor alpha (TNF α) is a cytokine released in excessive amounts in RA and is a major contributor to the synovial inflammation and cartilage destruction. For this reason, agents that specifically target this inflammatory process have been developed and these so called Anti-TNF α agents have been demonstrated to be efficacious in the treatment of RA on clinical, radiological and lab measures, particularly when used in combination with Methotrexate (Chan et al., 2010). Despite the fact that 70-80% of patients will see a positive effect of biologic therapy, they are very expensive and therefore NICE (2010) recommends the use of Anti-TNF α agents only when patients have active disease (defined as a DAS28 score of greater than 5.1) on two occasions, one month apart and have previously failed to respond to two traditional DMARDs, one of which must be Methotrexate (unless contraindicated). Anti-TNF α therapy should be used in conjunction with Methotrexate, unless the use of MTX is contraindicated as clinical trials have suggested that this is the most efficacious administration (Soliman et al., 2011). However, some agents can be given as monotherapy. Due to the cost of administration, NICE (2009) recommend regular monitoring of disease activity as biologic therapy should only be continued if an adequate response has been identified within six months of initial administration and is maintained (an adequate response is defined as an improvement in DAS28 score of at least 1.2 points).

There are three commonly prescribed Anti-TNF α agents; 1) Adalimumab is administered subcutaneously fortnightly by the patient, 2) Etanercept is also administered subcutaneously by the patient once or twice per week and 3) Infliximab is administered intravenously in an outpatient setting every eight weeks. As these drugs block the inflammatory process, they also interfere with the body's normal process of fighting infection and so can have serious side effects such as increased risk of infection and a reaction at the administration site. Due to a lack of evidence, these agents are also not suitable for use during pregnancy. However, as well as reducing joint swelling and radiological erosions biologics have also been reported to greatly improve malaise and fatigue in RA patients (Maini, 2001).

1.7: Treatment phases of Rheumatoid Arthritis

There are detailed guidelines available for the treatment of rheumatoid arthritis (NICE, 2009; Luqmani et al., 2009; Combe et al., 2007; Smolen et al., 2010) and the treatment trajectory is well established. The main aim is to promote and maintain remission by reducing inflammation which in turn will preserve joint function. There is strong evidence by Tsakonas, Fitzgerald, Fitzcharles et al. (2000) and Fries, Williams, Morfeld, Singh & Sibley (1996) that people with RA who are treated early and continue therapy have better functional outcomes than those who are treated intermittently. For that reason, the treatment course of RA can be conceptualised in a way presented in Figure 1.2.

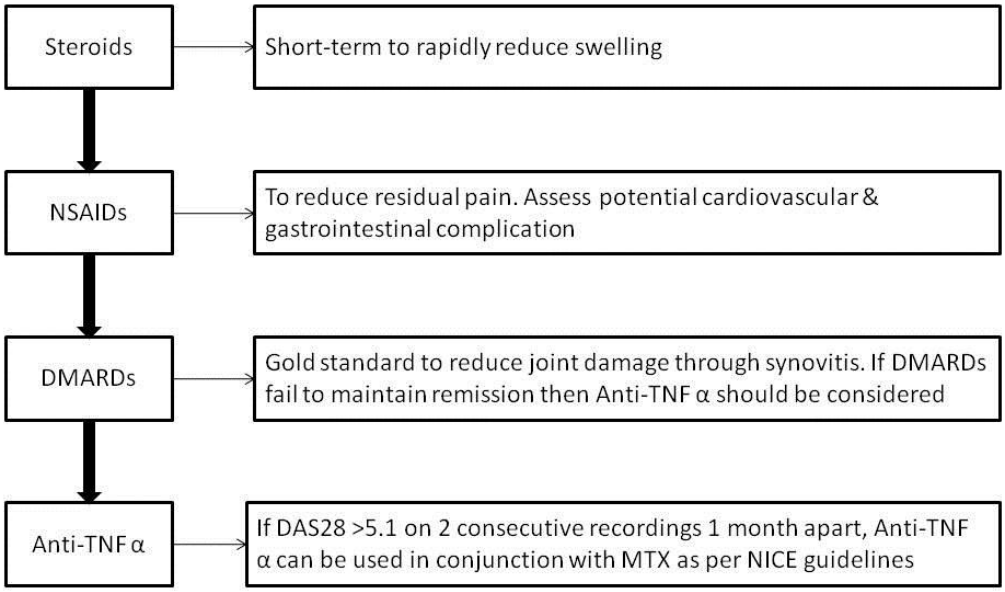


Figure 1.2: Typical treatment phases for rheumatoid arthritis

The treatment strategies described in Figure 1.2 demonstrate distinct phases of treatment for RA; 1) newly diagnosed when treatment is focussed on rapid reduction in inflammation and choosing an efficacious and well-tolerated DMARD for long term therapy; 2) established disease that can be controlled with DMARD therapy and 3) serious disease which requires Anti-TNF α therapy to maintain remission and functioning. Some patients may react well to traditional DMARDs and remain on this therapy for life. However, some patients may suffer serious, progressive disease which requires more aggressive treatment and result in more serious consequences.

1.8: Impact of Rheumatoid Arthritis

1.8.1: Impact on the patient

As the joints become damaged, more patients require help, aids and adaptations to the home for everyday functioning (Eberhardt & Fex, 1995; Young et al., 2000). Despite these adaptations the disease often leads to many patients being unable to work with some studies reporting up to 85% work disability for RA patients (Barrett, Scott, Wiles & Symmons, 2000; Wolfe & Hawley, 1998; Young et al., 2000) resulting in many RA patients having a reduced income (Albers et al., 1999). This will differ between patients as education and socioeconomic status is shown to be protective of work disability, most likely because of more flexible and less physical working conditions (Barrett et al., 2000; Wolfe, 1996). However, as being in employment has been shown to improve psychological wellbeing (Albers et al., 1999), this level of work disability can have a profound effect on RA patients.

The unpredictable and progressive nature of the disease can lead to a feeling of loss of control and helplessness by the patient which can have an impact on mental health. Depression and anxiety are more prevalent in people with RA (Brown, 1990; Pincus, Griffiths, Pearce & Isenberg, 1996) with estimates of between 6-42% of RA patients having a diagnosis of clinical depression (Fifield et al., 2001; Murphy, Dickens, Creed & Bernstein, 1999; Pincus et al., 1996; Walsh, Blanchard, Kremer & Blanchard, 1999) compared to around 5% for elderly people without RA (Beekman, Deeg, Geerlings, Schoevers & Smit, 2001). As well as the distressing and debilitating effects that negative mood has on the patient, there are also consequences for their family and society as outpatient visits and inpatient stays are disproportionately higher in depressed RA patients (Katz & Yelin, 1993).

As well as the joint damage characterised by rheumatoid arthritis, patients often also suffer from fatigue and general malaise (Belza, 1995; Huyser et al., 1998) which can have a negative impact both on physical and psychological wellbeing (Nikolaus, Bode, Taal & van de Laar, 2010; van Hoogmoed, Fransen, Bleijenberg & van Riel, 2010). Fatigue can also increase as the disease progresses (Belza,

Henke, Yelin, Epstein & Gillis, 1993) which, when coupled with joint erosion and functional impairments can leave patients highly disabled.

1.8.2: Impact on society

The greatest impact of rheumatoid arthritis on society is the economic burden through the direct cost of treating patients and the indirect cost of loss of productivity through disability and mortality. As previously mentioned, a large proportion of RA patients stop work prematurely, with approximately one third doing so within the first two years and more as disease duration increases (Young et al., 2002).

An inception cohort of early inflammatory polyarthritis in Norfolk, UK found that the mean cost for the first six months from symptom onset was approximately £2800 per person, of which 14% were due to costs of medication, hospitalisation and other costs of treatment (Cooper, Mugford, Symmons, Barrett & Scott, 2002). The costs of loss of earnings and productivity are often higher than treatment costs (Liang et al., 1984; Meenan, Yelin, Henke, Curtis & Epstein, 1978; Stone, 1984) although this can alter dramatically if a patient is experiencing a flare as inpatient hospital costs can be particularly high. As a general rule, medication, physician and inpatient care costs contribute the most to treatment costs for the National Health Service (NHS), although the National Audit Office (2009) have shown that by treating patients earlier and more aggressively, long term treatment costs can be reduced. The National Rheumatoid Arthritis Society (NRAS) calculated in 2010 that RA costs the UK economy an estimated £8bn per year which includes £700m of direct costs to the NHS (NRAS, 2010). Despite the lack of data and knowledge surrounding the true costs of rheumatoid arthritis, it is clear that as well as the direct cost on the NHS (in the UK), there are additional costs through lost productivity, increased disability and co-morbidity creating a significant burden on society. For a more comprehensive discussion of the economic costs of rheumatoid arthritis, see Chapter 10.

1.9: Self-management

It is clear from this chapter that a diagnosis of rheumatoid arthritis can be a major obstacle for many patients. Adequate adjustment to the requirements of a chronic illness is key to effective management and improved psychological wellbeing in patients (de Ridder, Geenan, Kuijer & van Middendorp, 2008). The pain, functional limitation and loss of identity by some patients can lead to serious problems in self managing their illness; however it is recommended that patients have an active and equal participatory role in treatment decisions to improve outcomes and adherence to recommendations (Stevenson, Cox, Britten & Dundar, 2004). As well as managing the initial

symptoms, RA patients are also required to take an active role in monitoring and managing many other complementary treatment requirements shown in Table 1.2.

Table 1.2: Typical self-management behaviours required by rheumatoid arthritis patients

Self-management behaviours
• Booking and attending outpatient appointments • Taking medication as prescribed including the correct timing, dosage, any special requirements (e.g. with food) as well as ordering and collecting repeat prescriptions • Having timely monitoring blood tests (usually every eight weeks) • Monitoring and reporting side effects, particularly potentially serious episodes such as contraction of viral infections (e.g. chicken pox) • Remembering to have recommended vaccinations (e.g. annual influenza) and not have prohibited vaccinations (e.g. Yellow Fever) • Modifications to diet and exercise, particularly for physiotherapy or occupational therapy

Given the demands that are made of patients, in addition to coping with a painful and disabling chronic illness, it is clear that some RA patients may struggle to effectively manage all areas of their treatment at all times. For this reason, issues surrounding self-management are being actively researched with an aim of improving the patient-provider relationship and providing patients with the tools that they need to successfully manage their disease.

1.10: Rheumatoid Arthritis in the context of this programme of research

The aim of this chapter was to give an overview of the burden that patients with rheumatoid arthritis face in order to successfully manage their disease, both physically and psychologically. After diagnosis, patients typically endure a changeable course of treatment until remission is promoted, however many will experience an unpredictable disease course which will last for the remainder of their life (Weinblatt & Maier, 1989; Young, 1992). This often leads to a heterogeous clinic population for clinicians and specialist nurses to manage as patients move through the stages of illness described in section 1.7, resulting in different needs and difficulties with self-management and adherence. Patients are also required to make substantial changes to their lifestyle as well as incorporate and manage a number of new health behaviours including attending outpatient appointments, taking medications and the associated monitoring tests that are necessary. As effective and continued therapy is paramount to maintaining function and quality of life for patients (Fries et al., 1996; Tsakonas et al., 2000), the correct management of medication is clearly an important part of managing and coping with RA. However, advertisement of serious side effects through pharmacy leaflets, contra-indications with alcohol intake and pregnancy and requirements for regular blood tests and vigilant side-effect monitoring have the potential to seriously

compromise DMARD adherence. For this reason, this programme of research will focus on adherence to medication required for the disease and the different ways in which patients at different stages in their disease progression cope with this demanding and sometimes unpleasant requirement to stay as healthy as possible.

Chapter 2

Literature review of using social cognition models to explain adherence to treatment regimens in chronic illness.

2.1: Introduction

There have been a number of excellent reviews published in recent years focussing on the issue of adherence to treatment regimens, particularly in chronic illnesses (DiMatteo, 1994, 2004; Elliott, 2008; Hill, 2005a, 2005b) including Cochrane reviews (Haynes, 2001; Kripalani, Yao & Haynes, 2007) and a World Health Organisation publication (WHO, 2003) as well as hundreds of studies investigating various issues of adherence in a number of chronic illnesses. For these reasons, a systematic review of all of the literature on medication adherence is inappropriate for this chapter. However, definitions of adherence, its importance and current issues surrounding adherence are introduced and discussed, as well as a narrative review of the literature that has measured or utilised the current social cognition models of health behaviour to explain adherence to treatment by rheumatoid arthritis patients. The aim of this chapter is to give a comprehensive overview of the literature surrounding treatment adherence and to guide the reader towards an understanding of how social cognition models, which concern beliefs individuals hold about health behaviours, have been used to explain adherence behaviour in rheumatoid arthritis.

2.2: Definitions of adherence

Adherence to medical regimens is an important part of treatment, particularly in a chronic illness such as rheumatoid arthritis. The terms “adherence” and “compliance” have been used interchangeably in the literature but adherence is defined by Treharne, Lyons, Hale, Douglas & Kitas (2006; pg 1) as “the extent to which patients take prescribed medication “as directed””. A variation of this definition has been used by many adherence researchers (e.g. Haynes et al., 1979; WHO, 2003). It is important to differentiate between adherence and compliance as adherence implies that people are free to choose to undertake the behaviour, whereas compliance implies obeying a prescription. There is a clear motivational difference between the two which is paramount as most of the models of health behaviour have a motivational aspect inherent within them (Brawley &

Culos-Reed, 2000), therefore the term "adherence" will be used throughout this programme of research.

Adherence to treatment has been a popular area for research over the past fifty years, however the evidence is still disparate as to which factors influence adherence to different regimens and therefore the best interventions to employ.

2.3: Different types of adherence; intentional and unintentional

Non-adherence is complex and multifaceted and can comprise of a deliberate decision not to take medications (which will hereafter be termed "*intentional* non-adherence"), or can simply be a result of forgetting to take all of the doses prescribed (which will be termed "*unintentional* non-adherence"). Unintentional non-adherence can be due to a number of reasons, and has been shown to increase as patients become older (Salzman, 1995), if they are out of their usual routine (for example on holiday; de Klerk, van der Heijde, van der Tempel & van der Linden, 1999) or if the regimen is complex (McDonald, Garg & Haynes, 2002).

Intentional non-adherence has been shown to be related to a number of factors surrounding experience of illness and treatment (Johnson, Williams & Marshall, 1999; Lumme-Sandt, Hervonen & Jylha, 2000; Svensson, Kjellgren, Ahlner & Saljo, 2000) and will be discussed in more detail below. Unintentional non-adherence has received less attention and there have been conflicting results for chronic illness, particularly among older people. Woods et al. (2008) found that deficits in prospective memory (i.e. "remembering to remember") was a strong predictor of medication non-adherence by HIV positive patients. However, Hertzog, Park, Morrell & Martin (2000) found that although prospective memory and cognitive ability decreased with age in RA patients, adherence increased. They speculate that this may be because older patients were compensating for memory loss with other cues, a view supported by Kippen, Fraser & Ellis (2005) who found that older people often link medication taking to other daily activities such as eating and Elliot, Ross-Degan, Adams et al. (2007) who found through interviewing older patients that levels of forgetting were very low because they used written aids or dose boxes as cues.

These types of non-adherence are not mutually exclusive but it is expected that they would have different underlying mechanisms; unfortunately, the *type* of non-adherence is often not reported in the literature. However, the importance of differentiating between intentional and unintentional non-adherence is starting to receive more attention with Johnson (2002) developing a model of adherence in elderly patients incorporating the different types. Lehane & McCarthy (2006) and

Lowry, Dudley, Oddone & Bosworth (2005) demonstrate how important this differentiation is as they reported much higher levels of unintentional non-adherence than intentional. However, few researchers have systematically measured and evaluated the two appropriately.

2.4: Rates of non-adherence

Typical rates of treatment non-adherence in chronic illnesses have been variable but relatively high at 30-50% (Barber, Parsons, Clifford, Darracott & Horne, 2004; DiMatteo, 1994; Dunbar-Jacob & Schlenk, 2001; Haynes, 2001), although a meta-analysis by DiMatteo (2004) reported average non-adherence of 24.8%. However, non-adherence rates for DMARDs in RA are often higher with Viller et al. (1999) reporting 41% and Grijalva et al. (2007) finding 54% of patients stopped their DMARD for more than 90 days. When a more stringent measure of adherence is used including correct dosing and/or timing, non-adherence rises with Park et al. (1999) claiming 62% and de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden (2003) showing 75% for Sulfasalazine. During the literature search three systematic reviews and meta-analyses were found that attempt to quantify non-adherence (DiMatteo, 2004; Haynes et al., 2001; Kripalani et al., 2007). Although reported adherence rates differ depending on the method of measurement and type of treatment, there is a consistently held opinion in the literature that non-adherence is a major factor contributing to poor outcomes that will only worsen as populations increase and morbidity rates worsen.

2.5: Importance of adherence to treatment regimens

Non-adherence to treatment in chronic illness leads to poor prognosis for patients (Irvine et al., 1999) and has been shown to be the primary cause of unsatisfactory blood pressure control in hypertensive patients (Waeber, Burnier & Brunner, 2000) whereas good adherence leads to reduced complications (Rogers & Bullman, 1995). Non-adherence in RA has the potential to increase illness progression as DMARDs are most effective when taken as prescribed by the specialist doctor. A patient who regularly misses or changes doses of prescribed medication may experience personal effects such as delayed recovery (Grijalva et al., 2007), increased morbidity and mortality (DiMatteo, 1994) and increased treatment complications (Hughes, Bagust, Haycox & Walley, 2001; ten Wolde et al., 1996). This will also have a societal effect as patients with increased disease activity are more likely to require frequent hospital and GP visits (DiMatteo, 1994; Steiner & Prochazka, 1997) and the apparent treatment “failure” can then lead to unnecessary escalation of treatment. Ausburn (1981) reviewed admittance details for 205 patients in hospital medical wards and found that 20% had probably been admitted due to non-adherence to prescribed medication. This subsequently results

in higher health service costs (DiMatteo, 1994; Grijalva et al., 2007; Hughes et al., 2001; Urquhart, 1999). As adherence is a primary determinant of the effectiveness of treatment (Cramer, 1998), poor adherence attenuates optimum clinical benefit (Dunbar-Jacob & Schlenk, 2001; Sarquis et al., 1998). For this reason, Haynes (2001) concludes that increasing the effectiveness of adherence interventions may have a greater impact on public health than improved medical treatments.

2.6: How has adherence been measured?

Non-adherence has been measured in a number of ways with various degrees of success and accuracy. The World Health Organisation (2003) publication on adherence highlights these problems as both healthcare providers (Norell, 1981) and patient self-report generally overestimate adherence which could be due to inaccurate memory or socially desirable reporting of behaviour. The gold standard for assessing medication adherence in patient groups is to test biological markers of the drugs in the blood, however this is very expensive and can be subject to contaminated results through variable levels of absorption, excretion and pharmacokinetics of the drug in individuals (Vitolins, Rand, Rapp, Ribisl & Sevick, 2000). Pill counts have also been used whereby the number of pills left over after a given period of time (e.g. one month) are counted and compared to the number of pills that should have been taken in that period as per the prescription. This method has been used in a number of studies, however there is no guarantee that the pill has actually been taken and information regarding correct dosing or timing is not available (Matsui et al., 1994). These limitations have been improved upon to some extent by using electronic medication event monitoring (eMEMs) to record the time and date of pill bottle opening to infer adherence. However, both of these measures are costly and time consuming and can be subjected to “white coat compliance” where patients are deliberately more adherent in the run up to a clinic appointment (de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden, 2003) because they are aware that their adherence is being measured.

The more objective measures mentioned above are not compatible with long term adherence monitoring, particularly in the case of polypharmacy which is common among chronic illness and the elderly. To increase the utility in large scale clinical studies, the most common methods of assessing medication adherence are self-report questionnaires. Questionnaires can measure attitudes, intentions and behaviours and although they are prone to biased results from socially desirable answering, if item construction and validation is carried out correctly, these problems can be overcome. An additional advantage of questionnaires is that they can help to establish *how* and *why* a patient is non-adherent which can then be addressed, whereas eMEMs and biological monitoring

give very basic information which cannot help to inform interventions. The descriptive data given by the questionnaires therefore increases the predictive validity of identifying the different *types* of non-adherence. Garber, Nau, Erickson, Aikens & Lawrence (2004) reviewed concordance between self-reported adherence and more objective measures such as pill counts or eMEMs. Of 86 pairs of self-report and objective measures, 43% were highly concordant. Questionnaires were the best self-report measure (compared to diaries or interviews) with 55% being highly concordant with the objective measure. Of those pairs that were not highly concordant, the self-report measure over-estimated adherence. However, there was no indication of how accurate the objective measure was at actually measuring adherence. For this reason, it is advisable to use a multi-method approach which combines self-report and an objective measure (WHO, 2003). However as this is often not feasible, self-report questionnaires seem to have the most clinical utility to not only identify people with low adherence, but to establish the reasons behind it which can then be addressed in the clinical setting.

Although there are a number of ways to measure adherence, it is worth considering the purpose of measurement and its clinical utility. Most often, "percentage of adherence" is reported but it is important to consider what this means. For example, as Pullar (1991) rightly acknowledges, an "adherence rate of 60%" does not convey whether each patient took 60% of their doses or whether 60% took all of their doses. He suggests that the most appropriate method of reporting would be the number of patients falling into adherence bands (e.g. good, bad). However, this banding in itself has some inherent problems as thresholds defining "good" and "bad" adherence are generally arbitrary based on clinical expertise rather than any empirical evidence base (WHO, 2003). It would be incredibly difficult to definitively define a universal level of "good" adherence for a number of reasons. Firstly, the response to treatment for chronic progressive illnesses like RA is generally a continuum over a long period of time. Secondly, the efficacy of a drug is based upon its performance during clinical trials in which adherence rates are particularly high and thirdly, periodic or low levels of non-adherence (for example taking a break to reduce side effects or forgetting the third of a thrice daily dose) may not be clinically important. The acceptable threshold for non-adherence would also depend heavily on the type of illness and treatment as not taking insulin for a few days could prove fatal to someone with Type I diabetes, whereas missing the same number of DMARD doses would not have as large an effect for RA patients. It is therefore important to consider for each patient group what the effect of non-adherence would be over the short and long term and what the optimum adherence rate might be (Elliott, 2008).

Although there are weaknesses inherent in measuring adherence, with estimated non adherence rates being as high as 60%, it is important to establish adherence patterns, causes (intentional or unintentional) and psychosocial determinants in order to improve self-management among patients, particularly those with a chronic illness. Based on the evidence presented above, self-report questionnaires appear to offer a reasonably reliable and cheap method of measuring adherence and also have the advantage of providing additional explanatory information. For this reason, a self report questionnaire has been chosen to measure adherence in this programme of research.

2.7: Measuring adherence in this programme of research

The Compliance Questionnaire for Rheumatology (CQR19; de Klerk et al., 1999) is a nineteen item scale that measures behaviours and attitudes concerning medication taking which is measured on a 4 point Likert scale ranging from *"Don't agree at all"* to *"Agree very much"*. The authors have reported excellent sensitivity at detecting low adherers at 98% with a kappa of 0.78. This was established by validating the scale against eMEMs and suggests that it is a good questionnaire for establishing medication adherence to DMARDs. Other researchers have also successfully used this scale as a measure of adherence (de Thurah, Norgaard, Harder & Stengaard-Pedesen, 2010; Garcia-Gonzalez et al., 2008; Treharne, Lyons & Kitas, 2004). However, de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden (2003) report a moderate level of internal consistency. As the only adherence questionnaire specifically designed for use by rheumatoid arthritis patients, the CQR will be used in this programme of research to measure intentional non-adherence. The structure, reliability and validity of the CQR are discussed further in Chapter 6. However, a limitation of the CQR is that it does not measure unintentional non-adherence and therefore one statement from the Reported Adherence to Medication scale (RAM; Horne, Weinman & Hankins, 1999); *"I sometimes forget to take my medication"* will also be used. Patients are asked to indicate the level to which they agree from *"definitely do not agree"* to *"definitely agree"*.

2.8: Introducing the social cognition models of illness

Based on the evidence established over the past five decades, it is clear that there is a triad of factors that influence self-management and adherence to treatment regimens. These include; 1) the patient-provider relationship which refers to the level of satisfaction with communication between the doctor and patient and concordance, 2) organisational factors including the structure of collecting prescriptions and different economic models (e.g. the UK's National Health Service or an insurance scheme) and 3) patient factors which include demographics, attitudes and behaviour of

the patient. Although the patient-provider relationship (Viller et al., 1999) and factors relating to the healthcare organisation (for example the logistics of seeing a doctor or collecting a prescription) are associated with adherence (WHO, 2003), this programme of research will concentrate on patient factors as these are some of the least well known and researched areas that can and need to be addressed in rheumatoid arthritis.

An obvious dimension of patient related factors are demographics such as age, gender, education and socioeconomic status. Although these have been researched, there has been little evidence to suggest that they reliably and actively impact on adherence to medications. For example, there appears to be no consistent association between gender and adherence in RA (Brus, van de Laar, Taal, Rasker & Weigman, 1999; Treharne et al., 2004; Viller et al., 1999). There is conflicting evidence surrounding age with the assumption that non-adherence will increase as cognitive ability decreases, however Treharne et al. (2004) and Park et al. (1999) both found that adherence to DMARDs *improved* with age. Issues surrounding ethnicity, education and socio-economic status have also been variable, which is partly due to different healthcare systems around the world. For example, African-American and Hispanic patients in the US tend to have worse adherence than white Americans (Garcia-Gonzalez et al., 2008; Garcia Popa-Lisseanu et al., 2005) although this is likely to be confounded by reduced levels of education and employment resulting in worse levels of health insurance. Although adherence may mediate the effect of demographics on disease status, there is not enough evidence thus far to determine whether demographics can reliably predict adherence (Elliott, 2008).

Self-efficacy, motivation and intentions to perform a health behaviour are related to adherence (Armitage & Conner, 2001) and are best conceptualised within the social cognition models of illness that have been extensively researched since the 1960s. The three most useful models are the Theory of Planned Behaviour (TPB), Health Belief Model (HBM) and the Self Regulatory Model (SRM) which are described in more detail below. These are all social cognition models of illness that are based on the concept of expected utility (Edwards, 1954) which assumes that people make a rational decision of behaviour based on the expected costs and benefits of performing the behaviour.

2.8.1: The Theory of Planned Behaviour

The Theory of Planned Behaviour (Ajzen, 1988; Figure 2.1) is an extension of the Theory of Reasoned Action necessitated by the assumption by Ajzen (1988) that the performance of any behaviour is dependent on the amount of volitional control an individual has over the behaviour. This builds on

Bandura's (1977) work on self-efficacy and control. Intention to perform the behaviour is central to the theory and is assumed to capture the motivational aspect of behaviour (Ajzen, 1991). Intention to perform the behaviour is the single most predictive factor of behaviour (Ajzen, 1991) and in general, the stronger the intention, the more likely the behaviour will be performed. Attitudes and Subjective Norm are taken from the Theory of Reasoned Action and Perceived Behavioural Control is added, which all explain behavioural intention. Perceived Behavioural Control is also a direct predictor of behaviour as even if intention is high, if the person feels that they are not capable of carrying out the behaviour, the likelihood of success is low.

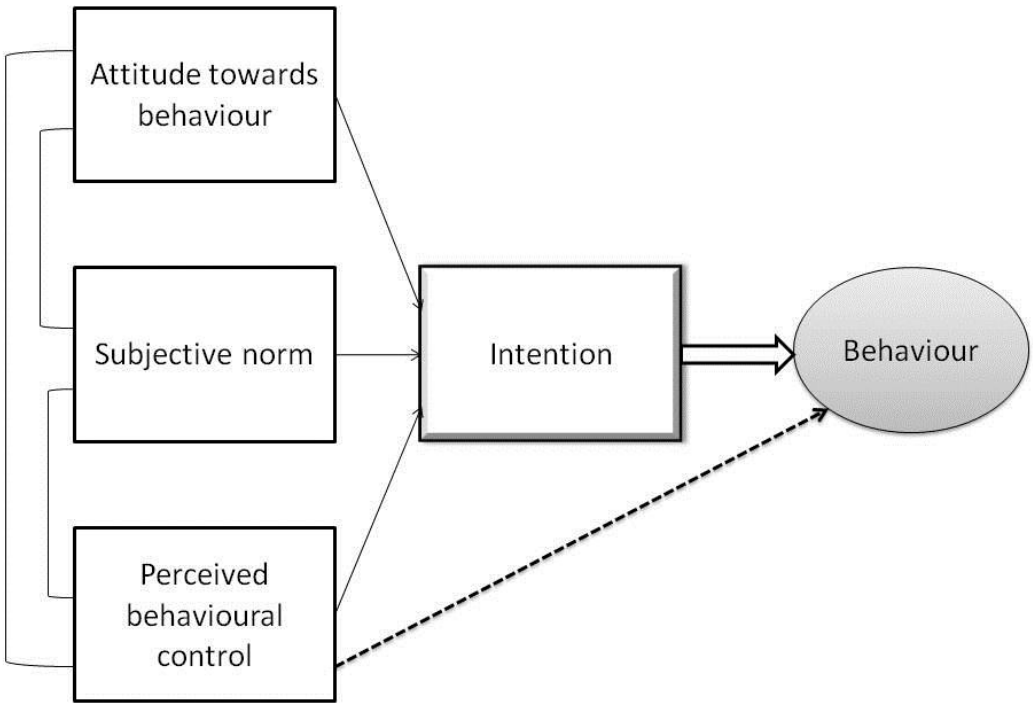


Figure 2.1: The Theory of Planned Behaviour from Ajzen I. (1991) The Theory of Planned Behaviour. Organizational Behavior and Human Decision Processes 50; 179-211 (pg 182)

Ajzen (2007) proposes that behaviour can usually be predicted with considerable accuracy from intention and control. There are three factors that are seen to influence intention in the TPB; Attitudes, subjective norms and perceived control. *Attitudes* refer to the accessible beliefs about the behaviour and the perceived consequences. This follows an expectancy-value model of the perceived likelihood that the behaviour will lead to a particular outcome and the evaluation of that outcome.

Armitage & Conner (2001) performed a meta-analysis across different behaviours and found a correlation of 0.5 between Attitudes and actual behaviour. Similarly, Albarracin, Johnson, Fishbein & Muellerleile (2001) found a correlation of 0.56 in a meta-analysis between Attitudes and condom use. *Subjective norm* refers to the subjective assessment by the individual that "important others" think that they should (or shouldn't) perform the behaviour. Subjective Norm must be evaluated with respect to the motivation the individual has to comply with the wishes of the reference group (which can include friends, family and health professionals). Armitage & Conner (2001) found similar correlations of 0.5 between Subjective Norm and behaviour. *Perceived Behavioural Control* is influenced by the individual's belief that they have access to the necessary resources and skills to perform the behaviour successfully. This may be based in part on past experience but can also be influenced by information from others and the media.

Although the evidence suggests that the TPB is good at predicting behaviours under volitional control (Alberaccin et al., 2001; Armitage & Conner, 2001; Azjen, 2007), behaviours which require particular skills, knowledge or resources that the individual does not possess will not be well predicted by the TPB (Fishbein, 1993). This may prove challenging with respect to medication taking if there are cognitive, financial or logistic barriers to the behaviour such as an inability to pay for the medication or a lack of transport to collect the prescription.

Although there have been a number of studies investigating the utility of the Theory of Planned Behaviour to explain preventive health behaviours such as condom use, exercise and smoking cessation which have prompted a number of reviews (e.g. Abraham, Sheeran & Johnston 1998; Armitage & Conner, 2001), few have used it to explain adherence to medications. Some studies have implicitly measured Perceived Behavioural Control and social norms but have not truly used them to determine adherence. For example, DiMatteo (2004) performed a meta-analysis of the effect of social support on adherence and found that adherence is likely to mediate the effect of social support on adjustment to chronic illness but that the *quality* of the relationship has a stronger effect than the *number* of relationships.

2.8.1.1: Empirical findings of the Theory of Planned Behaviour and medication adherence in rheumatoid arthritis

There have been no studies that explicitly evaluated the Theory of Planned Behaviour in relation to medication taking in rheumatoid arthritis. There has been a little research that has focussed on social support and Owen, Friesen, Roberts & Flux (1985) found that a strong motivation for adhering to

medications for rheumatoid arthritis patients was pressure from their spouse and the doctor. Although it is safe to assume that a patient's family and doctor will encourage them to take their prescribed medication, the level of motivation that the patient has to comply with this encouragement will affect the influence that they have.

2.8.2: The Health Belief Model

In response to public health failures in the US in the 1950s, the Health Belief Model was designed by Rosenstock (1966) and further refined by Becker and colleagues during the 1970s and 1980s and therefore is one of the earliest and most cited models to attempt to explain health behaviour (Harrison, Mullen & Green, 1992). Initially, the model relied on the expectancy value model and stated that the perceived cost of carrying out a health behaviour would be weighed against the perceived benefit. The model was originally applied to preventive health behaviours but has been amended and applied to other health behaviours more recently.

The HBM focuses on two aspects of health and health behaviours; threat perception and behavioural evaluation. Each of these components can each be further broken down (Figure 2.2). Firstly, threat perception can be broken down into perceived *susceptibility* and perceived *severity*. Susceptibility is related to the possibility or probability of becoming ill with a new or recurrent illness compared to a reference group of either other people of the same age or a patient's personal health related history. The severity refers to the perceived consequences of suffering from the illness (Rosenstock, 1966). Although traditionally, the threat perception constructs of the HBM have referred to contracting an illness, they can also be applied to medication taking with the patient's perceived susceptibility of experiencing side effects and the perceived severity of those side effects. The second part of the model refers to behavioural evaluation and includes the perceived benefits of undertaking a behaviour which is weighed against the perceived costs. Later versions of the model added a health motivation component (Becker, Haefner & Maiman, 1977b) and cues to action (Mattson, 1999) which include internal (symptoms) or external (health leaflet) cues. Harrison et al. (1992) carried out a meta-analysis of studies that included all four of the major constructs (susceptibility, severity, benefit, barriers) and found that they all had significant correlations ($r \geq 0.3$) to health behaviours, although the effect sizes were largest for the benefits and barriers constructs. The four constructs together generally explained about 10% of the variance in behaviour, although this could potentially decrease further had the constructs been allowed to correlate, allowing for covariance in the model. Perceived severity has been shown to be a weak correlate of health behaviour (Janz & Becker, 1984; Schwarzer & Fuchs, 1996). It may be that severity needs to exceed a threshold before it has an

effect. Once the threshold has been met, susceptibility may then have more of an effect on motivation (Schwarzer, 1998; Sheeran & Abraham, 1996).

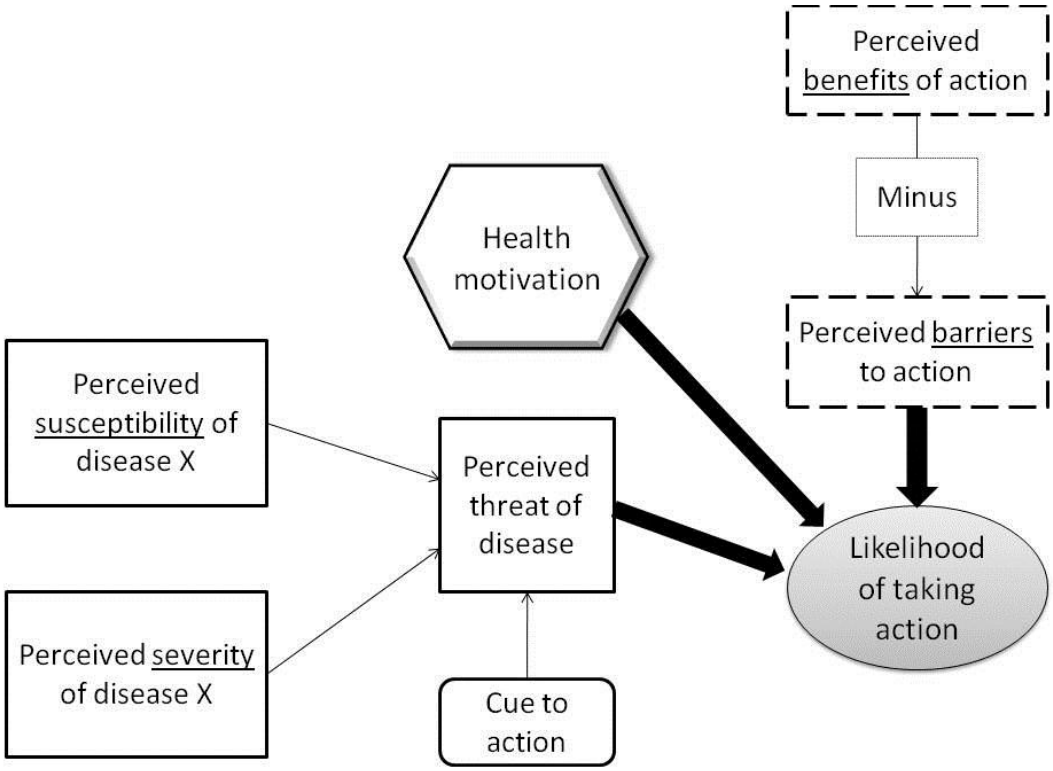


Figure 2.2: The Health Belief Model

The Health Belief Model has been used for a variety of health behaviours including preventive, adherence behaviours and clinical use, and therefore there is no standard questionnaire that can be used (Abraham & Sheeran, 2005). However, health beliefs have been elicited from physiological measures (Brady et al., 1987), behavioural observations (Hay et al., 2003), interviews (Grady, Kegeles, Lund, Wolk & Farber, 1983; Volk & Koopman, 2001) and self-report questionnaires (Champion, 1984; Nexoe, Kragstrup & Sogaard, 1999).

2.8.2.1: Empirical findings of the Health Belief Model and medication adherence in rheumatoid arthritis

A number of studies have implicitly or explicitly measured components of the Health Belief Model with respect to adherence, although there have been few specifically looking at adherence to medication in rheumatoid arthritis. Perceived efficacy of medication and a fear of side effects are often associated with adherence (Johnson et al., 1999; Kane, 2006; Lumme-Sandt et al., 2000;

Svensson et al., 2000) which clearly demonstrates aspects of the benefit and cost constructs of the model. Berry, Bradlow & Bersellini (2004) found that the main benefits of medication given by rheumatoid arthritis patients were reduction of pain (71%), easing joint stiffness (73%) and reduced joint swelling (52%) but that side effects were perceived to be the biggest costs. Existing patients perceived the costs to be significantly higher than new patients, although they did not report more side effects. However, although they perceived the costs to be greater, the existing group had better adherence than the new group suggesting that they still perceived the benefits to be greater. Similarly, Owen et al. (1985) interviewed 178 RA patients and found that the biggest motivations were the benefits of pain relief and treating the arthritis.

Goodacre & Goodacre (2004) sought to add to the social cognition models by interviewing 16 established and 13 newly diagnosed RA patients over a nine month period. Patients believed that they had "no choice" about taking DMARDs because they were necessary to preserve joint function and quality of life. However, they expressed concern about becoming reliant on the "powerful" and "toxic" medication and compensated for their perceived "dependence" on drugs by minimising their intake of other medication such as analgesia. When the RA medication was not perceived to be beneficial, patients reported more side effects and the rationale for the medication was questioned. This clearly demonstrates the cost-benefit decision being made about DMARDs as although these patients perceive there to be high costs to taking DMARDs, they still persevere in order to gain the benefit of reduced stiffness and increased quality of life. These patients go even further by limiting their intake of other drugs in order to keep the cost-benefit balance for DMARDs. This also seemed to be a dynamic process as newly diagnosed patients were more confident that the DMARDs would be beneficial than the established patients who had more experience on which to base their cost-benefit decision.

Although there have been a few studies testing the Health Belief Model in relation to adherence to DMARD medication in rheumatoid arthritis, they have mostly been cross sectional and looking at purely bivariate associations between the components and self-reported adherence. Also, many studies have not specifically measured the subdivisions of the illness threat, i.e. susceptibility or severity of either RA itself or the practice of taking the DMARD medication. Most studies specifically in rheumatoid arthritis have been mainly qualitative with very small samples and a lack of a valid measurement of adherence. Although reviews of other health behaviours have demonstrated some promising results for the Health Belief Model (e.g. Harrison et al., 1992), there is clearly a lack of

evidence regarding the predictive value of the full HBM to explain medication adherence in rheumatoid arthritis.

2.8.2.2: Beliefs about Medications

An extension to the Health Belief Model which directly addresses the perceived benefits and barriers of taking medication was developed by Horne, Weinman & Hankins (1999). The Beliefs about Medications Questionnaire (BMQ; Horne et al., 1999) was developed with the aim of determining whether there are ranges of specific and general beliefs about medications which can be summarized into common themes and how these may relate to each other and to adherence behaviours. Scales were derived from items identified in the literature and in interviews about medication beliefs. The factor structure revealed two main factors (specific and general), each with a further two factors (*"specific-necessity"* and *"specific-concern"*, *"general-overuse"* and *"general-harm"*). The specific scale represents the two sides of the cost-benefit analysis of the cognitive models; the necessity of the drugs and the undesirable affects that they can have. These were tested in a chronic illness sample of 524 patients which reflected a variety of illnesses and treatment characteristics. This was to ensure that items both represented the attitudes of different patient groups and that they could be used to discriminate between them.

2.8.2.2.1: Empirical findings of Beliefs about Medications and medication adherence in rheumatoid arthritis

Few researchers have investigated the effects of "general" medication beliefs on adherence in chronic illness, possibly because they are perceived both by researchers and patients as less important once a chronic illness has been diagnosed. The internal reliability of this scale was also not as good in the original construction (Horne et al., 1999). Owen et al. (1985) investigated general medication beliefs in RA patients through interview and found that those that had no objection to taking medications in general were more adherent to their NSAID medication.

More commonly, the "specific" factor of the BMQ has been evaluated with regards to medication adherence. Treharne et al. (2004) measured necessity and concerns about DMARD medication in 85 RA patients aged between 29 and 86 years. They found that necessity was highly correlated with adherence (r=0.69) but that concerns was not. After controlling for the number of medications and demographic variables, they found that the explained variance in adherence was increased by 43% with the addition of psychosocial variables including the BMQ subscales. However, only the necessity and overuse variables were significant showing that higher perceptions of the necessity of DMARDs

to treat RA and lower perceptions that medications in general are overused by doctors lead to better adherence. More recently de Thurah et al. (2010) measured adherence to Methotrexate by 85 RA patients using the CQR19 over nine months and termed non-adherence as having a CQR19 score in the bottom quartile. Twenty-three percent of patients were identified as non-adherent, which did not change over the nine month follow-up. For the non-adherers, 37% had low perceptions of necessity whereas only 14% had high perceptions of necessity. This did not differ between baseline and follow-up. At baseline, there was no variation in levels of concern, but at follow up, only 18.9% had low concerns whereas 37.7% had high concerns. This indicates that people who do not adhere to their Methotrexate generally have lower perceptions of its necessity but concerns differ over time and increase as patients have more experience. However, the authors found that only necessity was related to adherence, which supports the findings of Treharne et al. (2004).

A number of studies have utilised the BMQ to investigate medication adherence in other chronic illnesses and Horne (1999) found that specific medication beliefs have explained 15-20% of the variance in adherence across different illness groups. Across a number of different studies it would appear that specific beliefs do go some way to explain adherence to medications but that patients' perceptions of the necessity of their medication is most important. This appears to be a useful addition to the Health Belief Model and many researchers have used it to extend both this model and the Self Regulation Model to improve knowledge about medication adherence and to design interventions.

2.8.3: The Self Regulation Model (and Illness Perceptions)

Leventhal and colleagues (Leventhal, 1980, 1984) developed a model of health behaviour based on problem solving models with an emphasis on the cognitive and emotional processes that are elicited from an illness threat. Traditional problem solving models involve three stages; 1) interpretation of the problem, 2) coping with the problem and 3) appraisal (assessment) of the coping strategy. Leventhal aimed to model patients' representation of a health threat (presentation of an illness), the procedures used to cope with the threat and the evaluation of the coping mechanism (Leventhal, Diefenbach & Leventhal, 1992). The model has two largely independent processing systems, the first being the objective psychological representation of the health threat and the second being an emotional processing system that runs in parallel to the representational arm (Figure 2.3). Leventhal proposed the need to describe how emotional processes interact with the psychological illness representation and the appraisal of the interaction. The model posits that it is not possible to evaluate an illness solely objectively without an emotional response to the threat.

The Self Regulation Model retained the three processing stages of traditional problem solving models. The first of these is interpretation of the illness threat. This involves accessing illness cognitions that a patient has based on the information they already have and their experience of the symptoms. Five dimensions of illness cognitions were elicited through multidimensional scaling and interviews (Bishop, 1987; Linz et al., 1982) which were termed *illness perceptions* (Table 2.1). These dimensions are interrelated (Petrie, Jago & Devcich, 2007; Petrie & Weinman, 2006; Weinman et al., 1996) and have good discriminant validity as different types of illness showed different patterns of illness perceptions. For example, life threatening diseases are often perceived to be chronic, caused by internal factors with severe consequences whereas infectious diseases are the opposite.

Table 2.1: the Illness Perceptions of the Self Regulatory Model

Perception	Definition
Identity	The illness label or diagnosis and the associated symptoms
Consequences	The expected effects of having an illness on the patient's life
Timeline	Perceptions of the expected duration of the illness. Typically acute, cyclical or chronic
Control/cure	Perceptions of the extent to which the illness can be controlled or cured through treatment or behaviour
Cause	The factors that the patient believed caused the illness. Generally subdivided into internal (e.g. genetic) and external (e.g. environment) factors

The underlying processes of each of the stages rely on integration of current information using two types of memory structure. Schematic memory refers to memory *of* prior illness episodes. This is important for the automatic elicitation of emotional reactions to an illness. Conceptual memory refers to memory *about* illness with causal and outcome expectations based on judgements about illness. This is important for labelling and reasoning about the illness state and the emotional reaction (Leventhal, 1980, 1984). Symptoms form an important part of the Self Regulation Model as it is attention to the stimuli that guide behaviour (Cioffi, 1999; Lazarus, 1966; Leventhal, 1970; Leventhal, Brown, Schacham & Engquist, 1979). This is where memory *about* an illness may be combined with memory *of* an illness to create an erroneous representation which leads to non-adherence. This has been demonstrated with asymptomatic illnesses such as hypertension where patients attribute headaches as a symptom of high blood pressure and therefore take their hypertension medication only when they have a headache.

> "I know I can tell when my blood pressure is up, like if I have a headache... I take it, I have a [blood pressure] cuff and it's high! And I take my medications, whenever I have a headache or if my face feels warm. So, I know I can tell and I don't need meds all the time" [a nurse describing her self-care routine: She only takes her blood pressure when she experiences symptoms] (Leventhal, Diefenbach & Leventhal, 1992 pg 144)

Here, the information *about* illness (that an illness must have symptoms) is combined with the memory *of* illness (the patient has high blood pressure when she has a headache) to create a representation which leads to non-adherence as she does not take her blood pressure reading when she does not have a headache. This can also cause conflict within rheumatoid arthritis as the patient may believe that having RA must mean that they should experience symptoms. Therefore, if a patient is in remission without symptoms, the illness must have gone away, leading to non-adherence to medication.

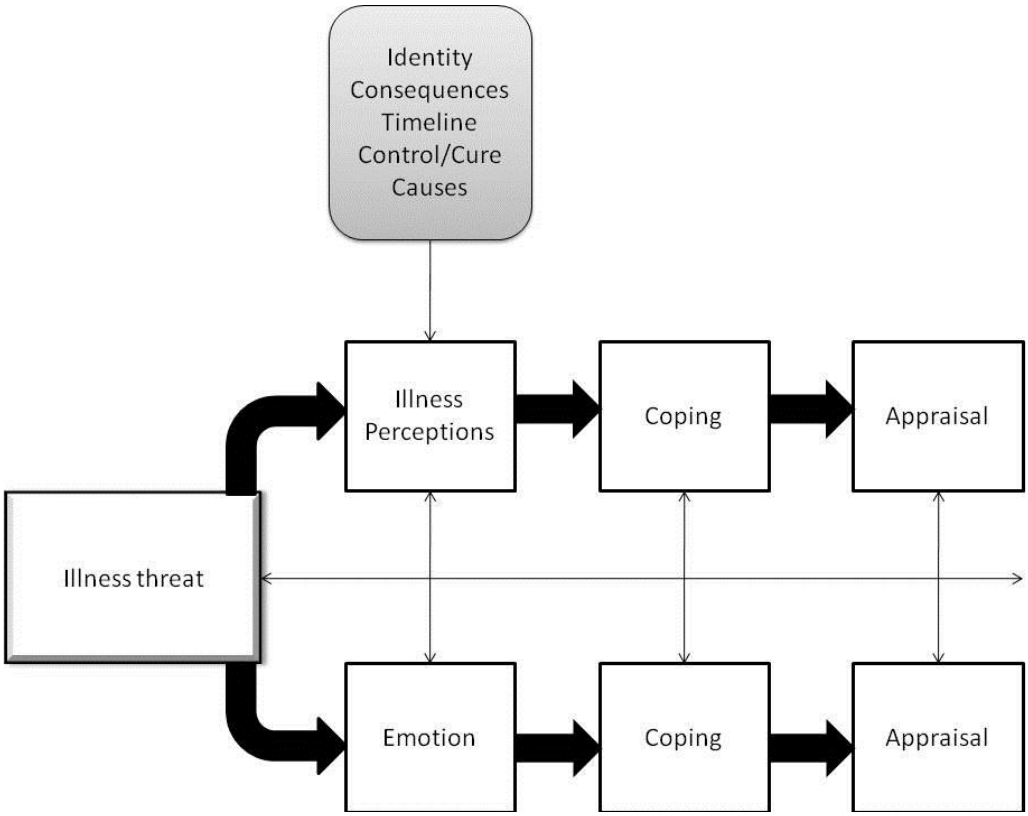


Figure 2.3: The Self Regulatory Model

The SRM is self regulatory because the model of illness and behavioural response to the threat is continually updated by the information and experience the patient acquires through the appraisal of the coping strategy. The aim for the patient is to maintain the status quo; therefore as more symptoms develop or more information is gathered which is at odds with the current representation, the patient must employ different coping strategies in order to return to "normality". For example if a patient becomes more disabled because of the increased joint damage caused by rheumatoid arthritis, they may decide to use a walking stick to help them move around. If this helps them to walk more easily, they would appraise this coping system favourably. In this circumstance, the patient may now perceive their RA to have higher consequences, more symptoms and less controllability than previously. As this model is regulatory, it would be expected that the illness perceptions also change as circumstances change. It is assumed that this regulation is based on common sense (indeed the model is sometimes referred to as the common sense model of illness; Leventhal, Meyer & Nerenz, 1980).

Ongoing research has shown that patient behaviour is influenced by illness representations, for example patients who feel they have a high level of control or low levels of identity features generally have a better prognosis than those that do not. Changing these perceptions has been shown to improve recovery through self regulatory interventions in acute and chronic illnesses (Petrie, Cameron, Ellis, Buick & Weinman, 2002; Petrie et al., 2003).

The Illness Perception Questionnaire (IPQ) developed by Weinman, Petrie, Moss-Morris & Horne (1996) is based on the five cognitive constructs of the Self Regulatory Model and has a total of 80 items. Scharloo et al. (1998) used the 80 item IPQ to test for coping and functioning in patients with chronic illnesses including RA. They found good internal consistency for most of the factors although the Cronbach's alpha coefficients were lower in the RA group with the timeline, consequences and control being 0.53, <0.5 and 0.55 respectively. For this reason, the authors did not use the consequences and control items in the subsequent multiple regression analysis. The IPQ items and answers to a coping scale were entered into a multiple regression analysis to predict functioning in each of the illness groups. After controlling for disease duration and severity, the "identity" and "control" factors explained the most amount of variance in functioning in RA patients at approximately 20% each.

Moss-Morris et al. (2002) developed the Revised Illness Perception Questionnaire (IPQ-R) which consists of eight factors measuring Leventhal's five constructs (with control being split into "personal control" and "treatment control") as well as an emotional representation and comprehensibility of

the disease. Broadbent, Petrie, Main & Weinman (2006) proceeded to test the validity and reliability of the IPQ-R in six chronic illness groups, most of which had more than one hundred participants. Test-retest was used in the renal group to test the reliability. Pearson's r correlations of between 0.42 and 0.75, (all significant to $p<0.001$) were found for all questions three and six weeks after initial presentation.

2.8.3.1: Empirical findings of the Self Regulatory Model and adherence in chronic illness

As emotional response is an important component of the SRM that is not included in the other social cognition theories, there has been a tendency in the literature to use illness perceptions to investigate psychological wellbeing and adjustment to chronic illness rather than health behaviours such as medication adherence. However, there have been some studies that have looked at various adherence behaviours. Cooper, Lloyd, Weinman & Jackson (1999) measured illness perceptions of 152 patients that had suffered myocardial infarction and measured their adherence to clinic appointments up to six month later. Those that displayed lower perceptions of controllability and didn't consider their lifestyle to be a causal factor were less likely to attend follow-up clinic appointments. As 60% of patients did not attend these appointments, these perceptions are potentially playing an important role in the way these patients react to their situation.

Although illness perceptions in respect of DMARD taking have not been investigated in RA, there have been a number of studies that have looked at adherence to treatment in long term illness, although they have demonstrated variable results. In univariate analysis, Chilcot, Wellsted & Farrington (2010) found that patients with end-stage renal disease that did not adhere to fluid restrictions had significantly lower perceptions of the chronicity and consequences of the illness than adherent patients. However, in regression analysis, only lower perception of consequences was a significant predictor of non-adherence. In contrast, Ross, Walker & MacCleod (2004) and Patel & Taylor (2002) found that lower emotional reaction, and less personal control significantly predicted non-adherence to hypertension medication.

In other studies, illness identity, which is based upon symptoms, has been shown to be important in the regulation of the response to illness. Llewellyn, Miners, Lee, Harrington & Weinman (2003) measured adherence to prophylaxis medication by haemophilia patients and found in regression analyses that only illness identity and necessity of medications (measured by the BMQ) significantly predicted non-adherence. Similarly, Horne & Weinman (2002) found that if asthma patients modeled their illness on their symptoms and therefore considered themselves to be well when they were

symptom free differed in their illness perceptions and did not adhere to preventer medication. Those who perceived their illness as chronic with potentially serious consequences were more adherent to corticosteroids.

Although the studies reviewed above have shown variable results with regards to medication adherence, this may partly be due to the fact that the aetiology and treatment of these illnesses is quite disparate which could lead to the development of different illness perceptions. For example, haemophilia patients would be aware of their illness from birth and self-managing regular treatment from a young age, whereas end-stage renal disease patients will generally be older at onset and less aware of how to manage treatment until they develop some experience. Generally, perceptions of consequences and controllability show univariate and bivariate differences although do not necessarily predict adherence in multivariate analysis. The model as a whole has been shown to explain around 20% of the variance in adherence. However, the studies that have been carried out to date are mostly cross sectional and have not taken into account the self regulatory process of adjustment to illness and how this would affect health behaviours. Reviewing studies that have used the SRM to explain adherence shows clearly that this model needs to be explored more efficiently in longitudinal studies to establish the changes that are likely to occur from initial diagnosis to self-management. There is a particular need for this within rheumatoid arthritis as illness perceptions have not been effectively explored in this patient group. This would be particularly interesting given the flare/remission nature of the disease and the fact that patients will inevitably face serious threats to their quality of life through the progression of the illness.

2.8.4: Addressing the chronic and variable nature of rheumatoid arthritis when using social cognition models

Although a number of studies have evaluated the social cognition models above in relation to medication adherence, few have addressed the specific difficulties faced by RA patients that would impact both on medication taking and the relative importance of various constructs of the models. For example, although rheumatoid arthritis is chronic, it also often has a flare/remission cycle which has the potential to greatly impact on DMARD adherence. Firstly, patients are required to continue taking their DMARDs when they are not experiencing symptoms (remission), which requires them to overcome the costs of side effects in a period when they will see no immediate benefit (e.g. reduced swelling of the joints). Secondly, it is possible that some patients will experience a flare in their symptoms despite taking their DMARDs adequately, leading to an unfavourable appraisal of medication taking.

Some studies have attempted to investigate some of these differences. For example, Berry et al. (2004) recruited both newly diagnosed and established rheumatoid arthritis patients. They clearly demonstrated the effect that knowledge and experience has on perception of illness as established patients perceived the risks of taking medication to be higher than newly diagnosed patients, although they did not report more side effects. Interestingly, the established patients also had better adherence than the new patients, indicating that although their perception of the costs were higher, they were placing less weight on them in the final decision. Similar results were found by Goodacre & Goodacre (2004) who also recruited newly diagnosed and established RA patients. Here, there was a clear cost-benefit analysis being carried out by the patients, however the newly diagnosed patients were more confident that the DMARDs would be beneficial. Again, this provides some evidence of a dynamic process of decision making as new information and experience is integrated. However, Goodacre & Goodacre (2004) did not find any change in these perceptions over a nine month follow-up period for any patients.

Few studies that have used these models longitudinally have found any change over the follow-up period. However, de Thurah et al. (2010) did find that patients that were non-adherent had higher concern scores on the BMQ at 9 months than at baseline using the Beliefs about Medications Questionnaire. In RA, the perceptions towards DMARDs would be especially important to measure over the evolution of the disease. For example, it has been shown above that newly diagnosed patients have different perceptions of DMARDs due to their inexperience of taking them. This would also be true of patients that have escalated up to biologic medication as DMARDs alone would have failed to initiate remission in these patients, although they are still expected to take them. As necessity has been shown to be a strong predictor of adherence, it could be assumed that patients on biologic medication would perceive their DMARDs to be less necessary and therefore not adhere to them. However, no studies have currently investigated adherence to DMARDs specifically by patients that are also prescribed biologics and therefore the changing model of medication adherence in these patients is unknown.

It is clear that aspects of all of the models would be susceptible to changing perceptions as patients become more experienced and knowledgeable about their treatment. It is particularly important to identify these changes in order to target specific interventions. For example, the Attitudes towards taking medications and Perceived Behavioural Control that are aspects of the Theory of Planned Behaviour are liable to change as patients become more experienced. However, by knowing how these changes occur, it may be possible to aid the patient to be more adherent; for example by

addressing concerns with the medication and talking through exactly how to take them. Similarly, the perceptions of threat and the behavioural evaluation at the core of the Health Belief Model would also change as patients understand more about their RA. A dynamic, changing model is particularly important with regards to the Self Regulation Model because it explicitly describes the process of adjusting to various coping mechanisms and the appraisal process. However, there is a serious lack of longitudinal studies with a sufficiently large sample size and follow-up period to evaluate how exactly illness perceptions change over time within the individual and the effect this has on medication adherence. Although this is important for any chronic illness, it is especially so for rheumatoid arthritis because of the unpredictable nature of flares and the progressive damage that impacts on treatment choice and therefore changing regimens for patients to cope with.

2.9: Summary of social cognition models

There are many similarities between the models, primarily because they are all based on an expected-utility model (Edwards, 1954) which assumes that a cost-benefit decision is made based on information available to the patient. The two major components of all of the models are social involvement from family, friends, doctors and other patients and self-efficacy. Perceived control in particular is a very strong predictor of both intention and actual behaviour. Although the models assume that all patients will carry out the same basic information processing, differences in behaviour occur because of the subjective nature of information gathering and the relative importance that each patient will place on each of the components.

Despite the similarities, Weinstein (1993) noted that there had been very little research comparing these health models empirically and there has been very little done since. To date, only one study has compared more than one model to explain adherence behaviour. Orbell, Hagger, Brown & Tidy (2006) used the Theory of Planned Behaviour and the Self Regulatory Model to predict prospectively whether 660 women with abnormal cervical screening tests would complete their course of treatment. Of these women, 83% attended all of their appointments, 7% attended all appointments after a prompt and 10% ceased treatment prematurely, even after a reminder. Factors from both the TPB and SRM correlated with intention and behaviour. In logistic regression, higher socioeconomic status, being employed and shorter travel time to clinic predicted intention. After controlling for these, illness perceptions accounted for an extra 4% of the variance in intention, although only treatment control was significant. The TPB variables however increased the variance over and above demographics by 42% with all variables being highly significant, although Perceived Behavioural Control had the highest β value at 0.59. With the two models combined in the second step, the

illness perceptions were no longer significant predictors of intention. However, the results for actual adherence to appointments were less encouraging as no illness perceptions were significantly related and only Perceived Behavioural Control of the TPB was related with an odds ratio of 1.85 (1.20:2.86). However, when intention was added to the model, this became the only significant predictor with patients with higher intention being 2.81 times more likely to complete the course of treatment. Although the Self Regulatory Model was not capable of predicting adherence in hierarchical regression, it was able to discriminate between attenders and non-attenders with the former reporting higher identity and coherence than non-attenders. These results show that although both models are good at discriminating between attenders and non-attenders, it is only demographic and personal control variables that can actually predict adherence behaviour. However, this study is important because it has actually compared the utility of two models within a prospective setting which is lacking considerably in the literature on health behaviour as a whole, but particularly with regards to adherence to treatment.

2.10: Conclusions and justification for this programme of research

A strong limitation of the research reviewed above is that most have not compared more than one model and few studies have systematically measured adherence to medication in a chronic but variable disease such as rheumatoid arthritis. For this reason, it would be useful to test each of the full models in an RA population to determine which aspects are most strongly predictive of adherence to medications. As well as measuring adherence *per se*, few studies have evaluated the effect that the models have on disease outcomes such as functional disability or quality of life. Although it is useful to know what psychological factors influence adherence, it is also very important to establish exactly what clinical effect this has on patients in order to identify the most appropriate areas for intervention.

A review by Hagger & Orbell (2003) of the Self Regulatory Model in various coping behaviours also established the need for more prospective work and, particularly in the case of the SRM, more studies that look specifically at the psychological process of adherence in newly diagnosed patients. This is especially important in RA as any damage that occurs to the joints before satisfactory remission is established is permanent, leading to more disability in the long term.

To address the issues raised in this review and to gain more explanatory and predictive knowledge about the social cognition models of adherence to DMARDs by RA patients, this programme of research will aim to test the three most prominent models of health behaviour; the Health Belief

Model, the Theory of Planned Behaviour and the Self Regulatory Model as well as Beliefs about Medications prospectively over six months in relation to adherence to DMARDs. In order to test the discriminant validity of each model it is also necessary to recruit patients with different treatment regimens as their motivation to adhere to treatment may differ. Therefore, patients that have been newly diagnosed, that are established in their DMARD treatment and those that have progressed to biologic therapy (but receiving at least one DMARD concurrently) will be recruited. Mechanisms of intentional and unintentional non-adherence will be evaluated separately in order to provide an understanding of these very different behaviours. Importantly, the effects of the social cognition models and of the different types of adherence themselves will be investigated in relation to disease related outcomes such as quality of life, disease activity, functional disability and healthcare costs in order to provide a more complete view of the concrete effects that non-adherence can have in rheumatoid arthritis.

Chapter 3

General Methods

3.1: Introduction

The rationale of this programme of research was to investigate non-adherence to DMARDs by rheumatoid arthritis patients. The main focus was to establish whether three social cognition models were able to predict and explain medication non-adherence over a period of six months. In addition, a number of complementary studies were carried out to provide a more holistic and comprehensive approach to tackling adherence in the clinical setting. Although the main focus of this research involves a large, prospective longitudinal study establishing the psychological predictors of adherence, the issue of measuring adherence, the clinical effects that non-adherence has and potential ways of addressing non-adherence were also investigated and are presented in subsequent chapters. Given this holistic approach, a number of methodologies and statistical analyses were carried out to provide a comprehensive evidence-base on which to consider the importance of research into medication non-adherence in rheumatoid arthritis. These methods are discussed in the chapters of the studies to which they pertain.

In order to fulfil the rationale, there were five distinct aims of this programme of research which are discussed in more detail below:

1) Establish the feasibility of using Information and Communication Technology (ICT) in the rheumatology clinic to provide a cheap, portable reminder to prevent unintentional non-adherence to treatment.
2) Establish a feasible and reliable method of measuring DMARD adherence in the clinic.
3) Investigate the ability of three social cognition models of illness to predict and explain DMARD non-adherence in a large, multicentre cross-sectional study.
4) Extend the cross-sectional study by investigating whether the social cognition models can predict non-adherence in a prospective longitudinal study over six months.
5) Investigate the clinical impact of non-adherence to DMARDs though health economic analysis.

3.2: Rationale of establishing the feasibility of using Information and Communication Technology to prevent unintentional non-adherence in the rheumatology clinic

The introduction of cheaper and more sophisticated ICT in recent years presents the opportunity for healthcare to implement services with the potential for improving care and reducing costs. Specifically, the practice of sending SMS (Short Message Service) text messages to remind patients of outpatient appointments has become routine within the NHS. However, there is little research that has evaluated the success of these messages, or the potential to extend them to prevent unintentional non-adherence to medication, particularly with patients with rheumatoid arthritis who are generally older and have more disabilities than the general population. For this reason, Chapter 5 reports on a survey assessing the feasibility of communicating with RA patients via email and/or SMS message that was carried out in the rheumatology clinic. The survey asked patients about accessibility to the internet and mobile phones, current use of email and SMS messages and whether they would accept appointment and medication reminders in the future.

3.3: Rationale for establishing a clinically viable measure of adherence to DMARDs

In order to investigate adherence to DMARDs, an effective measure of adherence was required for use in subsequent studies. Objective measures of adherence such as eMEMs and pill counts were not suitable for these studies because of the prohibitive cost and resource requirements from both researcher and patient and the fact that they are unsuitable for polypharmacy which is a common requirement of rheumatoid arthritis management. As discussed in Chapter 2, section 2.6, self-reported adherence measures are often used in research and a validated measure designed specifically for RA was chosen for this programme of research. The 19 item Compliance Questionnaire for Rheumatology (CQR19; de Klerk et al., 1999) has been shown to have good sensitivity and specificity in detecting non-adherence to DMARDs compared to eMEMs. However, a number of items have been shown not to add to the exploratory power of the tool (de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden, 2003), making them redundant and therefore reducing the parsimony of the questionnaire. In addition, a nineteen item questionnaire was deemed too long to use regularly in the clinical setting and within the battery of questionnaires in the main study. Therefore, to increase the clinical utility and to improve the reliability by removing redundant questions, an exploratory factor analysis was carried out in Chapter 6 with a confirmatory factor analysis to check the fit of the reduced questionnaire.

3.4: Rationale of testing the social cognition models of illness in relation to the stage of illness and adherence to DMARDs

This study contributed to the main focus of the programme of research. Three commonly used models of illness were evaluated in relation to adherence to DMARDs by RA patients. All three models were tested simultaneously to establish which was most predictive of non-adherence to test which psychological factors should be targeted for intervention in the future. As the aetiology of chronic illness differs, it is recommended to establish the models in each patient group (Hagger & Orbell, 2003) and very little research has systematically evaluated all three models in the same dataset. Therefore, in order to establish the possible psychological causes of non-adherence to DMARDs, a large, multicentre study was carried out across six hospitals in Hertfordshire and north London between February and October 2010. The cross-sectional analyses are shown in Chapter 7. As this type of research had not been carried out in rheumatoid arthritis, there was little previous information of effect size and power on which to base a sample size calculation. Therefore, the target sample size was based on the standard five cases per item required for regression analyses (Tabachnick & Fidell, 2007). To test all of the models simultaneously, 80 patients for each treatment group were required. As this study was longitudinal, an attrition rate of 20% over six months was assumed meaning that 100 patients per group were required for individual analysis and at least 100 in total for whole group analysis.

Patients were followed-up six months after recruitment and asked to complete the questionnaire again. There were two aims for the longitudinal analysis; firstly, to establish the stability of the social cognition models of illness over six months, particularly for newly diagnosed patients and secondly to identify the best predictors of non-adherence over six months. Chapter 8 focuses on the stability of the social cognition models with a particular emphasis on the different treatment groups to establish whether the social cognition models of illness are stable over time or subject to change in response to the illness. There is currently very little research investigating medication adherence longitudinally, but those that have, typically employed regression analyses to test the predictors of interest (e.g. Abraham, Clift & Grabowski, 1999; Orbell et al., 2006; Ross, Walker & MacLeod, 2004; Schuz et al., 2011). A more powerful way of testing causal pathways is to use Structural Equation Modelling (SEM) which allows for multiple regression analyses to be carried out simultaneously and is shown in Chapter 9.

3.5: Rationale of using health economic analysis in relation to adherence to DMARDs

A number of related health economic analyses were carried out to investigate the effect that non-adherence to DMARDs has on patients and the NHS. Firstly, a Cost of Illness (COI) analysis was carried out in relation to intentional, unintentional and overall non-adherence. The COI took an NHS perspective and aimed to establish the total cost of medications, GP visits, inpatient hospital stays, Accident and Emergency contacts and outpatient appointments over six months for patients that have low adherence. COI studies are carried out to gain economic information about an illness in order to raise the public profile. Although many standard COI studies have been carried out for RA in numerous countries, none have so far focussed specifically on the cost of medication non-adherence. For this reason, a pilot study measuring NHS costs prospectively over six months was carried out using the patients recruited for the social cognition models of illness and adherence study to provide preliminary evidence of the costs generated by these patients. The aim of this analysis was to provide a clinically useful, concrete outcome for non-adherence to encourage clinicians to become more aware of its importance.

Health Related Quality of Life (HRQoL) of patients was assessed using the EQ5D (Dolan, 1997; EuroQol Group, 1990). This measures five components of health which are combined into a single composite score ranging from 0 (death) to 1 (perfect health). The EQ5D utility score is used to calculate Quality Adjusted Life Years (QALYs) which combine quantity and quality of life to produce a standardised measure which can be used to compare different interventions for different illnesses. The QALY was calculated for each patient using the baseline and follow-up EQ5D scores and used to produce mean QALYs for adherence groups. More details of these calculations are presented in Chapter 10.

Finally, a simulated Cost-Utility Analysis (CUA) was carried out in Chapter 11 based on the QALYs calculated in Chapter 10 and evidence for a potential SMS based intervention provided by Chapters 4 and 5 and a study by Petrie, Perry, Broadbent & Weinman (2011). CUA is a special type of cost-benefit analysis which assesses the ratio of costs (measured in monetary terms) and HRQoL, usually via QALYs. As QALYs are designed to be universal, CUA can be used to compare across illnesses whereas traditional cost-benefit analysis cannot, however there have been criticisms of using QALYs in this way which are reviewed by Stamuli (2011) but discussion of which is beyond the scope of this chapter. By using CUA, a cost per QALY gained was generated to evaluate the utility of an SMS based medication reminder service which is presented in Chapter 11.

3.6: Summary of methods used

In order to provide a complete and comprehensive evaluation of the effects of non-adherence to DMARDs, a number of studies were carried out. Firstly, a measure of adherence with high clinical utility and easy interpretation was created using exploratory and confirmatory factor analysis of an existing measure specific to RA. Following that, the psychological predictors of adherence were evaluated in a large, multicentre prospective longitudinal study over six months in 2010. Using statistical modelling, the best predictors of adherence were identified with the aim of targeting these perceptions in a future intervention to improve adherence. In order to provide more evidence as to the importance of researching treatment non-adherence, a health economic analysis was carried out to determine the costs of non-adherence from the NHS perspective. A simulated cost-utility analysis was then carried out based on a feasibility survey of implementing an SMS reminder service for medication adherence. By using these different methodologies, a more comprehensive analysis of non-adherence was possible giving more evidence on which to base future interventions.

Chapter 4

Using technology to aid adherence in rheumatology clinics: Systematic review of the use of electronic reminders for chronic health management

4.1: Background

The issue of unintentional non-adherence (forgetting) affects all aspects of patient self-management including clinical review appointments, medication taking and monitoring tests (e.g. blood tests). However, forgetting could potentially be addressed with the use of reminders which would act as the "cue to action" proposed by the Health Belief Model for the patient to initiate the behaviour in question (e.g. taking medication or attending medical appointment). This could potentially overcome the issue of people that have a strong intention of performing the behaviour, but simply forget to do so. The Hospital Episode Statistics (HESonline) state that in England during 2010, 6.9 million outpatient appointments were classified as DNA (did not attend), constituting 8% of all outpatient appointments wasted due to patients not attending. This is a problem facing all NHS trusts which costs millions of pounds per year.

There has been little research that systematically differentiates between forgetting and other medication non-adherence, therefore there is little known about the prevalence. However, a study by Atkins & Fallowfield (2006) found that 38.9% of women prescribed medication for stable breast cancer sometimes forget to take it. Forgetting was also much more prevalent than intentional non-adherence at 83.6% of the non-adherent sample. "Forgetting" and "being busy" are two of the most common reasons given by HIV positive patients to miss medication (Chesney, 2000).

Woods et al. (2008) found that deficits in prospective memory (i.e. remembering to remember) were a strong predictor of medication non-adherence by HIV positive patients. They suggest: "a programmable electronic device that prominently notifies the patient when it is time to take a medication with a detailed text message that includes the medication dosage... might be maximally effective" (Woods et al., 2008; page 268). With the market penetration of information and communication technologies (ICT) such as the internet and mobile phones increasing year on year (Office of National Statistics, 2009), the potential to utilise these existing resources in an appropriate

way to aid self-management and adherence by chronic illness patients is huge. However, to date, there are no guidelines on the best way to initiate and integrate this type of reminder into clinical care in the most effective way to produce an improvement in adherence rates without over-burdening the patient. For this reason, a systematic review of the literature was carried out to determine how electronic reminders have been used to aid self-management in chronic disease and the best strategies to implement an intervention.

4.2: Methods

4.2.1: Search

Three frequently used Psychology databases were used to carry out a literature review of technology used to address adherence in chronic illnesses in the week commencing 6th April 2009; ISI Web of Science, PsycINFO and PubMed. For areas such as the disease type, the search terms needed to be reasonably wide (i.e. chronic illness as opposed to specifically rheumatoid arthritis) whereas the technology terms needed to be specific (SMS or email produced good results). This reflects the fact that there has not been a large amount of research conducted in this area as yet.

Table 4.1: Results for each of the search terms

Search terms	Search terms prefixed with Boolean operator AND	Search terms prefixed with Boolean operator AND	Retrieved	Title review	Abstract review
Adheren* OR complian*	Rheumatoid arthritis OR ra	Technolog*	8	0	0
Adheren* OR complian*	Rheumatoid arthritis OR ra OR chronic illness	Email OR text message OR mms OR mobile telephone OR msn OR computer	32	19	9
Elder* OR old*	Chronic illness OR disease OR pain OR patient OR health	Email OR text* OR sms OR internet	7	7	6

Appendix 4.1 shows the full list of available articles that were produced by this search. There were a total of 4 duplicated references. It is clear that the vast majority of papers are concerned with various aspects of internet use, with only twelve concerned with SMS or email use in chronic illnesses.

4.2.2: Eligibility

Studies were eligible if they included an email or SMS based reminder for any part of self-management in a patient sample. Participants had to be over 18 years of age and receive the reminder themselves. Due to the small number of eligible studies retrieved, all designs were considered. Eligible studies had to be in English but did not have to conform to the NHS model.

4.2.3: Scrutiny and data abstraction

Titles and abstracts of each of the studies returned were reviewed. A number of studies were removed because the intervention was entirely internet based or because the patients were <18 years. Although these studies will provide valuable information on integrating technology more generally into healthcare, they were deemed unsuitable to inform a reminder service to improve adherence. A standardized data extraction form was designed and completed for each eligible study. Due to the heterogeneity of the studies, it was not possible to do a meta-analysis and so articles were grouped into the type of reminder employed (appointment, medication, self-management).

4.3: "Results"

A small number of studies were found for each of the three categories above (Table 4.2) totalling 11. Due to this and the differences in design, it was difficult to compare equivalent results and so a narrative review of each of the sub-groups was undertaken in order to establish what research had already been carried out, what results could be gleaned and where these technologies could be employed in the future and how the research could support this.

Table 4.2: Eligible papers retrieved from the systematic search of the literature

Article category	First author	Year	Study design	N	Mean age	Setting	Outcome measure
Appointment reminder	Casey	2007	Survey	76	-	Urology outpatient clinic in Ireland	Percentage of DNA patients that requested a reminder
Appointment reminder	Chen	2008	RCT	1859	51	Heath promotion centre in China	Attendance rates for outpatient clinic (%) and cost per patient
Appointment reminder	Koshy	2008	Prospective observational	9959	-	Ophthalmology outpatient clinic in UK	Attendance rates for outpatient clinic and cost per DNA avoided
Appointment reminder	Leong	2006	RCT	993	38	2 public and 5 private primary care clinics in Malaysia	Attendance rates for outpatient clinic (%) and cost per DNA avoided
Self-management	Anhoj	2004	Intervention	12	39	Asthma patients home	Response rate of diary SMS messages (% days)
Self-management	Faridi	2008	Phase 1 clinical trial	30	-	Community health setting in USA – Type II diabetes	1) Adherence to uploading data to server 2) HbA1c control
Self-management	Kwon	2004		185	42	Home management – Type I & Type II diabetes	HbA1c, blood glucose, HDL cholesterol, weight, patient satisfaction
Communication	Castren	2005	Questionnaire	82	49	Physicians in Finland Student Health Centre	Use of email and telephone consultation
Communication	Huang	2006	Cross sectional intervention	177	-	Surgery patients in Taiwan	Participant satisfaction
Communication	Neville	2008	Qualitative	180	-	Appointment booking and repeat prescription ordering in GP practice in Scotland	Uptake rates and interviews related to service
Adherence	Vilella	2004	Intervention	2348	-	Travel vaccination clinic in Spain	1) Booster adherence rates 2) Correct timing of booster

4.3.1: Appointment reminders

Three papers were found that investigated the use of SMS appointment reminders for adults in health care (Table 4.3). One of these was a prospective observational study in an outpatient clinic in a UK hospital. Two were randomised controlled trials (RCT) based in all outpatient clinics in hospitals outside of the UK (one in China and one in Malaysia). An additional survey carried out in a UK urology clinic asked patients that did not attend their appointment whether they would like a reminder, although these were not implemented.

A study by Koshy, Car & Majeed (2008) audited all patients that had an ophthalmology outpatient appointment at Barts and the London NHS Trust between April and September 2006 (N=9959 appointments). Patients that received an SMS reminder were opportunistically selected; those that had a mobile phone number recorded on the internal Patient Administration System (PAS) were sent a reminder (N=447, 4.5%) and those without a number were not sent a reminder (N=9512, 95.5%). The time between the reminder and scheduled appointment differed by when the patient had booked. If the appointment was booked less than 7 days previously, the reminder was set for the day before, but if the appointment was booked more than 7 days previously, the reminder was set for 4 days prior to allow for cancellations. The following information was collected; whether the patient had received an SMS reminder, whether they were a DNA, and whether they cancelled. The authors found that patients that received an SMS reminder were 38% less likely to DNA than those not receiving a reminder (Risk Ratio RR=0.62, p=0.0002) and that there was an absolute reduction in DNA of 6.9% from 18.1% (no reminder) to 11.2% (SMS reminder). However, the authors acknowledge that they were not aware of the proportion of patients without a mobile number on PAS who also did not own a mobile phone and therefore would not be accessible via this method. These patients would also likely be of a lower socio-economic status and therefore at higher risk of DNA (McClure, Newell & Edwards, 1996; Hamilton, Round & Sharp, 2002). The authors report that the cost of an SMS reminder was 7.2p and that the number needed to be sent to prevent 1 DNA was 14 (10-31) at a cost of approximately £1. The cost of an appointment is cited as £65 making a saving of £64 for every DNA avoided.

The two RCTs carried out by Leong et al. (2006) in Malaysia and Chen, Fang, Chen & Dai (2008) in China have very similar designs but were carried out in different health care settings where the expectations of the patients are quite different. For example, at the health promotion centre in China, patients are assigned specific appointment times which they are expected to attend whereas in Malaysia, attendance was defined as any time during clinic hours of the allotted day. There was

also the issue that there were 7 clinics included in the Malaysian trial, 5 of which were private, whereas only one university based centre was included in the RCT in China. However, the procedure was the same for both studies. Patients were randomised into one of three groups; i) telephone reminder made by office staff to a landline number, ii) SMS reminder with the same information as the telephone reminder (name and appointment details) or iii) no reminder (control). Successful contact was assumed when the patient answered the telephone and when a "message sent" message was received for the SMS reminder. Leong et al.'s (2006) sample consisted of 993 patients, 64% of which were female with a mean age of 38. Chen et al.'s (2008) sample consisted of 1859 patients with a mean age of 50 with 43% being female. Within each setting, RCT groups were matched for age and sex. Both of these studies found that a reminder of any type resulted in higher levels of attendance than the control groups and that there was not a significant difference between attendance rates for the phone or SMS reminders. However, the authors of both studies conclude that an SMS reminder is more cost-effective as they are approximately 1.5 times cheaper than a telephone call. This was due to the increased staff time needed for the telephone calls as well as increased telecommunications costs. This could be further reduced in the future with an automated reminder system, eliminating the need for dedicated staff time.

A survey by Casey et al. (2007) asked patients that did not attend their appointments the reasons for this and also if they would like a reminder in the future. A large proportion of patients either forgot about their appointment or claimed that they did not receive the original notification. When asked, 34% requested an SMS reminder, 37% a phone reminder, 36% letter reminder and 6% email reminder.

4.3.2: Disease self-management

Three studies were retrieved through the search however the types of self-management interventions, patient groups and outcome measures are disparate. The majority were internet based with an additional SMS message component to send or receive clinical information.

Anhoj & Moldrup (2004) tested the feasibility of using a reciprocal SMS diary service for asthma patients to upload information about their peak flow measurement and sleeping patterns. This information could then be used to encourage and empower patients to tailor their medication for better self-management. Twelve patients ranging from 13 to 57 years (median = 38.5 years) received a sequence of text messages each day for two months at a self-selected time of day. The first two messages were reminders for controller medication and measuring peak flow. Patients were then

required to reply to the following messages giving information on; peak flow measurement, waking up because of asthma symptoms and the number of rescue doses in the past 24 hours. As this was a feasibility study to determine whether information could be provided via SMS message, only the percentage of responses and patient satisfaction were recorded. The authors found that the response rate was approximately 60% which did not decline over time. In any one day, patients tended to either reply to *all* of the messages or none, so the level of information gathered was generally high. Generally, patients felt the system gave them more confidence and control over their asthma and preferred this type of daily contact to face to face with a health professional. However, patients did complain of too many messages per day with too long a delay between them. They also wanted the messages to be tailored to arrive later on weekends and holidays. Overall, the SMS messages appeared to work well and provide a feasible way of capturing health related data. However, these patients were relatively young and highly motivated which could lead to a positive bias towards adherence. The authors have shown that is it possible and desirable to use SMS messages in conjunction with an online self-management programme for these patients.

Two studies were found that incorporated SMS messages into a web-based self-management programme for diabetes. A study by Kwon et al. (2004) required patients to upload information on blood glucose, blood pressure, body weight and any questions to a secure website via SMS message to be converted into an electronic chart for both the patients and medical team to review. HbA1c, blood glucose and weight were measured pre and post the 3 month period that the website was used. The authors found that patients were reasonably happy with technical aspects of the website and that there was a trend towards improved diabetes control, although this was non-significant over a relatively short period of time. It appears this website could be a useful aid for self-management, however there does not seem to be any benefit of uploading the information via SMS as opposed to directly online or whether the system would be cost-effective based on the improved blood glucose control. The authors also noted that older patients got their children to upload the information, prompting questions about the suitability of such a system for older patients less experienced with the intricacies of uploading and reviewing information online.

Faridi et al. (2008) implemented a similar diabetes self-management website called NICHE which sent personalised SMS messages based on pedometer and blood glucose readings uploaded daily by the patient. This intervention had only 15 patients plus 15 control patients who did not receive the SMS messages over a 3 month period. The authors found that adherence to uploading blood glucose and pedometer readings were very low with a third never submitting readings. Patients identified a number of technical issues that acted as barriers to use, however they indicated that they would

prefer the NICHE to usual care if it was simpler and more reliable. There was a trend towards better blood glucose management and self-efficacy in the intervention group only, although this was not statistically significant. There was no change in control patients. It would appear that the SMS component of the NICHE study is well received and perceived to be useful by these patients to improve self-efficacy and control although improvements to the methodology and a larger sample are needed to clarify how efficacious and cost-effective the system is.

4.3.3: Adherence to treatment

Only one study was found that investigated the use of electronic reminders on adherence to treatment. Vilella et al. (2004) sent SMS reminders to travellers requiring Hepatitis A+B or Hepatitis A vaccination. Participants were recruited opportunistically from two offices from the International Clinic Vaccination Centre in Barcelona in the summer of 2001. Those that had a mobile phone were offered a reminder for their second and third booster jabs for the respective vaccinations. People attending a third office at the centre during the same period acted as controls with no reminder offered. Only one person who was offered a reminder refused. Although patients were not randomised, *post hoc* analysis of the demographics found that patients did not differ on socio-economic status or duration of holiday. Results were based on i) whether a participant attended follow-up for a second and third booster at any time and ii) whether the attendance was within the recommended time period of 30 days +/- 10 days for the second dose and 190 days +/- 30 days for the third dose from initial administration.

For the Hepatitis A+B vaccine, the reminder did not make any difference to attendance rates for the second dose at any time (RR=1.00), however, those that had a reminder were 10% more likely to attend within the recommended timing. There was a larger effect of a reminder on the third dose as they were 44% more likely to attend at any time and 75% more likely to attend within the recommended 190 days. For Hepatitis A, those receiving a reminder were 60% more likely to attend for a second dose and 69% to attend within the recommended timing.

Vilella et al. (2004) found that an SMS reminder increased attendance for the final administration of the Hepatitis A+B vaccine by 17.2% in absolute terms from 39.2% (control) to 56.4% (reminder). A similar increase of 13.7% from 23% (control) to 36.7% (reminder) was found for follow-up administration of Hepatitis A vaccine. Patients were also more likely to attend within the recommended time for follow-up if they received a reminder. Although the absolute rates of

attendance are still relatively low for each vaccination, it has been shown that a reminder can significantly increase the level of adherence to this treatment course and is well received by patients.

Table 4.3: Results from each of the interventions

Study	Participants	Duration (months)	Procedure	Measures	Outcome
Casey et al. (2007)	76 urology outpatients, Ireland	1	Audit of DNA rates following reminder and survey	1) DNA rates 2) Reasons for DNA & reminder	DNA mostly related to forgetting or not knowing appointment date. 34% requested SMS reminder, 6% email
Chen et al. (2008)	1859 outpatients, China	2	RCT of SMS appointment reminder	1) DNA rates 2) Cost per patient	1) SMS and telephone reminder significantly reduced DNA rates 2) SMS reminder more cost effective; cost per patient = 0.42Y
Koshy et al. (2008)	9959 ophthalmology outpatients, UK	6	Prospective audit of SMS appointment reminder	1) DNA rates 2) Cost per DNA avoided	1) SMS 38% less likely to DNA with absolute reduction of 6.9% 2) 14 reminders needed to avoid 1 DNA at a cost of £1 (saving £64)
Leong et al. (2006)	993 outpatients, Malaysia	7	RCT of SMS appointment reminder	1) DNA rates 2) Cost per patient	1) SMS and telephone reminder increased attendance by 50% 2) SMS reminder more cost-effective; cost per patient = RM0.45
Anhoj & Moldrup (2004)	12 asthma patients, Denmark	2	Feasibility study of using SMS to collect diary data	1) Response rate per patient 2) Response rate per day 3) Participant experience	1) Median response rate/patient = 0.69 (0.03-0.98) 2) 57% of days participants responded to all messages 3) Liked medication reminder but too many technical problems
Faridi et al. (2008)	30 Type II diabetes patients, USA	3	Phase 1 clinical trial of NICHE; self-management website with personalized SMS messages	1) Adherence to uploading 2) Participant experience 3) HbA1c	1) 13.3% completely adherent, 53.3% partially adherent, 33.3% completely non-adherent 2) Too many technical issues but happy to use if simplified 3) Trend towards improved HbA1c (-0.1) in intervention group only
Kwon et al. (2004)	185 diabetes patients, North Korea	3	Pre-post self-management website with SMS upload	1) HbA1c 2) Triglyceride 3) Patient experience	1) HbA1c mean reduction of 0.5 (p=.003) 2) Triglyceride mean reduction of 24.4 (p=.007) 3) Well tolerated but older patients needed help
Vilella et al. (2004)	2348 travel vaccinations, Spain	4	Case control SMS reminder for booster vaccination	1) Percentage of patients getting booster 2) Percentage of correct timing of booster	1) No difference for second dose but 46% improvement for third dose 2) Significantly improved optimum timing for all doses

4.3.4: Communication

Only one paper was found which formally investigated the potential for electronic media to improve communication between patients and physicians. Castren, Niemi & Virjo (2005) asked doctors at the Finland Student Health Service how many of their patient contacts were face to face, via telephone or via email and whether they felt that any of the contacts could be replaced by email. In the one working week in 2003 in which the study was set, 79% of the doctors had used email to contact patients and 98% had used the telephone. Email and phone usage by the doctor did not differ by age, gender or specialism. Over half of the sample were positive about the use of email for patient contact. The participating doctors estimated that 2% of the face to face contacts and 21% of the phone calls could be replaced with email. However, the authors found that approximately 73% of the emails sent were not recorded on patient files leading to questions of patient safety.

Although this study is useful in terms of identifying how email is currently being used within healthcare and the ways in which it could be used to reduce unnecessary face to face and telephone contacts, this study did not seek to determine the patients' opinions of this method of communication, particularly with regards to security and safety of advice offered via email. This would be pertinent before trying to reduce the number of phone contacts by 21% as suggested in the paper if, for example these patients would not be willing or comfortable with replacing a phone call with an email. However, particularly with this type of student patient group, it would appear that email contact allows doctors to reduce the cost of face to face appointments whilst maintaining contact with their patients.

4.4: Discussion

The few studies that have evaluated the use of SMS messages for outpatient appointments add evidence that these reminders are capable of reducing DNA's significantly for very little cost. Any type of reminder (i.e. by telephone call, letter or SMS message) would work well to remind people of a scheduled appointment, particularly for routine review appointments for chronic illnesses such as RA as these are often booked up to six months in advance increasing the potential to forget about it. Although the prospective audit by Koshy et al. (2008) measured whether appointments were subsequently cancelled after the reminder was sent (the appointment can then be offered to another patient), they did not evaluate the optimum time to send the reminder to allow for cancellations without leaving enough time for the patient to forget again. This was also not addressed by Leong et al. (2006) or Chen et al. (2008). The evidence given by these studies indicates that SMS reminders are a cheap and effective way to reduce the number of DNA appointments, however it is now imperative to establish i) the optimum window for the reminder to be sent, ii) how

well received these messages are by patients and iii) whether the reminders are being received by those most at risk of non-attendance, for example people from a lower socio-economic status or those that aren't highly motivated and therefore do not sign up to a reminder system. Only once this information is available will the true benefit of these reminders be known and therefore the true cost-effectiveness of a reminder system evaluated. However, due to the very low cost of SMS messages, it could be assumed that "blanket reminders" that are not targeted will still be effective at reducing the wasted cost of DNA appointments. There appears to be a dearth of evidence from the NHS, with many trusts already employing outpatient reminders and reporting reduced DNA rates without seeming to properly evaluate the consequences.

Only the study by Vilella et al. (2004) explicitly sought to improve adherence rates, in this case to booster Hepatitis A and A+B vaccination. Although this was not an RCT, the large number of people that did receive an SMS reminder had better adherence rates than controls. The effect was heightened when the timing of the booster was taken into account with a large improvement, although the absolute values remained low. The authors reported that only one person refused a reminder suggesting a well tolerated approach. Although the cost of such an intervention is less relevant for this type of reminder because of the nature of the travel clinic, it does provide a model to remind people of routine tests that are not immediately required, such as 8 weekly blood monitoring tests required for rheumatoid arthritis patients. The increase in timing adherence could be particularly beneficial for RA patients to ensure that the result of a recent blood test is available to review in their clinic appointment in order to discuss potential problems with the clinical care team. It would appear that this type of reminder removes the burden from the patient of remembering when a test is required and planning it to coincide with the appointment as this could be automatically generated by the clinic.

The quality and relevance of the self-management studies was not particularly high as they dealt with asthma and diabetes and suffered from a lot of technical problems leading to low participation rates, impacting on the generalisability of the studies. However, despite the small sample sizes and intensive interaction with the clinical care team that these patients experienced, it seems that SMS reminders and interactive exchanges can be used to prompt patients to perform self-management behaviours and share the information to improve self care. Again, the focus of these studies was not specifically on the SMS system and therefore unanswered questions remain with regards to the optimum timing and number of reminders and the ability of all patients to respond with relevant questions. Some patients complained at the frequency of messages in the study by Anhoj & Moldrup (2004) and indicated that one message a day that was tailored for weekends and holidays would be preferable. Others had difficulties with uploading information due to the level of technical

knowledge required. Although these studies did not specifically seek to find the optimum reminder schedule, they give some indication that a single reminder that is tailored to their circumstances is preferred which requires very little specialist knowledge. Technological advances since these studies were carried out have made it possible to more simply upload information to a website via SMS message which would circumvent some of these problems.

Overall, although the studies that actually report using electronic reminders are very heterogeneous in their design and outcomes, they provide some evidence that SMS reminders are a cheap, well accepted method to provide patients with a prompt for self-management behaviours. It was interesting to find that none of these studies used email as a way of communicating information which may be easier than SMS message. However, SMS messages have the advantage of being more portable and readily available at times when a behaviour may be required (for example taking a tablet or testing blood glucose). Although there are gaps in the evidence provided by some of these studies; for example the proportion of patients who have this type of technology already and whether patients who are not highly motivated would be willing to participate in this type of service, the results are encouraging. However, the relevance to a rheumatology patient sample is limited due to the mostly younger age of participants in these studies and the fact that very few of them would be expected to suffer from a disability that could potentially impact on technology use (such as joint deformity in the hands).

4.5: Conclusion

The conclusion that can be drawn from this systematic review is that currently there is not enough evidence published to be able to confidently predict who will benefit from a reminder system or in what guise. The optimum recruitment and administration system has not been reported to guide an intervention and no studies have been published concerning rheumatology patients. Therefore, it would seem that technology can and is being used effectively in a clinical setting but that further research is needed to determine the optimum intervention, both for all patients in the case of appointment reminders and for particular illness groups for self management programmes.

Chapter 5

Using technology to aid adherence in rheumatology clinics: testing the feasibility of implementing electronic reminders in a rheumatology patient sample

5.1: Introduction

The systematic literature review presented in the previous chapter demonstrates that although the use of ICT in healthcare is starting to receive some research attention, there is still a lack of knowledge about who regularly uses this type of technology and how best to utilise it for chronic illness patients. There is data available for the general population in the UK with the Office for National Statistics (ONS) Internet Access survey in 2009 stating that 18.31 million households in the UK have access to the internet in their homes; 70% of the population. The survey also stated that the most popular online activity was sending and receiving emails with 90% of respondents participating in this activity (up from 87% in 2008). This suggests that the possibility of utilising emails in a health setting, particularly by reminding patients about medications or appointments is becoming more plausible. A survey by Wilson et al. (2008) in South Australia found that 65% of those surveyed with internet access would be willing to receive unsolicited health information via the internet, suggesting that health related emails would be welcomed.

In 2008, a survey aggregating real time data from all UK mobile phone operators stated that there were 65 million active mobile devices and that 216 million SMS messages were sent per day on average; a growth of 38% from 2007 (Mobile Data Association, 2009). The systematic review in Chapter 4 indicates that the area of SMS messaging in health settings is becoming more evident. A number of mobile phone based interventions have been found to be successful in dietary education and weight loss (Kubata, Fujita & Hatano, 2004; Wang, Kogashiwa & Kira, 2006) and smoking cessation (Bramley et al., 2005; Lazev, Vidrine, Arduino & Gritz, 2004; Obermayer, Riley, Asif & Jean-Mary, 2004; Rogers et al., 2005; Vidrine, Arduino, Lazev & Gritz, 2006a, 2006b), as well as in chronic illness (Anhoj & Moldrup, 2004; Faridi et al., 2008; Kwon et al., 2004).

Although there have been some studies relating to chronic illness, they have tended to focus on younger patients and those that are not expected to have some of the potential disabilities that rheumatoid arthritis patients might have. There is some encouraging research as Dey, Reid, Godding

& Campbell (2008) found that 75% of women aged 41-88 years use a computer and Wilson et al. (2008) found that 59% of people aged 50-76 had internet access. van Lankveld, Derks & van den Hoogen et al. (2006) and Tak & Hong (2005) found that older patients with arthritis did not have additional difficulties using the internet, but that overall access rates were low at 28%.

Very little research has been carried out regarding the current usage of mobile phones in older people. Qualitative studies by Kurniawan (2006, 2008) and Bachu, Hine & Arnott (2008) indicated that people over 60 used their mobile phones infrequently, mostly to call family to notify them of an emergency. They reported rarely sending SMS messages, although they received them on average once a week and were able to access and understand them. Some potential problems with small buttons and screens were identified in all of these studies as barriers to use, although this was not the case for the actual participants.

A review of the literature indicated no studies had asked about the current use of text messaging among older people, particularly by patients with arthritis who would be especially prone to problems handling a mobile phone. This would obviously impact on a potential ICT intervention to improve adherence. For this reason, a feasibility survey was carried out to determine the levels of current use of email and SMS messaging among rheumatology patient groups to determine whether the interventions that have been successful in other healthcare settings such as smoking cessation and appointment attendance would be possible to implement in this cohort without the need for extensive training or set up costs.

5.1.1: Aims

1) Establish current use of the internet, email and SMS messaging among rheumatology patients.

2) Assess the acceptability of using email and/or SMS reminders for appointments and medication doses in the future.

5.2: Methodology

5.2.1: Patients

A total of 121 patients were eligible and 112 agreed to take part, giving a response rate of 93%. Patients that refused were all female and aged over 40. The median age range was 55-64 and 67.8% of patients were female (Table 5.1), which is consistent with the demographics of rheumatic disease. Over half of the sample (58.9%) were educated to GCSE or A-level, 29.9% to degree or postgraduate level and 11.2% had no formal qualifications. All patients came from the local Hertfordshire area.

Table 5.1: Age distribution of the sample

Age range	Frequency (%)	Percentage female	Percentage high school education only
18-24	5 (4.5)	40.0	20.0
25-34	10 (8.9)	88.8	11.1
35-44	12 (10.7)	81.8	25.0
45-54	24 (21.4)	75.0	33.0
55-64	29 (25.9)	75.9	55.2
65-74	23 (20.5)	52.2	66.6
75+	9 (8.1)	37.5	57.1
Total	**112 (100)**	**67.8**	**43.9**

5.2.2: Procedure

All patients attending a Rheumatology outpatient appointment at two Hertfordshire hospitals over eight half-day sessions in February 2010 were approached by a researcher and invited to participate in a survey of current technology use. An explanation of the content and purpose of the survey was given to patients and they were then left to decide whether or not to participate. Consent was assumed with submission of a completed survey. Patients were left to complete the survey alone unless they requested help from the researcher. All questionnaires were paper based and took approximately 15 minutes to complete. A full copy of the survey is shown in Appendix 5.1. Every effort was made to include patients in the survey who do not routinely use ICT. This study was given ethical approval by the Hertfordshire NHS Research Ethics Committee (REC); 09/H0311/105.

5.2.3: Office for National Statistics survey

The Office for National Statistics produces an annual survey called “Internet Access; Households and Individuals” which gives data on internet access for the UK population as well as some of the typical online activities such as email and shopping for adults aged over 16 years. Approximately 1800 adults were contacted each month between January and March 2009 with a response rate of 60%.

The population data available in the ONS survey is particularly useful for this feasibility study as these patients could potentially differ from the population through socio-economic status and disabilities. Firstly, the fact that the patients were all taken from the same geographical area could impact on internet access due to high broadband availability in Hertfordshire and the traditionally high socio-economic status, *increasing* the likelihood of uptake (Fogel, Albert, Schnabel, Ditkoff & Neugut, 2002, 2003; Wilson et al., 2008). Secondly, the reduced dexterity resulting from the arthritis (Weiner, 1967) could *reduce* the uptake of these technologies.

Therefore, in order to establish whether or not the sample differed from the population, the current survey was designed to be used in conjunction with the ONS survey, regarding age groups and frequency of internet and email used.

5.2.4: Statistical analysis

It is important to consider how many patients overall could potentially be accessed as well as those that are already very familiar with the technology in order to gain an understanding of potential barriers to implementing a reminder service in this patient group. Therefore, results are generally presented in two ways; i) the percentage of the entire sample (N=112) to establish the proportion of the entire patient population that could be accessed via ICT and ii) the percentage of patients that have stated that *they already use the internet* at least once per week (N=86) or *own a mobile phone* (N=104) to establish the proportion of patients that would be immediately accessible via these technologies.

For all technologies, differences between age groups are considered using χ^2 tests and odds ratio statistics. The χ^2 tests were used to identify differences between all of the age groups. To determine odds ratios, the sample are dichotomised into those that are aged 18-64 and 65+ years. These age ranges were chosen because they created the most homogenous groups to determine differences between older and younger patients to establish whether patients over 65 were less likely to benefit from any potential ICT based interventions. Given the traditional view that older people do not use ICT, odds ratios were used to look at a younger versus older patient group.

It is expected that younger patients will be very familiar with ICT and so as well as calculating odds ratios, the absolute percentage of patients using email and SMS are shown to determine current experience of older adults.

5.3: Results

5.3.1: Internet access and use

Of this sample, 81.6% had internet access at home, which is comparable to the ONS (2009) survey for the London area (80%). Ninety-three percent of these patients had broadband access, again comparable to the ONS survey. Of those aged over 65, 76.5% had internet access at home.

Home internet access increased with education, with 97% of patients with a degree or above having access, 100% with A levels, but only 66% of those with GCSEs or no formal qualifications having home internet access. Again, this trend is comparable to the ONS survey which gives 95%, 89%, 81% and 52% respectively. Although $\chi^2(3) = 7.82$, $p = 0.05$ this is on the cusp of being significant, indicating

that the patient sample and the ONS survey do not differ substantially on home internet access by education groups.

Table 5.2: Frequency and percentage of patients in each age group that have used the internet

Age range	< 3 months		> 3 months ago		Never	
	N	%	N	%	N	%
18-24	5	100	0	0	0	0
25-34	10	100	0	0	0	0
35-44	11	92	0	0	1	8
45-54	23	96	0	0	1	4
55-64	23	79	1	3	5	18
65-74	12	52	2	9	9	39
75+	3	33	0	0	6	66
<65	72	90	1	1.2	7	8.8
65+	15	46.9	2	6.3	15	46.9
Total	**87**	**77.7**	**3**	**2.7**	**22**	**19.6**

The majority (77.7%) of patients indicated that they had used the internet within the last 3 months (Table 5.2). A very small minority had used it more than 3 months ago and 19.6% had never used it, showing that if patients have used the internet it has been relatively recently. Table 5.2 shows that the patients that have never used the internet are generally older, which is supported by the fact that the OR shows that patients <65 are 8.4 (2.8 : 25.7) times more likely to be weekly users than older patients.

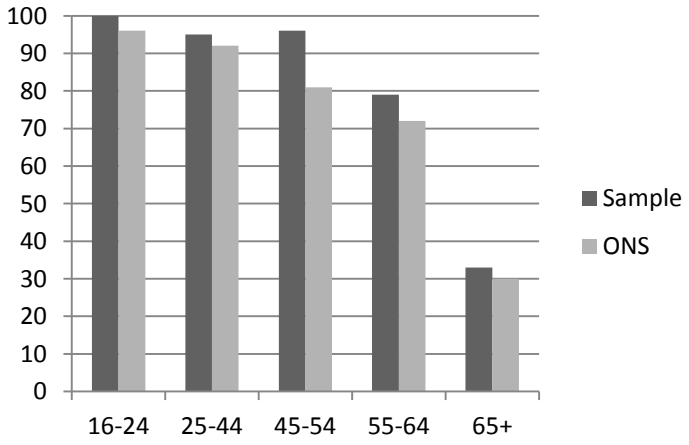


Figure 5.1: Percentage of patients in this sample and in the ONS survey that have used the internet *within the past 3 months*

The same proportion of patients across the age groups had accessed the internet in the past 3 months as in the ONS survey; $\chi^2(4) = 4.02$, $p = 0.40$. A small difference is shown in Figure 5.1 in the 45-54 and 55-64 age groups as the patient sample had a very high level of internet use in these ages

at over 79%. There was however a sharp decline at 65+ with only a third of patients having accessed the internet within the past 3 months both in this sample and the population. For those patients that had accessed the internet *within the past 3 months only*, (N=87) there was no difference between the patients and the ONS survey, $\chi^2(4) = 2.7$, $p = 0.61$, in frequency of internet access. The absolute values were also very high at >93% of the patient sample accessing at least once per week.

5.3.2: Email

There is no information regarding the use of email in the ONS survey and therefore comparisons cannot be made between the patients and the general population.

The proportion of patients with an email address was high for the total sample (79.1%); however this dropped to just over half for patients over 65. A high proportion of weekly internet users <65 had an email address (98.5%) as well as those aged over 65 (86.7%). Nearly all of these email addresses were personal with only 3.4% of patients having *only* a work address. The majority of patients up to 75 years that had an email address accessed it at least once per week, shown in Figure 5.2.

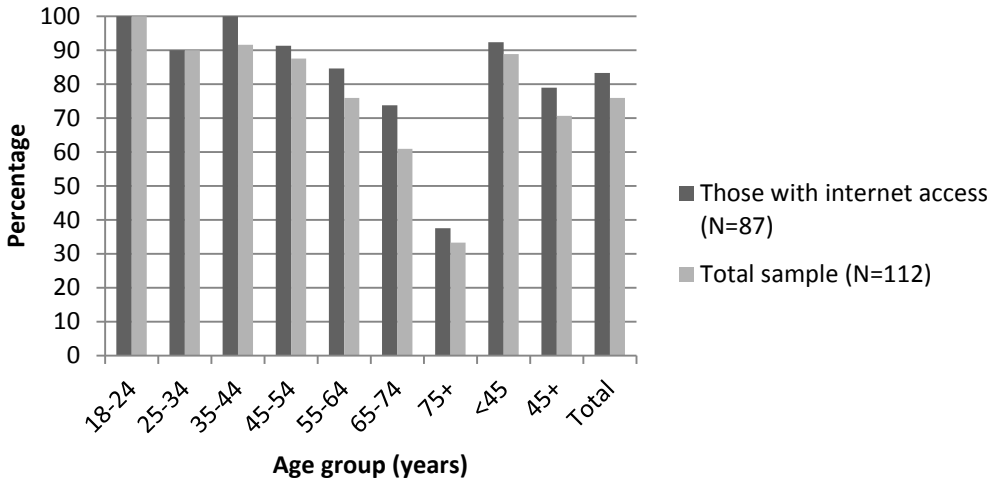


Figure 5.2: Percentage of patients for the total sample (N=112) and only those with internet access (N=87) that access emails at least *once per week*

5.3.3: Mobile phone use

Mobile phone ownership was very high with only 8 patients stating that they did not own a mobile phone in the entire sample, a trend which was maintained across the age groups. The majority of patients had their phones switched on at least during the day. Although there was a tendency for older patients to report having it on less often, the differences between age groups was not significant, $\chi^2(18) = 26.70$, $p=0.09$.

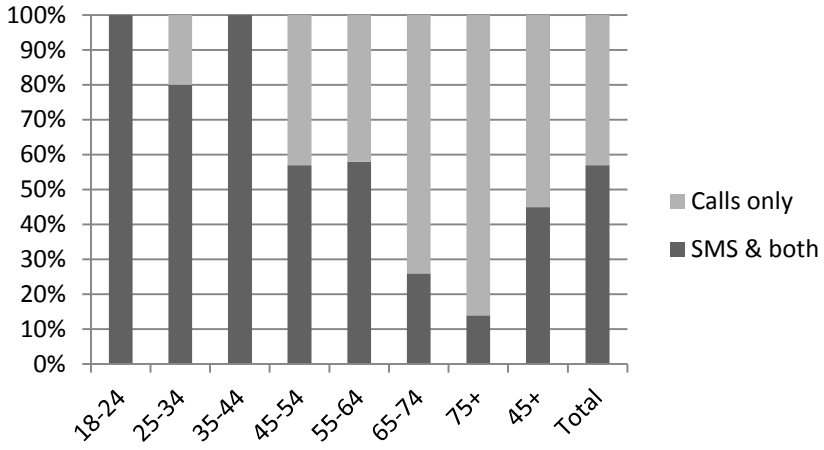


Figure 5.3: Distribution of mobile phone use among patients of all ages that own a mobile phone (N=104)

Patients were asked about their usual mobile phone activity, specifically whether they use their phone mainly for calls, mainly for SMS messaging or about the same for both. Over half (57.4%) of the total sample used their phones mostly for SMS messaging or equally for SMS and phone calls. However, Figure 5.3 indicates that the older patients were more likely to use their phones mostly for phone calls with a gradual decline from age group 45-54 in using the phone mostly for SMS messaging.

The decline in Figure 5.3 is not mirrored when it comes to how often patients receive SMS text messages on average. Although those aged 45-64 report that they use phone calls more frequently, there is still a large proportion of them that receive text messages at least once a week and a very small minority (N=3) that report never receiving a text message. Therefore, although these patients report that they mostly use phone calls, the majority are also receiving SMS messages on a regular basis.

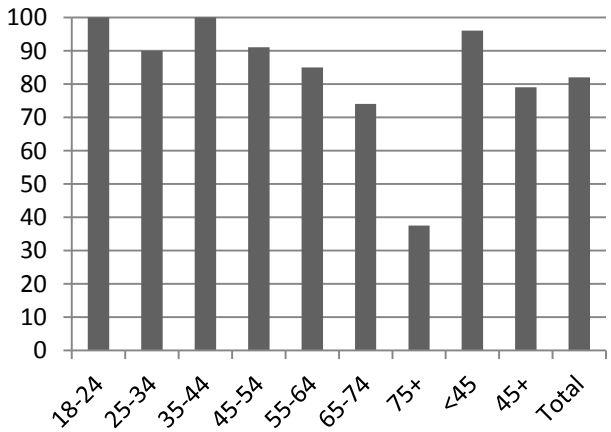


Figure 5.4: Percentage of participants that are confident at *reading* SMS text messages

In anticipation of the likely one way application of an SMS reminder, patients were asked how confident they were in *reading* text messages. Figure 5.4 shows that all age groups, other than those aged 75+, had more people reporting that they are confident (either very or quite confident) in *reading* text messages than not confident. Only group 75+ had a higher proportion that were not confident whereas the other age groups had only 30%, showing a decline with age.

5.3.4: Disease specific difficulties with ICT use

Due to the nature of arthritis, patients were asked whether or not they experienced some specific difficulties when using a computer which could potentially be a barrier to its use. Only 8% of patients reported problems using a computer with only one patient claiming that these difficulties were a barrier to use (Table 5.3). Five people accounted for 13 out of the 17 problems reported. The most problematic element was movement of the mouse with 7% of people indicating problems with this. There were twice as many arthritis related problems (pressing keys and moving mouse; N=10) as age related (sight; N=5). However, there were very few incidences of technical difficulties. None of the problems identified differed between the age groups.

Table 5.3: Potential difficulties experienced by patients when using ICT

Difficulty when using a computer (N=87)	***N***
Seeing the screen	4
Seeing the keyboard	1
Pressing the keys	4
Moving the mouse	6
Maintaining email	2
Difficulty when using a mobile phone (N=104)	***N***
Seeing the screen	6
Seeing the buttons	6
Holding the phone	8
Pressing the buttons	15
Using SMS features	11

Similarly, very few people identified difficulties using mobile phones as sixteen people accounted for 40 out of the 46 problems reported. The most problematic area was pressing the buttons with 15% of people responding positively to this. As with computers, there were twice as many arthritis related problems (holding the phone and pressing the buttons; N=23) as age related (sight; N=12). In contrast to the computer problems, there were a lot more technical difficulties reported with SMS (N=11) than with email (N=2). As with the computer based difficulties, none of these differed between the age groups and no patients reported not using a mobile phone because of these problems.

5.3.5: Electronic reminders

Patients were asked whether or not they would be willing to receive an electronic reminder for appointments and/or medications that are due in the future. Table 5.4 shows the percentages of patients willing to receive a particular reminder for the total sample as well as only those with access to the relevant ICT. A large number responded positively to an appointment reminder and about a quarter of people would be willing to receive a medication reminder.

Table 5.4: Percentage of all patients wanting electronic reminders

	Appointment reminder email	Appointment reminder SMS	Medication reminder email	Medication reminder SMS
Total sample (N=112)	43.8	44.6	25.9	25.9
Have email address (N=87)	56.3	NA	33.3	NA
Own mobile phone (N=104)	NA	48.1	NA	27.9

There was no difference between all age groups for an email appointment reminder, email medication reminder or an SMS appointment reminder. There was a small difference, χ^2 (6) = 13.52, p=0.04 for SMS medication reminders with a higher proportion of younger patients willing to receive one. Younger patients were more willing to using SMS as fifty percent of those under 65 would be happy to receive an SMS appointment reminder compared to 29% of those aged 65+. Similarly, 28.8% of the under 65s would be happy to receive an SMS medication reminder compared to 18.8% of the over 65s. There was no preference between the mode of reminder with very similar results for SMS and email.

5.4: Discussion

This survey found that a large proportion of patients within the rheumatology outpatient clinic had access to and frequently used ICT. It is encouraging to find that this patient sample did not differ in their levels of access to the internet from the general population, as shown in the ONS (2009) survey. As has been found in previous research (Fogel et al., 2002, 2003; Wilson et al., 2008) as well as the ONS survey, internet access increased with education. For those with no formal qualifications in particular, there were low levels of internet access (66% in the patient sample and 52% in the population). This could potentially impact on any healthcare interventions involving internet delivered programmes as a subset of people that are already at increased risk of adverse health outcomes (Eysenbach, 2000; Gordon-Larsen, Nelson, Page & Popkin, 2006) would be less likely to benefit from these interventions. This is an area that the UK government is aiming to address with

the Digital Britain initiative which plans to roll out 2mg/second broadband internet across the country by 2015.

A high proportion of people that had an email address accessed it at least weekly which indicates that if a reminder was sent sufficiently in advance, particularly of an outpatient appointment, the majority of patients with an email address would read it. This is maintained across the age groups until age 75+ wherein this type of reminder would not be particularly useful as there was a only small proportion with an email address and even those that did have one did not check it regularly. However, as an additional means of reminding patients of information that they are already aware of (e.g. appointment times), email seems a cheap and feasible method.

The penetration of mobile phones was very high with ownership at 93% of the total sample. There appears to be an age effect as seven of the people who did not own a mobile phone were aged over 45. As the majority of people had their phones switched on during the day and are confident in reading text messages this could be a very effective method of reminding patients about appointments and medications that are due. Also, as mobile phone ownership was so high, the overall effect on the clinic population would be strong and it would not be necessary to give additional training or hardware thus reducing the cost of a potential intervention. This suggests that it would be possible to obtain similar levels of success at reducing missed appointments as those in Paediatrics (Milne, Horne & Torsney, 2006) and Ophthalmology (Koshy et al., 2008) despite the typically older average age of patients.

Interestingly, there were very low levels of “problems” reported for both computers and mobile phones by these patients. A very small number were responsible for the majority of the problems reported, which were mostly arthritis based, i.e. pressing buttons and holding small objects, as opposed to sight related problems. Only two people reported “technical” problems with computers such as maintaining an email account whereas 11 people reported equivalent problems with mobile phones. This suggests that although mobile phone ownership is higher than internet access, more people struggle with complicated phone features such as predictive text than with using an email account. Although they may find mobile phones more difficult to use, this is not acting as a barrier as they still report regular use.

A quarter of the sample would like a medication reminder and approximately 44% would like an appointment reminder. Patients did not discern between email or SMS for the reminders indicating that patients would take advantage of any type of reminder to improve their ability to self-manage. More patients requested an appointment reminder which may be due to the fact that most patients would be monitored via outpatient clinics every six months whereas medication has to be taken

much more regularly allowing people to develop a routine. Reducing the number of forgotten doses would not only improve the prognosis for the patient but also help to save costs on unnecessary treatment and hospital contacts. As email and SMS messages are so cheap to deliver, any potential savings would far outweigh the costs of an intervention.

There was a marked decrease in technology use for those aged over 65 although there was only a very small sample for this age group. However, as Figures 5.2 and 5.3 show, over 70% of patients aged up to 75 were regularly using ICT which would result in a high penetration rate of reminders across the entire sample. It may be more difficult to introduce these measures in an older sample that are not already competent with the technology and who rely on paper based or telephone call reminders for appointments. However, these technologies are firmly entrenched in society with cheaper hardware becoming available to improve access for everyone. Therefore, as the patient sample ages, they will become more adept at using email and SMS messages which can be used to the advantage of the patient and healthcare provider to improve self-management and save wasted resources.

This survey reports current use of ICT among the rheumatology patient population which had the potential to be different from the general population due to the typically older age and likely disability from joint damage. Although the cross section of patients recruited was representative of the rheumatology clinics in this area, it should be noted the socio-economic status of this geographic area is historically high given its proximity to London and therefore may overestimate ICT access compared to the general population across the country (Fogel et al., 2002, 2003; Wilson et al., 2008). Encouragingly, the patient population did not differ from the general population for the area and so rheumatology patients should not be assumed to have reduced ICT use, particularly for mobile phones as no patients reported not using a mobile phone despite some functional difficulty. The sample size for the two oldest age groups was a little low, particularly for the over 75 group and more research is needed into how exactly these patients prefer to manage chronic illness and whether reminders would be suitable given that they are more likely to be given assistance from family and/or carers.

5.5: Conclusion

Current penetration of ICT is high within the rheumatology population in these Hertfordshire hospitals. These patients are also regularly using email and SMS text messaging up to age 75. The high level of knowledge and experience of this group suggests that implementing appointment and medication reminders would be feasible without additional training or hardware and that it would be welcomed by a number of patients to improve self-management of their rheumatic disease. This

survey has provided detailed information on how this patient group currently uses ICT to inform future interventions to use technology to aid self-management of chronic illness in light of a population that is becoming more technologically aware and more prone to serious chronic disease as life expectancy and morbidity increases.

Chapter 6

Exploratory and confirmatory factor analysis of the 19 item Compliance Questionnaire for Rheumatology

6.1: Introduction

As discussed in Chapter 2, the "gold standard" for assessing medication adherence in patient groups is to test biological markers of the drugs in the blood or to use electronic medication event monitoring to record the time and date of pill bottle opening to infer adherence. However, both of these measures are costly and time consuming and can be subject to "white coat adherence" resulting in patients being deliberately more adherent immediately prior to a clinic appointment (de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden, 2003). A cheaper and simpler way of measuring adherence is to use self-report questionnaires. These have the additional benefit of attempting to measure the psychological constructs behind medication adherence by measuring attitudes and emotions associated with illness and medication taking to infer adherent behaviour. This can provide some indication of areas to target to improve sub-optimal adherence. They have been shown to be strongly correlated with adherence as measured by other questionnaires, and more direct measures such as prescription filling and eMEMs (Garber et al., 2004).

The number of questionnaires that directly measure medication adherence behaviour has been very limited. Those that have been used are often dichotomous and have not been statistically validated (Butler, Peveler, Roderick, Horne & Mason, 2004; Morisky, Green & Levine, 1986). One questionnaire that has been developed specifically for this reason is the Compliance Questionnaire for Rheumatology (CQR19; de Klerk et al., 1999). The authors have reported excellent sensitivity at detecting low compliers at 98% with a kappa of 0.78. This was established by validating the scale against eMEMs and suggests that it is a good questionnaire for establishing medication adherence. Other researchers have also used this scale as a measure of adherence successfully (de Thurah et al., 2010; Garcia-Gonzalez et al., 2008; Treharne et al., 2004). However, de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden (2003) report a moderate level of internal consistency. This could be due to the fact that the authors claim that the scale is uni-dimensional and analyse it as such, although as part of construction, the instrument was classified as being multi-dimensional and no factor analysis has been reported detailing the factor structure. As self-report measures can be problematic with regards to construct validity, it is important to subject scales to rigorous statistical

testing to ensure that they are reliable and valid. To reduce the CQR19, factor analysis will be carried out to check the factor structure of the scale. This will also give statistics that can be used to assess the suitability of each item with regards to the construct validity and the amount of variance that the items share. The reduced version will also be validated using confirmatory factor analysis to ensure that it provides good model fit.

6.1.1: Instrument

The CQR (Table 6.1) is a 19 itemed, self-administered questionnaire that is designed to measure the level of adherence to the prescribed medication regimen of patients suffering from a range of rheumatic diseases (de Klerk et al., 1999; de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden, 2003). The items were generated from patient interviews and focus groups and categorised by two Rheumatology consultants. The most descriptive statement for each category was then chosen for the questionnaire, resulting in 19 items which are measured on a 4 point Likert scale ranging from *"Strongly agree"* to *"Strongly disagree"*. The aim of the questionnaire was to correctly identify patients that were classified as "low" adherers (taking <80% of their medication correctly). Further validation by the authors with eMEMs found that a weighted CQR19 explained 46% of the variance in adherence as measured by the eMEMs (de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden, 2003). Four items (items 3, 5, 7 and 12) combined explained 35% of the variance, indicating that it may be possible to reduce the number of items whilst still predicting an acceptable amount of medication adherence.

Table 6.1: The original Compliance Questionnaire for Rheumatology (CQR19)

	Questions
Q1	If the rheumatologist tells me to take the medicines, I do so
Q2	I take my anti-rheumatic medicines because I then have fewer problems
Q3	I definitely don't dare to miss my anti-rheumatic medications
Q4	If I can help myself with alternative therapies, I prefer that to what my rheumatologist prescribes
Q5	My medicines are always stored in the same place and that's why I don't forget them
Q6	I take my medicines because I have complete confidence in my rheumatologist
Q7	The most important reason to take my anti-rheumatic medicines is that I can still do what I want to do
Q8	I don't like to take medicine. If I can do without them, I will
Q9	When I am on vacation, it sometimes happens that I don't take my medicines
Q10	I take my anti-rheumatic drugs, for otherwise what's the point of consulting a rheumatologist?
Q11	I don't expect miracles from my anti-rheumatic medicines
Q12	If you can't stand the medicines you might say: "throw it away, no matter what"
Q13	If I don't take my anti-rheumatic medicines regularly, the inflammation returns
Q14	If I don't take my anti-rheumatic medicines, my body warns me
Q15	My health goes above everything else and if I have to take medicines to keep well, I will
Q16	I use a dose organizer for my medications
Q17	What the doctor tells me, I hang on to
Q18	If I don't take my anti-rheumatic medicines, I have more complaints
Q19	It happens every now and them, I go out for the weekend and then I don't take my medicines

6.1.2: Aim

The aim of this study was to reduce the number of items in the CQR19 whilst retaining a high level of explained variance and internal reliability. This will be achieved by carrying out an exploratory factor analysis of the CQR19 to reduce the number of items (Study 1) and the model fit will be tested using Confirmatory Factor Analysis (Study 2).

Study 6.1: Exploratory factor analysis of the Compliance Questionnaire for Rheumatology (CQR)

6.2: Methodology

6.2.1: Participants

A total of 70 patients were recruited that had been diagnosed with any poly inflammatory arthritis disease and were currently taking at least one of the following DMARDs; Methotrexate, Sulfasalazine, Hydroxychloroquine or Leflunamide. Patients were required to be aged between 18 and 75 years to participate. Table 6.2 shows the demographic and clinical details of these 70 patients (Hertfordshire dataset). In accordance with arthritis prevalence rates, the majority of the participants were aged over 40 years (84.3%) and most were female (71.4%). The most commonly prescribed DMARD was Methotrexate (50%) with 24.3% prescribed more than one.

Table 6.2: Demographics of the Hertfordshire and Dudley (and combined) datasets

	Hertfordshire dataset		**Dudley dataset**		**Combined dataset**	
	Number	Percentage	Number	Percentage	Number	Percentage
Total sample size	70		155		225	
Gender						
Male	19	27.1	33	21.3	52	23.1
Female	47	67.1	122	78.7	169	75.1
Missing	4	5.7	0	0	4	1.8
Age category						
18-29	4	5.7	2	1.3	6	2.6
30-39	7	10	13	8.4	20	8.8
40-49	15	21.4	20	12.9	35	15.6
50-59	15	21.4	35	22.6	50	22.2
60-69	15	21.4	51	32.9	66	29.3
70+	10	14.3	34	21.9	44	19.6
Missing	4	5.7	0	0	4	1.8
Disease duration						
<1 year	0	0	1	0.6	1	0.4
1-4 years	21	33.3	25	16.6	46	20.4
5-9 years	14	22.2	63	42	77	34.2
10-19 years	18	28.6	35	23.3	53	23.5
20-29 years	4	6.3	12	8	16	7.1
30+ years	6	9.5	13	8.6	19	8.4
Missing	7	10	5	3.3	12	5.3

6.2.2: Procedure

Participants were recruited in two ways; i) consecutive patients arriving for a scheduled outpatient appointment were approached by the researcher and invited to participate in the study, and ii) in order to increase the sample size, questionnaires were posted to eligible patients to be completed and returned in a pre-paid envelope. The CQR19 was given among a battery of questionnaires in order to obtain comparative measures with which to establish the validity of the scale.

Exploratory factor analysis (EFA) was carried out on the CQR19 to determine how many factors were present and how each item loaded onto the factors, to aid item reduction. To reduce the number of items in the CQR19, those with an MSA value of <0.5, and therefore not adequately sampling the construct of adherence, were removed from the analysis. Ethical approval was granted for this study by the Hertfordshire NHS REC: 08/H0311/74.

6.2.3: Statistical Analysis

Initially, the CQR19 was subjected to an exploratory factor analysis as this allows for analysis of the dimensionality of the scale and to reduce the number of items by removing those not adding to the explained variance of the latent variable (in this case adherence). In order to carry out EFA, a sample size of at least 3 cases per item are required (Tabachnick & Fidell, 2007), which was fulfilled by this study. EFA using the unweighted least squares with non-orthogonal rotation was used to extract factors which were defined as having Eigen values >1, as well as through inspection of scree plots. Before carrying at the EFA, the measures of sampling adequacy were interrogated to establish suitability for factor reduction. Firstly, the inter-item correlations and anti-image correlations were established to be >0.5. Secondly, the Kaiser-Meyer-Olkin (KMO) measure was required to be >0.7 and Bartlett's test of sphericity to be significant for EFA to be suitable. Following the extraction of factors, each item was tested for suitability by insuring that the communalities of the items, the factor loadings and inter-item correlations were all above the threshold of 0.3 (Tabachnik, 1989). Once the final model was determined, the internal consistency was tested using Cronbach's α with a threshold of >0.8 being considered as having high internal consistency (Nunnally, 1978).

6.3: Results

The initial analysis of all 19 items showed that the Kaiser-Meyer-Olkin (KMO) measure of sampling was not very high at 0.71. This indicates that there is some degree of inter-correlation leading to a possibly weak factor structure. This is supported by the fact that there were 6 Eigen values of >1 which explained 57.77% of the total variance. This suggests that the items included were not all suitable to measure the adherence construct as the factor loadings were mostly very low on all but

the first factor. For factors 2, 4 and 5 the highest loadings were around 0.5 but this was only for one or two items per factor.

Table 6.3: Exploratory factor analysis of the full and reduced versions of the Compliance Questionnaire for Rheumatology (CQR)

Factor analysis – no. of items	KMO	Items removed	MSA of removed items	Highest factor loading of removed item	Number of factors	Total variance explained
1-CQR19	0.711	NA	NA	NA	6	57.77%
2-CQR15	0.809	4	0.428	0.569	5	74.52%
		8	0.443	0.574		
		11	0.417	0.590		
		12	0.448	0.576		
3-CQR13	0.836	1	0.681	-0.420	4	70.96%
		19	0.633	0.578		
4-CQR10	0.851	7	0.770	0477	4	70.96%
		15	0.797	0.492		
		16	0.605	0.434		
5-CQR9	0.829	9	0.836	0.423	2	61.96%
6-CQR8	0.846	5	0.746	0.504	2	66.4%
7-CQR7	0.822	18	0.905	0.582	2	70.24%
8-CQR6	0.813	13	0.794	0.668	1	58.58%

Table 6.3 shows that for EFA 2, 3 and 4, the MSA values of the items removed were all below 0.8 and the factor loadings were all low. After each successive EFA, the MSA and factor loadings were re-calculated. Although from the fifth analysis on, some of the MSA values are above 0.8, they are still the lowest of the remaining items and the factor loadings are still low. The necessity of reducing the number of items to increase the utility of the scale justified removing more items. A uni-dimensional factor structure was suggested by the Eigen values and scree plot shown in Figure 6.1. The percentage of explained variance of the one factor CQR6 is reasonably good at >50%. The uni-dimensional nature of the CQR6 also allowed for the construct validity to be tested, with a high Cronbach's α of 0.85.

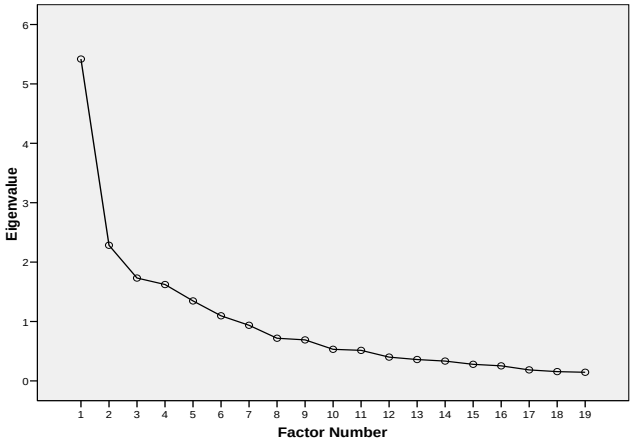


Figure 6.1: Scree plot of the factor structure of the CQR19

The final scale has a KMO value of 0.81 and the amount of variance that is explained by these six items is 58.58% which is satisfactory for this type of scale. The communalities of the items after extraction are all reasonably high at >0.42 indicating that the items share some common variance. The factor loadings are also high at 0.65 (item 3) to 0.80 (item 17), indicating that they are all strongly related to the latent construct. The inter-item correlations for the CQR6 were checked and the Pearson's r correlations between the items were at or above the recommended level of 0.30 (Tabachnik, 1989) at between 0.30 (items 3 and 13) and 0.64 (items 13 and 14). In contrast, the CQR19 had inter-item correlations of between 0.004 (items 8 and 15) and 0.68 (items 14 and 18) with the majority being below 0.30. The Cronbach's α for the CQR6 is 0.85 which shows a high level of internal consistency. To check the criterion validity, Pearson's r correlations were calculated between the items on the CQR6 and the Beliefs about Medications Questionnaire. The correlations between the BMQ and CQR6 were all >0.3 with the highest being 0.53 (CQR item 14 and BMQ item 3), indicating that the CQR is closely related to beliefs about medications.

6.4: Discussion

The CQR19 was developed by de Klerk et al. (1999) based on literature reviews and interviews with patients. However, the authors report moderate levels of internal consistency (de Klerk et al., 1999). Although the CQR19 was validated against eMEMs and regression analyses showed 98% sensitivity of the scale for detecting low adherence, a factor analysis has not been reported meaning the factor structure is unknown. This could explain the low Cronbach's α that is reported by de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden (2003).

The CQR19 was also found to be weak in this study. A number of items were shown to not adequately measure the construct of adherence. The study by de Klerk, van der Heijde, Landewe, van

der Tempel & van der Linden (2003) also suggested that some items were superfluous as when they carried out a multiple regression analysis, they found that four items explained 35% of the variance (items 3, 7, 5 and 12) and that the remaining 15 items together explained only 10% of the variance. Added to this, they performed a stepwise regression with each of the 19 items entered as a separate step. This would have inflated the amount of variance explained by each step by chance alone suggesting that the 15 items explained an inconsequential amount of the variance and were therefore unnecessary. Although the aim of this study was simply to reduce the number of items substantially, the apparently weak structure of the CQR19 warranted a factor analysis with the view to identifying the factor structure to allow a reduction in the number of items, therefore increasing the reliability. The first four factor analyses using the unweighted least squares method allowed nine items to be removed as they had low MSA values and low loadings on all of the extracted factors. This suggests that they were not adequately measuring the construct of adherence and therefore were reducing the reliability of the measure. Removing these items also reduced the number of factors from 6 to 4, indicating that they were not factors at all but that individual or small numbers of items were not loading onto the main factor and therefore creating new "factors" in themselves. It is interesting to note that the first items to be removed were those that were worded negatively. Although using reversed items is common in questionnaire research to increase the reliability of a measure, in this case they appear to have had the opposite effect. This may be because they have been worded in a confusing manner, thereby eliciting variable responses.

At EFA 5, it was decided to remove item 9 because this was cited by de Klerk et al (1999) as being one of the questions that was left answered, although this was not the case in this sample. Items 13 and 18 were missed most often in this sample. This could be because patients who had not missed doses of their medication cannot accurately answer the questions, which was expressed to the researcher by respondents on a number of occasions. Also, the issue of increased symptoms as a result of not taking the medications is addressed by items 2 and 14 which have been included in the final CQR6 and therefore the decision was made to use this version of the scale as a final measure of adherence. This also means that the scale has been greatly reduced, increasing the clinical utility.

The CQR6 appears to be a more reliable measure than the CQR19 because the Cronbach's α is reasonably high at 0.85. The unidimensional factor structure is also much clearer with high factor loadings of all of the items in the CQR6 whereas the factor structure was unclear and weak in the CQR19. The amount of explained variance is satisfactory at 58.58% and is comparable to other scales of this type. As no objective measure of adherence was used in this study, it is unclear as to how useful the CQR6 is in measuring and predicting medication adherence. This should be tested in a larger cohort as the reduction is based on a sample size of 59 as only fully completed questionnaires

were included. As the structure of the inter-item covariance was not clear in the original CQR19 and an objective measure of adherence was not available in this study to compare missing answers, it was not possible to replace the missing items with substitutes. The EFA resulted in a questionnaire that is short, appears to have good internal consistency, correlated well with other validated measures and is easy to use due to its unidimensionality.

Study 6.2: Confirmatory factor analysis of the reduced CQR in two datasets.

6.5: Introduction

Study 6.1 showed that reducing the number of items in the CQR19 is possible without losing a sizable amount of explained variance, creating a briefer, more clinically viable questionnaire. The reduction from 19 items to 6 also allowed for a more comprehensive factor structure with each question loading highly onto a single factor.

As the sample size in Study 6.1 is relatively small at 66 (4 removed due to missing data), the same methodology was used to carry out an exploratory factor analysis in a separate sample Rheumatology patients from Dudley, UK (hereafter termed the "Dudley" dataset). This sample was collected independently of this programme of research and is used with permission of the primary author (Dr Gareth Treharne, Department of Psychology, University of Otago, New Zealand). Using the same methodology as for the original sample (hereafter termed the "Hertfordshire" dataset), this larger sample (N=155) also demonstrated that the original 19 item CQR could be reduced without losing significant amounts of explained variance. As the methodology was identical to that described for the Hertfordshire dataset and the results very similar, the exploratory factor analysis for the Dudley dataset is not shown but is summarised below. The Dudley dataset produced a reduced CQR with 10 items (CQR10), retaining all of the same items as the CQR6 with the exception of item 10 which was removed due to a lack of validity in the Dudley sample. This produced a uni-dimensional scale that explained 41% of the variance in the sample. In order to determine whether the CQR6 or CQR10 is more suitable, it is necessary to carry out a confirmatory factor analysis (CFA). This will test the fit of the identified model, showing how much each item contributes to the measurement of the latent construct of adherence. Therefore, the CFA will show how much variance in medication adherence as measured by the CQR is explained by the reduced models as a whole, as well as clarifying which individual items are most useful. The aim of the second study therefore is to test the reduced versions of the CQR and determine which models produce the best fit to explain adherent medication taking behaviour.

6.6: Methodology

6.6.1: Samples

Two separate samples were used in this study, which were combined to increase the power of the confirmatory factor analysis. The details of each of the samples are shown in Table 6.2. The first

sample, named the "Hertfordshire" dataset was collected at St Albans City Hospital and Hemel Hempstead General Hospital during the summer of 2008. The method of collection is described in Study 6.1. The second sample, named the "Dudley" dataset was collected in Dudley and is described by Treharne et al. (2004). An ANOVA test showed that the mean age of the Hertfordshire dataset was significantly younger than the Dudley dataset ($F(1, 219) = 7.27$ $p=0.01$), but that the two samples did not differ significantly on gender or disease duration. However, as the effect size of the differences between the ages was small with Cohen's $d = 0.17$, the two datasets were combined to increase the power of the confirmatory factor analysis.

6.6.2: Procedure

Following the exploratory factor analyses that created the CQR6 and the CQR10 in the Hertfordshire and Dudley datasets respectively, a confirmatory factor analysis was carried out using Lisrel 8 student edition. Firstly, each of the models that resulted from the EFA in each of the datasets was tested in the other dataset; i.e. the CQR6 model that was generated by the Hertfordshire dataset was tested in the Dudley dataset and the CQR10 model that was generated in the Dudley dataset was tested in the Hertfordshire dataset. These two datasets were then combined in order to increase the sample size, and subsequently the power of the CFA. As the data were categorical, new polychoric and asymptotic covariance matrices were created from which the subsequent analyses were performed as there was a non-normal response pattern. Datascreening was then carried out in order to check for univariate and multivariate normality and missing cases. The three models that were identified *a priori* by the EFA were tested using Robust Maximum Likelihood and their fit to the data was evaluated using standard goodness-of-fit indices. As these models did not provide a satisfactory fit, some model modification was carried out using the modification indices given by Lisrel. These included analysing the correlated residuals and covariances among items. Models that showed sufficient fit to the data had their measurement and structural models tested. The final models were tested in a random sample of 500 created using the bootstrap test in Stata with the user written "cfa" command by Kolenikov (2009). New goodness-of-fit indices and R^2 values were generated for each item. These were assessed to the same criteria as above.

6.6.3: Statistical Analysis

Goodness-of-fit indices were chosen to include at least one index from each fit class; absolute, parsimony and comparative, as recommended by Brown (2006). It is necessary that the specific indices that are used are tailored to each study as they are each influenced by different aspects such as sample size or the use of categorical data. For the purposes of this analysis, the following fit indices were used with the respective cut-off values, recommended by Hu & Bentler (1999). Absolute

fit indices; χ^2 and Satorra-Bentler Scaled χ^2 because the latter adjusts for the fact that a polychoric correlation is being used, Root Mean Square Residual (RMR; <0.08). Parsimony fit indices; NCP and Root Mean Square Error of Approximation (RMSEA; <0.08). Comparative fit indices; Normed Fit Index (NFI; >0.9) and Comparative Fit Index (CFI; >0.9).

In addition to these model fit indicators, the measurement and structural parts of the model were also inspected. To test the structural model, the direction and strength of the estimated parameters were checked to ensure that they were in the hypothesised direction. For this model, all parameter estimates should be positive, with a t value of >1.96 (significant to α=0.05).

To test the measurement model, two calculations were carried out by hand to determine i) the composite reliability and ii) the average variance extracted. Both equations make use of the indicator loadings and indicator error variances. These tests can show how reliable the model is as well as how much of the variance is captured by the construct in relation to the amount of variance due to measurement error.

$$\rho_c = \frac{(\sum \lambda)^2}{(\sum \lambda)^2 + \sum(\theta)}$$

Where ρ_c = composite reliability

$\lambda = \text{indicator loadings}$

$\theta = \text{indicator error variances}$

$\sum = \text{summation over the indicators of the latent variable}$

(Equation 6.1)

Using equation 6.1 allows the composite reliability to be calculated using information provided by Lisrel (Diamantopoulos, 2000). This shows the reliability of the latent construct, and values should be >0.6 (Bagozzi & Yi, 1988).

$$\rho_v = \frac{\sum \lambda^2}{\sum \lambda^2 + \sum(\theta)}$$

(Equation 6.2)

Equation 6.2 (Diamantopoulos, 2000) enables a calculation of the average variance that is extracted and shows directly the amount of variance that is captured by the construct in relation to the

amount of variance due to measurement error (Fornell & Larcker, 1981). Therefore, ρ_v>0.5 indicates that more than half of the variance is accounted for by the construct, whereas ρ_v<0.5 indicates that most of the variance is accounted for by measurement error alone. Therefore, in order to evaluate how reliable the model is, it is desirable for ρ_v>0.5.

Bootstrap tests were used to test the final models in a randomly selected sample of the combined datasets. The method in Stata by Kolenikov (2009) sets the seed at 1010101 and uses Bollenstine strapping with 500 repetitions in 20 iterations. This gives parameter estimates and R^2 values for each item, as well as fit indices for the model as a whole. These were all assessed to the same criteria as for the models in the combined dataset.

The original authors of the CQR19 give a weighted regression model that can be used to classify patients as "high" (>80% of medication taken) or "low" (<80% of medication taken) medication adherers (de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden, 2003). In order to test the discriminant ability of the CQR5, each patient was classified as either a "high" or "low" adherer, based on this regression model and a discriminant function analysis was carried out. This determined whether the model can reliably distinguish between high and low adherers. This test also gives the weights for each question to create a regression equation to be used with the reduced questionnaire to optimise classification. The sensitivity, specificity, positive and negative prediction value were calculated by hand.

6.7: Results

The CQR6 model that was extracted from the Hertfordshire dataset appears to fit reasonably well to the Dudley dataset (Table 6.4) however, the average amount of unique variance explained in the model by the latent factor of adherence is very low at 0.39. The reasonable fit indices could be the product of a more parsimonious model, rather than being a result of an actually well fitting model.

Table 6.4: Goodness-of-fit tests for the Hertfordshire and Dudley models

	Hertfordshire CQR10	**Dudley CQR6**
χ^2	1086.55 (p<0.001)	75.62 (p<0.001)
Satorra-Bentler Scaled χ^2	282.57 (p<0.001)	26.93 (p=0.0014)
NCP (90% CI)	247.57 (197.7 ; 304.92)	17.93 (6.00 ; 37.47)
RMSEA (90% CI)	0.17 (0.16 ; 0.19)	0.093 (0.054 ; 0.13)
NFI	0.91	0.95
CFI	0.92	0.97
RMR	0.11	0.077
Construct validity	0.919	0.778
Average variance extracted	0.536	0.389

As the *a priori* models did not fit well in the individual datasets, they were combined in order to create more power for the CFA. In addition, as the CQR6 was a nested model of the CQR10 but with the addition of item 10, a model that included all of the items retained across both datasets (subsequently called the CQR11) was tested in the combined dataset. Datascreening of the combined dataset showed that there were 11 missing values and 1 missing case. Once listwise deletion had been implemented, the resulting effective sample size was N=187. Of these 187 cases, there were 154 distinct response patterns, indicating that the majority of participants responded completely differently to everybody else. The two most common patterns were; i) answering *"strongly agree"* to every question (N=17) and ii) answering *"agree"* to every question (N=7). A similar pattern was not found with the *"disagree"* responses; therefore it is possible that these participants were showing social response bias as *"agree"* responses indicate high adherence rates. However, the bivariate normality appeared to hold with nearly all of the p values being non-significant and two being very close to non-significant (item 10 *vs* item 2, p=0.01 and item 18 *vs* item 3, p=0.03).

The χ^2 values and goodness-of-fit tests of the three *a priori* models in the combined dataset are shown in the first three rows of Table 6.5. The RMSEA, NFI, CFI and RMR values are all outside of the acceptable thresholds indicating that the models do not fit the data sufficiently well. The CQR6 model appears to fit slightly better although both the parameter estimate and R^2 value for item 10 are very low, and there are five standardized residuals that are higher than the accepted $\pm$2.00 (not shown) indicating that the CQR6 is not a well fitting model, particularly with the inclusion of item 10.

Table 6.5: Goodness of fit tests for model comparison

Model	χ^2 (p value)	Satorra-Bentler χ^2 (p value)	NCP (90% CI)	RMSEA (90% CI)	NFI	CFI	RMR
CQR11	465.34 (p<0.001)	172.05 (p<0.001)	128.05 (91.48;172.2)	0.11 (0.095 ; 0.13)	0.94	0.95	0.094
CQR10	420.64 (p<0.001)	144.78 (p<0.001)	109.78 (76.38;150.7)	0.12 (0.097 ; 0.14)	0.94	0.96	0.097
CQR6	95.42 (p<0.001)	28.65 (p=0.001)	19.65 (7.13 ; 39.77)	0.097 (0.06 ; 0.14)	0.96	0.97	0.071
CQR5	56.64 (p<0.001)	14.14 (p=0.015)	9.14 (1.49 ; 24.38)	0.089 (0.036 ; 0.15)	0.98	0.99	0.054

Model modification was carried out by looking at the residuals and suggested modification indices given by Lisrel. As item 10 showed very little unique variance accounted for by the latent factor (R^2 = 0.16), model modification was carried out on the CQR10 model, as this doesn't include item 10. Through subsequent modifications, it was found that 6 items consistently had the highest

standardised residuals and the lowest R^2 values, indicating that these items produced the most error and explained little of the variance in medication adherence. For these reasons, they were removed from the model to produce the CQR5 shown in Figure 6.2.

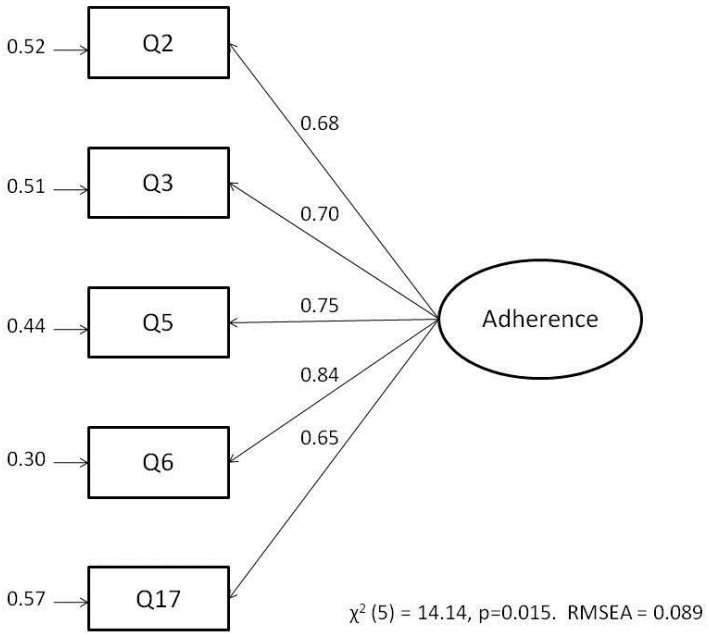


Figure 6.2: Model diagram with parameter estimates for the CQR5

The fit indices for the CQR5 were much improved and showed an acceptable model. Although the χ^2 values were beyond the acceptable values for a good fit, these are susceptible to sample sizes >100 (Hu & Bentler, 1999), making p>.05 overly sensitive and so it should be interpreted in conjunction with other indices. The RMSEA, NFI, CFI and RMR are all within the acceptable levels and show a good fit to the data. All of the t-values for the parameter estimates are positive and highly significant, which is indicated by the large parameter estimates shown in Figure 6.2. The R^2 values for the parameter estimates range from R^2=0.65 (Q17) to R^2=0.84 (Q6) showing that each of the items explained a large amount of variance in medication adherence. The average variance extracted is above the threshold of 0.5 (Bagozzi & Yi, 1988) at 0.53 showing that there is more variance explained by the items than by error and the construct validity is acceptable at 0.85, indicating a reliable measure (Bagozzi & Yi, 1988).

Although this model appears to be a good fit for the data, this may simply be that the model modification carried out *ad hoc* had over fit the model to this dataset only, which could result in it not being well applied to other datasets. In order to test this, a bootstrapping method was used to test the CQR5 in 500 randomly selected samples from the dataset. The goodness-of-fit indices show that the model still has adequate fit and so the CQR5 was tested for discriminant ability.

6.7.1: Discriminant Function analysis of the CQR5

Once the CQR5 model was established as a good fit, discriminant function analysis was carried out to determine whether it was as successful as the CQR19 at classifying patients as high or low medication adherers. The canonical linear discriminant analysis was highly significant, $F(5, 228) = 45.10$, $p<.001$, indicating that the CQR5 can effectively discriminate between high and low adherers. The effect size η^2 is large at 0.50 and the explained variance is very high at 70.5%. The structure matrix gives the correlation between the items and the function showing an indication of which variables are most closely associated with the function. Question 3 (0.84), Q17 (0.30) and Q5 (0.20) are the most strongly related. This is supported by a one way ANOVA of the item means between groups which shows that these questions produce significantly lower means by patients classified as low adherers, indicating that they *"do not agree"* more often than those classified as high adherers.

As was found by the de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden (2003), the discriminant function of the CQR5 showed that it is most effective when used as a regression equation, rather than simply as a summed score and the structure matrix gives the optimal linear combination of the questions to maximise the discriminant ability. Fisher's classification function coefficients result in the following equations:

$$D_0 = -27.611 + (4.407*Q2) + (0.939*Q3) + (6.101*Q5) + (2.366*Q6) + (2.531*Q17)$$

(Equation 6.3)

$$D_1 = -33.304 + (2.801*Q2) + (5.008*Q3) + (6.471*Q5) + (1.215*Q6) + (3.252*Q17)$$

(Equation 6.4)

Given the two parameters D_0 and D_1, if D_0 is greater than D_1 then the respondent should be classified as likely to be a low adherer. Conversely, if D_1 is greater than D_0 then the respondent should be classified as likely to be highly adherent. Table 6.6 shows the percentage of cases correctly classified by the CQR5.

Table 6.6: Classification results for the CQR5

CQR5			Predicted group membership		
		Group	0	1	Total
Original	Count	0	48	22	70
		1	5	159	164
	%	0	68.6	31.4	100
		1	3	97	100

88.5% of original grouped cases correctly classified

The sensitivity of the CQR5 for correctly classifying low adherers was 69% and the specificity was 97%. The positive predictive value was 0.91 and the negative predictive value was 0.88 indicating that the CQR5 is adequate at identifying patients with low adherence to DMARDs.

6.8: Discussion

This chapter found that reducing the CQR to just 5 items did not dramatically reduce its explanatory power and the sensitivity of identifying low adherers remained high. The exploratory factor analysis allowed for the factor structure to be made simpler and more robust with the removal of extraneous items, which reduces the burden on the patients whilst completing the questionnaire, and makes interpretation easier for clinicians.

The confirmatory factor analysis confirms that the CQR5 fits the data well and explains a good amount of variance in medication adherence for a very short, self-administered questionnaire. The parameter estimates are high and the whole questionnaire explains 52.9% of the variance in adherence, which is good for this type of measure. The CQR5 also performed at a similar rate in a bootstrapped sample of 500 repetitions, confirming that the scale had not been over-fitted to this particular dataset, but that it is likely to be applicable to the wider RA population.

Further evidence of this generalisability is shown by the fact that two of the items identified in the CQR5 (Q3 and Q5) correspond to two of the four items that the original authors found to explain 35% of the variance in their sample (de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden, 2003). As the full CQR19 only explained 46% of the variance in their sample, these items are clearly highly predictive of medication adherence.

The discriminant function analysis of the CQR5 suggests good specificity by identifying 97% of the high adherers classified by the full CQR19 and sensitivity of 69% at identifying low adherers. As the CQR5 is a nested model of the CQR19, which was used as the dependent variable to classify patients, good sensitivity and specificity would be expected. However, the good discriminatory power that the

CQR5 shows provides more evidence that the other 14 items of the CQR19 are extraneous and are not providing additional explanatory power over and above the five retained items, demonstrating the clinical utility of the more parsimonious questionnaire. The CQR5 performs equally as well as the CQR19 at correctly classifying patients, but with only a quarter of the number of questions. However, as the CQR19 was used as the dependent variable for the discriminant function analysis, the sensitivity and specificity of the CQR5 should be interpreted with caution unless it is shown to be as good when using an objective measure of adherence (such as electronic medication event monitoring) as the dependent variable.

As was found by de Klerk, van der Heijde, Landewe, van der Tempel & van der Linden (2003), the CQR5 is most predictive when used as a weighted discriminant equation. This is the optimum combination of weighted questions to classify patients as either high or low adherers, and is the function that should be used when implementing the CQR5. The structure matrix indicates that Q3; *"I definitely don't dare to miss my anti-rheumatic medication"* is the most indicative of high or low adherence as high adherers tend to *"agree"* whereas low adherers tend to *"disagree"*. It may therefore be possible to get an indication of the overall result from the answer to this question with a positive (answer 3 or 4) response indicating high adherence and a negative (answer 1 or 2) response indicating low adherence.

The utility of the CQR5 is also suggested by the fact that within this sample of 234 patients, 22% (N=53) were classified as being low adherers based on their CQR5 scores. This is in accordance with previously published figures (DiMatteo, 1994; Treharne et al., 2004; Treharne et al., 2006) of sub-optimal adherence to medication regimens.

Four of the removed items explore issues of medications in general and the patients' expectations of their medications. These constructs are well measured in Horne et al.'s (1999) Belief's about Medications Questionnaire (BMQ) which has been tested and found to be reliable and valid. It could therefore be suggested that the BMQ should be used in conjunction with the CQR5 to specifically address this construct. The two other removed items are concerned with reduced medication adherence on weekends and holidays. Unsurprisingly, it was found that these two items were strongly correlated ($r = 0.64$, $p<0.001$), although neither of them correlated strongly with any other item. Higher non-adherence when away from the home is common (Garcia-Gonzalez et al., 2008) and should be acknowledged within the clinical setting to plan and account for periods of sub-optimal adherence to DMARDs.

Above all, this study shows that it is possible to reduce the number of questions of the CQR19 without losing its explanatory properties, thus improving the clinical utility.

6.9: Conclusions

Although electronic medication event monitoring remains the gold standard, the CQR5 is cheap and easy enough to be widely used in the clinic and is short enough so as not to burden patients. This makes it ideal as an indicator of medication adherence when assessing efficacy of medications, as well as for research involving medication adherence as it can easily be incorporated into the appointment or within a battery of questionnaires. A further advantage of the CQR5 over other more expensive monitoring techniques is that the answers to the questions could give an indication of the reasons behind the non-adherence that can then be addressed by the clinical care team. For these reasons, the CQR5 will be used in this programme of research to assess adherence to DMARDs by rheumatoid arthritis patients.

Chapter 7

Using social cognition models of illness to predict adherence to DMARDs by rheumatoid arthritis patients: Cross-sectional analysis

7.1: Introduction

Chapter 1 discussed the significant burden of self-management on patients once diagnosed with RA. Patients are required to attend outpatient appointments, have regular blood tests as well as manage an often demanding treatment regimen consisting of polypharmacy with differing administration requirements, all whilst the patient copes with the pain and malaise generated by the disease itself. There is strong evidence that early and sustained treatment with disease modifying anti-rheumatic drugs (DMARDs) leads to better outcomes in the short term (van der Herijde et al., 1996) as well as in the long term (Fitzcharles et al., 2000; Fries, Williams, Morfeld, Singh & Sibley, 1996) because continued synovitis leads to irreversible joint damage (Neidel, Schulze & Lindschau, 1995). However, medication non-adherence has been shown to be as high as 41-75% in RA (de Klerk et al 2003; Viller et al., 1999). Non-adherence can result in delayed recovery (Grijalva et al., 2007) and increased mortality and morbidity (DiMatteo, 1994) leading to higher health service costs (DiMatteo, 1994; Grijalva et al., 2007; Hughes et al., 2001; Steiner & Prochazka, 1997; Urquhart, 1999). A Recent estimate of the annual cost to the NHS of treating RA in the UK was £689 million with an additional £7.9 billion per year of lost productivity due to sick leave and early retirement (NRAS, 2010). As well as the cost to society, as being employed has been shown to improve psychological functioning (Albers et al., 1999) it is clear that reducing the effects of RA through appropriate drug management is imperative for both patients and the wider society.

DMARDs are the corner-stone of treatment for RA and should be initiated within three months of symptom onset (NICE, 2009) and sustained over the duration of the disease to maintain disease suppression (Nikiphorou & Young, 2010). Many patients can be maintained on DMARDs such as Methotrexate, however some patients require escalation to anti-TNF α therapy although this is very expensive and has potentially more serious side effects. However, the benefits of DMARDs can be difficult for patients to perceive because of a delay of 8-12 weeks to experience positive effects whereas unpleasant side effects can emerge very quickly (Young, 2008). This is particularly relevant for newly diagnosed patients who will be required to take at least one DMARD whilst coming to terms with their diagnosis and potentially experiencing no benefit for three months. As well as

developing a routine for taking medication, their beliefs about their illness and treatment could be strongly influenced by the lack of an immediate effect of DMARDs leading to potentially low adherence. DMARDs are also required to be taken regularly even during periods of quiescence where the lack of an immediate association with the benefit can increase the likelihood of non-adherence (Garcia-Gonzalez et al., 2008; Kane, Cohen, Aikens & Hanauer, 2001; Kane, Huo, Aikens & Hanauer, 2003). This would be relevant to patients with established but low-activity disease who may struggle with the cost-benefit analysis of taking DMARDs that is inherent in the social cognitive models of illness if the benefit is difficult to see. Despite this delay, DMARDs have been shown to be very efficacious at promoting and maintaining remission and are well tolerated by most patients (ten Wolde et al., 1996) and so it is imperative that patients with established disease continue to adhere to their prescription to avoid joint damage and disability. For these reasons, adherence to DMARDs is the focus of this study to reduce the burden to the patient and the NHS of non-adherence to these cheap and mostly efficacious medications.

Although adherence to DMARDs has been researched in RA (de Klerk et al., 2003; de Thurah et al., 2010; Goodacre & Goodacre, 2004; Grijalva et al., 2007; Park et al., 1999; Treharne et al., 2004; Viller et al., 1999), patients in different stages of the disease have rarely been separated to identify differences both in adherence and in the social cogntion models of illness. As experience of the illness forms a fundamental part of the models, there is a need to specifically target newly diagnosed, established and patients who have escalated to biologic therapy to establish the differences in adherence to DMARDs and the social cogntion models of health that these patients may exhibit.

As discussed in Chapter 2, non-adherence can be intentional, where a deliberate decision is made not to perform the behaviour or unintentional which is largely due to forgetting. Although there are likely to be different causes and effects of different adherence types, they have not been reliably separated in the literature. Studies by Lehane & McCarthy (2006), Lowry et al. (2005) and Atkins & Fallowfield (2006) have demonstrated very different prevalence of intentional and unintentional non-adherence to treatment in chronic illnesses other than RA with forgetting being much more apparent than intentional non-adherence. Although a thorough review by Clifford, Barber & Horne (2008) demonstrated the importance of differentiating between the two, few researchers have consistently and reliably measured and reported the differences in their research, particularly in rheumatoid arthritis. Therefore, this study will use the CQR5 developed in Chapter 6 to measure intentional non-adherence along with a separate measure of unintentional non-adherence to provide more evidence of the different processes behind them.

The review of social cognition models of health in Chapter 2 showed that there are three main models that have been used to explain health behaviours including medication adherence. The Theory of Planned Behaviour (TPB) and the Health Belief Model (HBM) were developed in the 1980s and 1960s respectively and have been applied extensively to preventive health behaviours but less so to medication adherence in chronic illness. Aspects of social influence have been measured by Owen et al. (1985) and DiMatteo (2004) who found that the quality of the relationship with friends, family and the healthcare team can influence adherence to treatment. Although not directly measuring the HBM, Johnson et al. (1999), Kane (2006) and Goodacre & Goodacre (2004) demonstrated that patients with RA consider the costs and benefits of medications which are related to adherence. The Self Regulatory Model and more specifically Illness Perceptions have been the focus of much recent research into adherence behaviours in chronic illness. There have been mixed results as higher perceptions of the chronicity and seriousness of an illness generally leads to worse outcomes (Hagger & Orbell, 2003), however with regards to treatment adherence in chronic, progressive illnesses similar to RA, these perceptions have been shown to be beneficial (Chilcot et al., 2010; Horne & Weinman, 2002). However, the review by Hagger & Orbell (2003) acknowledges the fact that the aetiology and experience of each disease will alter the illness perceptions and therefore they should be investigated separately to provide information for potential interventions. The addition of treatment beliefs as measured by the Beliefs about Medications Questionnaire (BMQ) have generally improved the predictability of the SRM to treatment adherence with higher perceptions of necessity being significantly associated with better adherence (de Thurah et al., 2010; Horne, 1999; Llewellyn et al., 2003; Treharne et al., 2004).

All of these models are based on a cost-benefit decision performed by the patient and therefore there is considerable collinarity with the factors that are being measured. For this reason, and the fact there are a number of proposed models of health, it would be advantageous to test each of the models in the same dataset to establish which factors or which models are the best predictors of adherence. However, only one study has tested the Theory of Planned Behaviour and the Self Regulation Theory together. Orbell et al. (2006) found that when combining the two models, Perceived Behavioural Control (TPB) was predictive of adherence to colposcopy follow-up treatments but that none of the illness perceptions were predictive, although treatment control was predictive when the SRM was tested alone. This suggests that illness perceptions are related to Perceived Behavioural Control and demonstrates the importance of testing these models together to establish which factors are redundant due to a lack of predictive validity and/or colliniarity. Being able to identify the most predictive and parsimonious model would increase the clinical utility by making it

easier to identify the reasons behind non-adherence to medications and suggesting areas for intervention.

To increase the clinical utility of identifying and understanding non-adherence to DMARDs, it is important to establish the effects that it may have on disease activity, disability and changes in medication to establish the effects on prognosis. With limited time and resources available for each patient, the ability to identify which patients are struggling to adhere to their treatment regimen and the possible psychological mechanisms behind it could incentivise clinicians to address the problem and provide information for targeted intervention. For this reason, clinical outcomes such as disease activity, functional disability, service use including medication changes and quality of life will also be measured in this study to provide a more complete picture of how adherence affects patients and the progression of rheumatoid arthritis. Although there is now a raft of literature concerning treatment adherence in many different conditions (DiMatteo, 1994, 2004; Elliot, 2008; Haynes et al., 2001; Haynes et al., 2007; Hill, 2005a, 2005b; Kripalani et al., 2007; WHO, 2003), there have been a lack of interventions to address the problem to improve adherence in the long-term.

7.1.1: Aims and hypotheses

The aim of this study is to test the predictive value of three commonly used social cognition models of health behaviour in a large sample of patients with rheumatoid arthritis to explain non-adherence to DMARDs. In addition, patients in different stages of the disease, namely newly diagnosed, established and concurrent biologic treatment will be investigated separately to establish differences in adherence and social cognition models of illness that may be evident. Clinical measures of disease activity will also be collected to establish the effects of DMARD adherence on disease progression. The majority of research into medication adherence has been cross-sectional which prohibits causal inferences being made and therefore this study will follow-up patients over six months to establish the causal effects of the social cognition models on adherence. The aim is to provide evidence of the psychological factors of medication adherence based on a large sample of rheumatoid arthritis patients which is currently lacking in the literature, on which a future intervention could be based to improve medication adherence and therefore prognosis for patients.

Based on previous research on adherence and the social cognitive models of illness, it is hypothesised that there will be a number of differences between the three *treatment groups*:

1) Intentional non-adherence will be higher in the biologic group because of previous failure of DMARDs to promote remission.

2) Unintentional non-adherence will be higher in the newly diagnosed group because of a lack of routine in taking medications (Atkins & Fallowfield, 2006; de Thurah et al., 2010; Woods et al., 2008).
3) Factors of the social cognition models will differ between the three treatment groups because of the influence of the differing experience of the disease (Berry et al., 2004; Goodacre & Goodacre, 2004).
4) Demographics of the three treatment groups will differ with the newly diagnosed group being younger with less severe disease activity.

There has been a large amount of previous research on the effects that social cognitive models of illness have on adherence on which the following hypotheses are based for the entire sample:

5) Different factors of the social cognition models will be predictive of intentional and unintentional adherence because of the different mechanisms behind them.
6) Theory of Planned Behaviour; higher Perceived Behavioural Control and perceptions of Subjective Norms will be predictive of higher adherence (Ajzen, 1991; DiMatteo, 2004; Owen et al., 1985).
7) Health Belief Model; higher perceptions of barriers to medication taking will be predictive of lower adherence whereas higher perceptions of disease severity will be predictive of higher adherence (Berry et al., 2004; Johnson et al., 1999; Kane, 2006; Lumme-Sandt et al., 2000; Svensson et al., 2000).
8) Self Regulation Model; higher perceptions of chronicity, consequences and treatment control will be predictive of higher adherence (Chilcot et al., 2010; Horne & Weinman, 2002).
9) Beliefs about medications; higher perceptions of necessity of DMARDs will be predictive of higher adherence but concerns about DMARDs and general beliefs will not be predictive (de Thurah et al., 2010; Horne, 1999; Llewellyn et al., 2003; Treharne et al, 2004).

The effects of adherence on rheumatoid arthritis specifically have received little attention cross-sectionally but based on evidence that lower adherence results in worse disease outcomes (DiMatteo, 1994; Grijalva et al., 2007; Hughes et al., 2001; ten Wolde et al., 1996) the following hypothesis was generated:

10) Non-adherence to DMARDs will be related to lower quality of life and worse disease outcomes.

7.2: Methodology

7.2.1: Patients

In total, 238 of the 263 patients approached agreed to participate, although 49 did not return questionnaires or later withdrew. An additional 161 questionnaires were mailed to less accessible patients including those concurrently prescribed biologic therapy and those who received a diagnosis of RA within the past 12 months. Thirty-eight (24%) postal questionnaires were returned. Analysis was thus performed on 227 participants. Figure 7.1 shows the recruitment process. The mean age was 57.69 (SD=15.03) years and 75.78% were female. Demographic and clinical details for the whole sample are shown in Table 7.2.

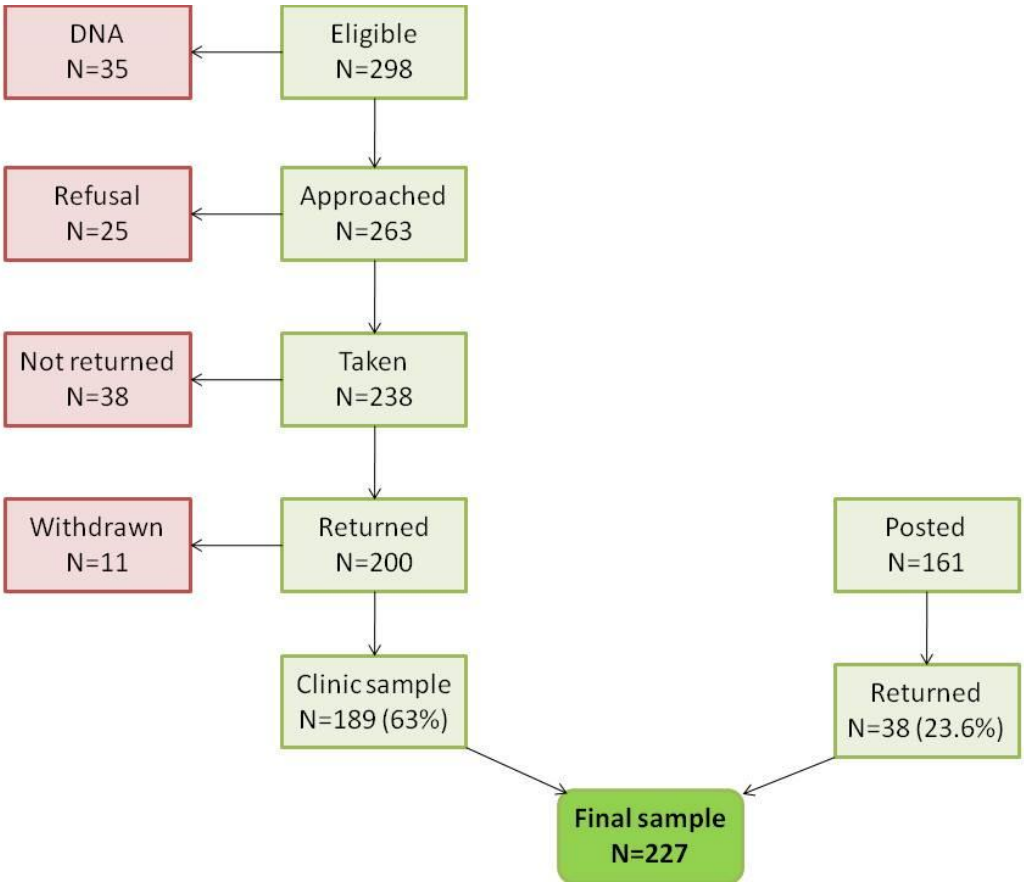


Figure 7.1: Recruitment flow chart

7.2.2: Materials and procedure

All consecutive patients aged over 18 diagnosed with rheumatoid arthritis and currently prescribed at least one DMARD in six hospitals across Hertfordshire and north London were invited to participate. In order to recruit patients in specific phases of treatment, dedicated clinics were targeted for recruitment and postal questionnaires were sent to patients. Patients were made aware that they would be required to complete the questionnaires again six months later and all patients gave written informed consent. Patients completed the questionnaires by themselves in the clinic or at home and returned in a stamped addressed envelope. A number of clinical variables were collected from the notes of patients who consented to the study including; DAS28, current prescription, date of diagnosis, date of first DMARD prescription and latest inflammatory blood markers (ESR and CRP). All data were confidential and assigned an anonymity identification number. The data were subject to double data entry to ensure there were no errors. The study was approved by the Hertfordshire NHS REC (09/H0311/102) and all data handling conformed to Good Clinical Practice Guidelines.

The full questionnaire is shown in Appendix 7.1 and described in more detail below. Questions included self-reported adherence (CQR5, RAM), quality of life (EQ5D and visual analogue scale), social cognition models of health behaviour including; Theory of Planned Behaviour (Orbell et al., 2006), Health Belief Model (Nexoe et al., 1999), Illness Perceptions (IPQ-R; Moss-Morris et al., 2002), Beliefs about Medications (BMQ; Horne et al., 1999) and self-reported functional status (HAQ; Fries et al., 1980).

Theory of Planned Behaviour

Attitudes

Participants are presented with eight pairs of statements that represent attitudes towards their DMARDs. They are instructed to circle one statement from each pair that would indicate a positive or negative attitude.

Subjective Norm

Three questions regarding the perception of other people's opinion of whether or not the patient should take their medication are scored on a 5 point Likert scale. A sumscore is generated to give a score of the patient's perceived level of subjective norm with regards to taking medications. Higher scores indicate a higher perception that other people think they should take their DMARDs.

Perceived Behavioural Control

Seven questions relating to the amount of control the person feels over successfully overcoming obstacles in order to take their medications accurately are scored on a 5 point Likert scale. Higher scores indicate more confidence by the patient that they have control over their medication taking.

Intention

Patients are asked to indicate their intention to take all prescribed doses of their DMARDs over the next month by circling one of four statements ranging from *"not at all"* to *"all of the time"*.

The Health Belief Model

Barriers

The barriers section contains six questions relating to various factors that could act as barriers to taking medications. They refer to conceptual and logistic issues such as *"I do not want to take medications"* and *"my medications are too expensive"* respectively. A sumscore for all of the barriers questions ranges from 6 to 30 with higher score indicating more barriers to taking medications.

Benefits

Four questions related to the potential for DMARDs to prevent the patient from becoming ill are scored on a 5 point Likert scale. The sumscore ranges from 4 to 20 with higher scores indicating a higher potential for benefits of taking DMARDs.

Severity

The final five questions relate to the arthritis itself and how a "flare up" could affect the patient's life. The questions are scored on a 5 point Likert scale with sumscores ranging from 5 to 25. Higher scores indicate that the patients perceive a flare up to be very severe.

Self Regulatory Model

Identity

Patients were presented with a symptom index of fourteen symptoms; 5 of which were specifically related to arthritis (e.g. swelling of the joints) and 9 of which were generic (e.g. headache). Patients were required to indicate i) whether they had experienced each symptom over the past two months and ii) do they believe this symptoms was caused by their arthritis. In line with guidelines, a sumscore of symptoms that were believed to be caused by the arthritis was used as the identity score.

Chronicity

Five questions relating to the chronicity of the arthritis were scored on a 5 point Likert scale from *"strongly disagree"* to *"strongly agree"*. Two of the items were reverse scored. After reversing, the sumscore ranged from 5 to 25 with higher scores indicating longer perceived chronicity of the arthritis.

Cyclical timeline

Four questions describing a cycling course of symptoms were scored on a 5 point Likert scale. Sumscores ranged from 4 to 20 with higher scores indicating more cycling or variability in symptoms.

Consequences

The consequences factor refers to factors that have a strong impact on the patient's life for example *"my arthritis has serious financial consequences"*. Six questions are scored on a 5 point Likert scale with one question being reverse scored (*"My arthritis does not have much effect on my life"*). The

sumscore generated ranges from 6 to 30 with higher scores indicating higher perceived consequences of the arthritis.

Personal control

Personal control refers to the level of perceived control by the patient to influence the symptoms and course of the arthritis. There are six questions, two of which are reversed. Sumscores range from 6 to 30 with higher scores indicating higher perceived personal control.

Treatment control

Six questions relating to the ability of medications to control arthritis are scored on a 5 point Likert scale with two reverse scored questions. Sumscores range from 6 to 30 with higher scores showing a higher perception that medications can improve arthritis.

Coherence

Five questions measured patients' *perceived* knowledge about their arthritis and the symptoms such as *"I don't understand my arthritis"*. It is important to note that the patients' actual knowledge about arthritis is not tested but rather it is an indication of how confident they feel about their knowledge. One question is reverse scored and sumscores range from 5 to 25. Higher scores indicates that the patient *does not* consider themself to have a high level of knowledge about their arthritis.

Emotional effects

A factor measuring general emotional affects of arthritis includes questions about feeling depressed, upset, anxious, afraid and angry specifically about having arthritis. Six questions are included, of which one is reverse scored. Sumscores range from 6 to 30 with higher scores indicating a more negative emotional effect of arthritis.

Beliefs about Medications Questionnaire

The BMQ has two subscales; general and specific which each have two further subscales. The general subscale has eight questions and refer to patients' feelings that in general, medicines are harmful (General Harm) and that in general, medications are over used (General Overuse). The specific subscale has ten questions that refer directly to the medications prescribed for rheumatoid arthritis and include five questions referring to concerns patients might have about taking these (Specific Concerns) and five questions related to the patients' perceptions that the medications are necessary in order to stay well (Specific Necessity). In all cases, questions are scored on a 5 point Likert scale with higher scores demonstrating a stronger association with the subscale.

Adherence measures

The Compliance Questionnaire for Rheumatology (CQR5)

The reduced Compliance Questionnaire for Rheumatology (CQR5) that was developed in Chapter 6 was used to measure intentional non-adherence. Based on the discriminant function scores, patients were classified as being "high" or "low" adherers.

Reported Adherence to Medications (RAM)

Two questions from the reported adherence to medication scale were used which measure unintentional non adherence (*"I sometimes forget to take my medicines"*) and intentional non adherence (*"I sometimes alter the dose of my medicines to suit my own needs"*). These were scored on a 4 point Likert scale from *"don't agree at all"* to *"agree very much"*. For the purposes of the analysis, responses were dichotomised as agree/disagree.

Disease related measures

Health Assessment Questionnaire (HAQ)

The HAQ measures the level of difficulty that a patient has faced in the past week carrying out eight everyday tasks such as dressing, walking and reaching for objects. It also measures whether a patient has needed an aid or device and/or help from another person to carry out the task. An index between 0 and 3 is calculated with 0 indicating no problems with these tasks and 3 indicating extreme disability. Although there is no specific cut-off value, scores over 2 are considered to indicate high disability.

DAS28

The DAS28 is described in Chapter 1, section 1.4.2 and was measured on the day of recruitment and taken from patients' medical notes.

Quality of Life (QoL) measures

EQ5D

The EQ5D (Dolan, 1997; EuroQol Group, 1990) is a measure of quality of life developed by the EuroQol group to be used for patients with a physical illness. It consists of a 200mm Visual Analogue Scale (VAS) asking patients to indicate their health state today from worst imaginable health state (0) to best imaginable health state (100) as well as a questionnaire measuring five components of health; mobility, self care, usual activities, pain and anxiety/depression. The five components are

measured on a three point scale; *no problems-some problems-unable to complete the task*. These five scores are then transformed into a weighted sumscore to give a utility value scoring from 0 (death) to 1 (perfect health). Due to the nature of the questions, it is possible to achieve a negative value which is considered to be "worse than death". The two measures are scored separately but used in conjunction to give a measure of quality of life.

7.2.3: Statistical analyses

Patients were classified into treatment and adherence based on the following criteria; 1) newly diagnosed patients, diagnosed within the six months prior to recruitment, 2) established patients, diagnosed more than six months prior to recruitment and not currently prescribed biologic therapy and 3) biologic patients, prescribed traditional DMARD concurrently with anti-TNF α therapy. Three adherence scores were obtained for each patient. Firstly, using the discriminant function analysis reported in Chapter 6, patients were classified as being either high (1) or low (0) intentional adherers. Secondly, using the RAM question 1, patients were classified as forgetting (agree or strongly agree) or not forgetting (disagree or strongly disagree). The overall adherence measure is a composite of these scores. If a patient was scored as a high intentional adherer *and* does not forget, overall adherence is high. If a patient scores as a low adherer on either the CQR5 or RAM or on both, they are classified as a low overall adherer.

Sumscores were generated for each psychological factor for each of the models for each patient. Mean sumscores were then established for; i) the entire sample, ii) each treatment group and iii) each adherence group. Differences in illness and treatment perceptions were tested using one way ANOVA with Bonferroni correction for multiple testing. Differences between categorical variables were tested using χ^2. All significance testing used α level of 0.05. In addition to univariate analyses, Pearson's r correlation was used to assess bivariate associations between all of the psychological factors and adherence.

To establish the predictive ability of the models to predict non-adherence, adherence was dichotomised so that 1=high adherence and 0=low adherence and logistic regression was carried out. Logistic regression is the most suitable analysis for binary categorical dependent variables (Tabachnik, 1989) and is evaluated by the -2 log likelihood statistics which can be interpreted as χ^2. The analysis also provides statistics of the number of cases correctly identified in each group based on the independent variables to evaluate the utility of the model. Although a true R^2 statistic indicating the amount of variance explained by the model is not possible with logistic regression, a number of proxies have been designed and Naglekerke's R^2 is used in this analysis to aid comparison of the different models. Each variable is evaluated using Wald's χ^2 statistic and the associated odds

ratio to interpret the effect that the variable has on predicting the dependent variable. Comparison of the models in this way was also carried out by Orbell et al. (2006) and allows comparability across the studies.

In order to establish the different social cognition models of illness for the treatment groups, a discriminant function analysis was carried out between the three treatment groups. The methodology is the same as that described in Chapter 6, section 6.6.3. To establish the utility of the social cognition models to predict non-adherence, logistic regression was carried out.

7.3: Results

7.3.1: Data screening

Missing data for most questionnaires was negligible, ranging between 0 and 3%. However, there were large numbers of missing responses for the Theory of Planned Behaviour Attitudes questions ranging from 26.9% for *necessary-unnecessary* to 52.9% for *pleasant-unpleasant*. Closer inspection indicated that this was likely due to patients misunderstanding how to answer the question as often only one option out of the eight possibilities was marked (e.g. only *"necessary"* was marked), rather than patients choosing the most appropriate response for each option (e.g. marking *"wise", "important", "satisfying"* etc). As so much of the Attitudes data was missing and it was not missing at random, this factor had to be excluded from further analysis.

The Theory of Planned Behaviour aims to explain both intention to perform the behaviour and the behaviour itself. For this reason, a question measuring patients' intention to take all of their DMARD doses over the next month was measured with the question; *"over the next month, my goal is to take my disease modifying anti-rheumatic medications: (not at all - some of the time - most of the time - all of the time)".* However, Figure 7.2 shows that there was very little variability in the responses to this question as 91.2% of patients responded *"all of the time"* and therefore it was not appropriate to use it as a dependent variable in any of the analyses.

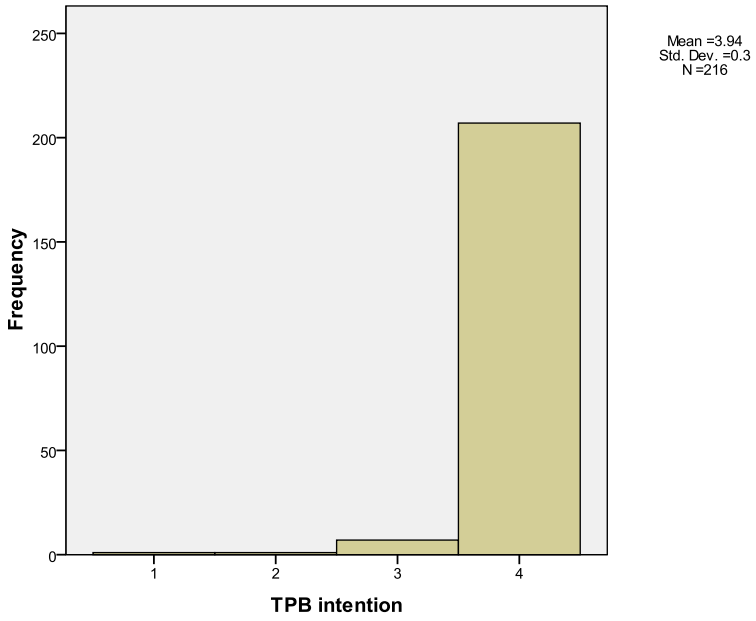


Figure 7.2: Distribution histogram of responses to Theory of Planned Behaviour "intentions" question

Most statistical packages use listwise deletion to remove cases that have incomplete datasets. However, as most of the data was shown to be missing at random (other than TPB Attitudes), it was possible to replace missing values with a suitable substitute. Ten multiply-imputed data sets were generated using the ICE package in Stata 11.1 for variables other than TPB Attitudes, which performs multiple imputation by chained equations (Royston, 2004). Analyses were then conducted separately on each of these datasets and averaged using Rubin's rule (Carlin, Galati & Royston, 2008).

Disease related factors were measured by the HAQ which is a questionnaire that was included in the battery of questionnaires completed by patients and the DAS28 which was entered by the physician on the day of the clinic visit. However, DAS28 can only be completed if a blood test was available on the day of the visit which led to 63 missing cases (27.8%). However, there is no reason to believe that cases are missing in a systematic way and so for analyses involving DAS28, listwise deletion was employed.

On inspection of the data, most of the categorical variables were negatively skewed. For this reason, all independent variables were z transformed so as not to violate the assumption of normality which is necessary for many of the statistical analyses that were carried out.

7.3.2: Reliability of scales used

The reliability of the scales used to measure the social cognition models of illness was tested for internal reliability using principle components analysis and Cronbach's α shown in Table 7.1. The

principle components analyses highlighted some issues with weak questions. Most notably, although three components were extracted for the Health Belief Model which would be expected, examination of the rotated component analysis shows that the loadings of the questions do not correspond to the predefined factor structure (Appendix 7.2). This is supported by the fact that the Cronbach's α for the named factors are less than satisfactory for barriers and benefits at 0.63 each. However, the internal consistency of the newly defined components was not improved (Appendix 7.2) and so the predefined structure was maintained for subsequent analyses in order to be comparable to previous research.

Table 7.1: Internal consistency shown by Cronbach's α for each of the psychological factors

Scale	Cronbach's α
Theory of Planned Behaviour	
Social Norm	0.53
Perceived Behavioural Control	0.78
Important others	*0.76*
Health Belief Model	
Barriers	0.63
Benefits	0.63
Severity	0.85
Self Regulatory Model	
Identity 1 – general unwell	0.74
Identity 2 – RA symptoms	0.66
Identity 3 – weight	0.66
Chronic timeline	0.85
Cyclical timeline	0.76
Consequences	0.82
Personal control	0.81
Treatment control	0.65
Cohesion	0.92
Emotion	0.88
Beliefs about Medications Questionnaire	
General harmful	0.67
General overuse	0.83
Specific concerns	0.80
Specific necessity	0.90

For the most part, the internal consistency was good for each of the other factors. Exceptions include the BMQ general overuse scale at 0.67, however similar α levels have been found in other studies (Menckeberg et al., 2008; Treharne et al., 2004). In the present sample, this is likely to be due to the fact that two questions also load onto the concerns factor. Similarly, the treatment control factor of the Self Regulation Theory had a low Cronbach's α at 0.65, but this has also been observed in both

RA (Groake, Curtis, Coughlan & Gsel, 2004) and non-RA samples (Chilcot et al., 2010; Scharloo et al., 1998).

The social norms factor of the Theory of Planned Behaviour also had low internal consistency (Cronbach's α = 0.53), however this was caused by the second question; *"most people who have rheumatoid arthritis take all of their medications"*. When this was removed, the internal consistency improved (Cronbach's α = 0.76) and so this new factor, termed "important others" was used in subsequent analyses.

7.3.3: Treatment groups

It was hypothesised that patients that newly diagnosed patients (diagnosed with RA within the past six months) would score differently for the social cognition models and that the scores would be more variable over time as patients' experience modifies their social cognition model of illness (through self-regulation). However, NICE guidelines have categorised "recent onset" RA to be within the first two years (NICE, 2009) and as the sample size of patients prescribed DMARDs in the past six months was small, the factor sumscores were compared for these patients (N=33) and those prescribed DMARDs in the past two years (N=49) shown in Appendix 7.3. No differences were found between these groups and so, to increase the power of subsequent analyses, patients starting DMARDs within the past two years were classified as "new". Although this also reduced the number of patients in the "established" group from 110 to 94, this group still had enough power to detect significance.

7.3.3.1: Adherence in the three treatment groups

The level of adherence was good as overall, only 37.4% of patients demonstrated sub-optimal adherence. Specifically, 25.6% of the sample showed intentional non-adherence and 18.5% sometimes forget their DMARDs. It was hypothesised that the biological group would have the highest levels of intentional non-adherence due to their previous experience of DMARD failure; however the highest reported level of intentional non-adherence was among the established group at 30.9%. Although this was not significant; χ^2 (2) = 1.86, p=0.40, it was substantially higher than newly diagnosed patients at 18.4% (Table 7.2).

Conversely, there was a trend for new patients to have the highest rates of forgetting at 20.4% which is consistent with the hypothesis, however this was again not significantly different from the other treatment groups as χ^2 (2) = 0.717, p=0.70.

Table 7.2: Mean sumscores for each model factor and disease outcome for the three treatment groups and the entire sample

	Whole sample	Newly diagnosed	Established	Biologic
Total N	227	49	94	84
Demographics				
Female (%)	171 (75.7%)	32 (65.3)	68 (72.3)	71 (84.5)
Age	57.39 (15.03)	56.91 (16.41)	**60.73* (14.14)**	**54.29* (14.57)**
Disease duration	12.54 (10.77)	**6.48 (10.90)*+**	**13.99+ (9.43)**	**14.20* (11.09)**
Theory of planned behaviour				
Important others	12.27 (1.76)	12.00 (1.76)	12.36 (1.81)	12.32 (1.71)
Personal control	30.60 (3.73)	29.96 (4.30)	30.72 (3.35)	30.84 (3.79)
Health Belief Model				
Barriers	15.65 (4.10)	16.16 (4.65)	15.57 (4.23)	15.48 (3.63)
Benefits	12.19 (2.29)	11.77 (2.61)	12.01 (2.34)	12.61 (2.00)
Severity	16.62 (4.09)	16.30 (4.67)	**15.93* (4.10)**	**17.58* (3.57)**
Self regulation model				
Identity	3.65 (1.34)	3.53 (1.37)	**3.43* (1.43)**	**3.96* (1.16)**
Chronic timeline	21.97 (3.64)	**20.11*+ (4.83)**	**22.33+ (3.01)**	**22.62* (3.18)**
Cyclical timeline	13.44 (3.44)	13.30 (3.44)	13.55 (3.39)	13.39 (3.53)
Consequences	21.48 (4.77)	**20.17* (4.88)**	**20.58+ (4.93)**	**23.24*+ (3.99)**
Personal control	18.93 (4.51)	19.79 (4.14)	18.57 (4.68)	18.84 (4.49)
Treatment control	20.10 (3.15)	20.89 (3.20)	19.77 (3.15)	20.02 (3.09)
Cohesion	12.43 (4.48)	**13.43* (4.14)**	12.81 (4.68)	**11.44* (4.29)**
Emotional effect	18.12 (5.42)	18.19 (5.31)	17.37 (5.48)	18.93 (5.38)
Beliefs about medications				
General harm	8.86 (2.51)	9.00 (2.67)	9.16 (2.60)	8.43 (2.26)
General overuse	10.41 (2.81)	10.66 (2.81)	10.52 (2.60)	10.15 (3.04)
Specific concern	13.50 (3.94)	13.98 (4.28)	13.41 (4.02)	13.34 (3.66)
Specific necessity	19.32 (3.78)	**16.89*+ (4.46)**	**19.51+ (3.24)**	**20.52* (3.31)**
Necessity-concerns differential	5.81 (4.86)	**2.91 (0.65)*+**	**6.10 (0.48)+**	**7.18 (0.54)***
Depression, Anxiety and Positive Outlook				
Depression	8.62 (4.39)	8.85 (4.31)	8.20 (3.94)	8.99 (4.91)
Anxiety	5.42 (3.15)	5.72 (3.30)	5.17 (2.91)	5.53 (3.34)
Positive outlook	10.50 (3.14)	10.17 (3.40)	10.36 (3.27)	10.86 (2.83)
Disease outcomes				
HAQ	1.27 (0.84)	**0.98* (0.79)**	1.26 (0.88)	**1.44* (0.78)**
DAS	3.52 (1.51)	3.52 (1.56)	**3.07* (1.22)**	**3.95* (1.63)**
EQ5D VAS	61.50 (20.45)	63.04 (19.52)	63.76 (20.84)	58.10 (20.30)
EQ5D utility	0.57 (0.28)	0.57 (0.27)	0.60 (0.29)	0.53 (0.28)
Adherence				
Low intentional	58 (25.7%)	9 (18.4%)	29 (30.9%)	20 (23.8%)
Forget	42 (18.6%)	10 (20.4%)	16 (17.0%)	16 (19.0%)
Overall low	85 (37.6%)	16 (32.7%)	38 (40.4%)	31 (36.9%)

*difference between pairs p<0.05, +differences between pairs p<0.05

7.3.3.2: Demographic and disease factors

One way ANOVA was carried out to determined differences between means of the treatment groups for psychological and disease related factors. As expected, the disease duration is approximately twice as long for the established and biological groups compared to the new group (ps<0.001). The biologic patients were also significantly younger than the established group (p=0.019) and had a higher proportion of females at 85.5% (χ^2 (2) = 7.82, p=0.02). This is in line with current prescribing practices for biologic medications.

The level of functional disability measured by HAQ was higher for the biologic group compared to new patients (mean difference 0.36) which is expected given the longer disease duration and active disease of the biologic group. However, both the new and biologic groups had DAS28 scores indicating moderate disease activity at 3.52 and 3.95 respectively. The established group however had a significantly lower DAS28 score than the biologic group at 3.07 (p=0.002). Based on current guidelines, all of the groups showed active disease with a DAS28 score >2.6 indicating low to moderate activity.

7.3.3.3: Psychological factors

7.3.3.3.1: Univariate analysis

Table 7.2 shows that there were no differences in mean sumscores for the three treatment groups on a number of factors including the Theory of Planned Behaviour factors and the psychological wellbeing factors. Most of the Beliefs about Medications scores did not differ, however the new patients perceived their medications to be less necessary than both the established and biologic patients (ps <0.001). As their concern scores were equally moderate, the necessity-concern differential was significantly lower for new patients than for both established and biologic patients (ps<0.05). The majority of the mean differences that were found were within the Illness Perceptions of the Self Regulation Theory and are shown in Figure 7.3.

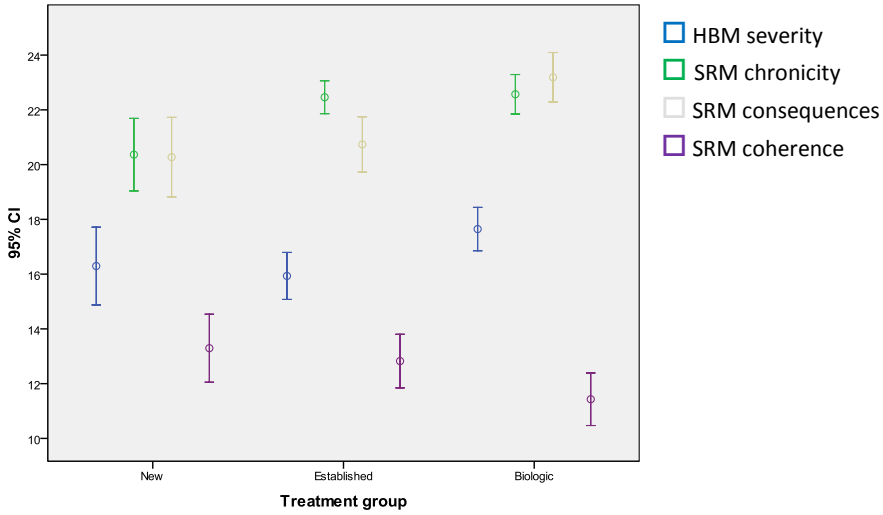


Figure 7.3: Mean sumscores for the model factors for each treatment group

7.3.3.3.2: Bivariate analysis

Table 7.3 shows that there were a number of significant correlations between the treatment group and the social cognition models, although the effect sizes ranged from small for the HBM factors to moderate for the BMQ necessity factor (r=0.34). The correlations were all positive suggesting that generally speaking, as patients become more experienced with their RA, their perceptions of illness severity, chronicity and understanding become higher and their perceptions of their medications become more favourable. However, there were no correlations between treatment group and the Theory of Planned Behaviour factors.

Table 7.3: Correlations between adherence groups, treatment groups and the model factors

	Intentional adherence	Forget	Overall adherence	Age	Gender	Treatment group
Intentional adherence 0= low 1=high						
Forget 1=forget 0=does not forget						
Overall adherence 0=low 1=high	.752**	-.610**				
Age	.238**	-.283**	.337**			
Gender 0=male 1=female						
Treatment group 1=new 2=established 3=biologic					.183*	
Theory of Planned Behaviour						
TPB important others						
TPB Perceived Behavioural Control		-.206*	.159*			
Health Belief Model						
HBM barriers	-.137*			-.330**	.141*	
HBM benefits				-.178*	.192*	**.143***
HBM severity				-.254**	.210*	**.139***
Self Regulatory Model						
SR Identity				-.228**		**.141***
SR timeline						**.234****
SR cyclical						
SR consequence	.263**				.149*	**.262****
SR personal control	-.158*		-.180*	-.164*		
SR treatment control						
SR cohesion						**-.173***
SR emotion				-.312**	.222**	
Beliefs about Medications						
BMQ harmful						
BMQ overuse						
BMQ concern				-.212*		
BMQ necessity					.300**	**.337****
BMQ necessity-concerns framework				.204*	.151*	**.306****
HAQ	.196*			.262**	.192*	**.201***
DAS		.182*				**.172***
EQ5D	-.216*					

*p<0.05, **p<0.001

7.3.3.3.3: Multivariate analysis

In order to determine effectively how the social cognition models differ between the treatment groups, a discriminant function analysis was carried out using the psychological factors that correlated significantly with treatment group which were; *SRM chronicity, SRM consequences, SRM*

cohesion, BMQ necessity and BMQ necessity-concerns framework. Fifteen cases had at least one missing discriminating variable and therefore the analysis was carried out on 212 cases.

Two discriminant functions were calculated, with both of them being significant (ps<0.05). Function 1 explains 75.5% of the between-group variance and has an effect size of 0.18. The second function explains 24.5% of the between-group variance but has a small effect size of 0.06. Therefore, the functions account for 18% and 6% respectively of the relationship between predictors and groups.

Table 7.4: Structure matrix for the discriminant functions of treatment groups

	Function	
	1	2
BMQ necessity	0.810	0.132
BMQ necessity-concerns framework	0.735	0.205
SRM chronicity	0.492	0.268
SRM coherence	-0.364	0.298
SRM consequences	0.421	-0.672

Table 7.4 and Figure 7.4 show the structure matrix and group centroids respectively. The first function is mostly related to perceived necessity of medications and the perceived chronicity of RA and discriminates the newly diagnosed patients from the established and biologic groups. Here, the perceptions of the necessity of medication is clearly correlated most strongly with the function; however this does not take into account covariance that would be evident, particularly for the two BMQ factors. The second function is related to perceived consequences of having RA and discriminates the established patients from those in the newly diagnosed and biologic groups. However, Figure 7.4 also demonstrates a lot of variability for the discriminant function means for all three groups.

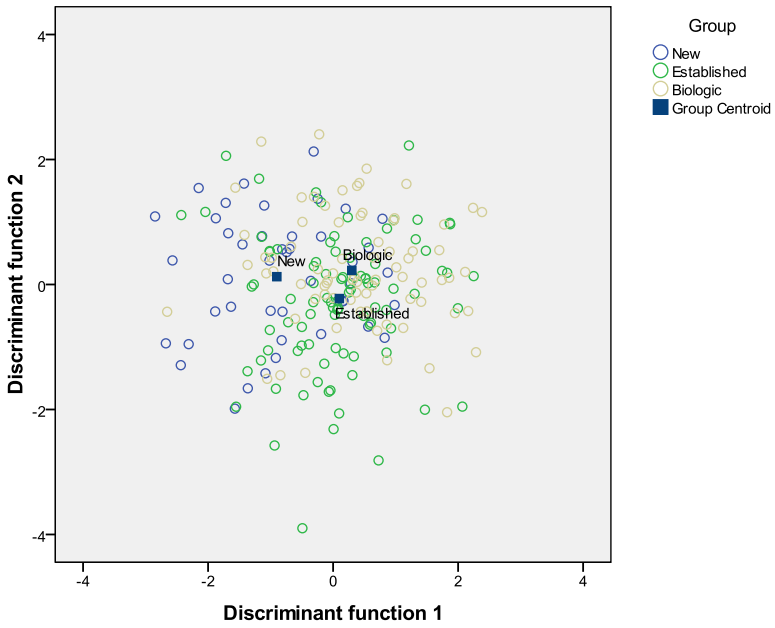


Figure 7.4: Group centroids and groups means of treatment groups for each discriminant function.

Using the two discriminant functions above, the patients were classified as being newly diagnosed, established or on biologic medication. Using sample proportions as prior probabilities, 56.1% of patients were correctly classified (Table 7.5). Most errors occurred by misclassifying new and biologic patients as established. However, this shows that the predictors can discriminate between treatment groups with more accuracy than by chance alone. This provides some evidence that illness perceptions and beliefs about medications differ between patients in different phases of their treatment.

Table 7.5: Predicted and actual treatment group membership using the discriminant functions

		Predicted group membership		
		New	Established	Biologic
Actual group membership	New	17 (38.6%)	21 (47.7%)	6 (13.6%)
	Established	6 (6.5%)	64 (69.6%)	22 (23.9%)
	Biologic	7 (9.2%)	31 (40.8%)	38 (50.0%)

7.3.4: Adherence groups

The mean sumscores for each psychological factor, disease related variables and demographics are shown in Table 7.6 for each of the adherence groups. Overall adherence is considered first (section 7.3.4.1) which is then separated into Intentional (section 7.3.4.2) and unintentional (section 7.3.4.3) due to the hypothesis that they will have different underlying psychological processes.

Table 7.6: Mean factor sumscores and demographics for each of the adherence types

	Intentional low	Intentional high	Forget	Do not forget	Overall low	Overall high
Total N	58 (25.6%)	157 (69.2%)	42 (18.5%)	174 (76.7%)	85 (37.4%)	131 (57.7%)
Demographics						
Female (%)	43 (20%)	118 (54.9%)	33 (15.3%)	129 (59.7%)	64 (29.6%)	98 (45.4%)
Age	51.86**(16.08)	59.92 (13.96)	49.18**(13.44)	59.85 (14.52)	51.47** (14.97)	61.76 (13.45)
Disease duration	10.90 (8.98)	13.21 (11.33)	9.24* (7.71)	13.26 (11.22)	10.53* (8.93)	13.87 (11.61)
Theory of Planned Behaviour						
Important others	12.22 (1.65)	12.32 (1.80)	12.48 (1.38)	12.22 (1.88)	12.24 (1.57)	12.29 (1.93)
Personal control	30.34 (3.79)	30.86 (3.52)	29.14* (4.25)	31.04 (3.43)	29.95* (3.96)	31.14 (3.41)
Health Belief Model						
Barriers	16.48* (3.99)	15.25 (4.03)	16.31 (4.50)	15.48 (4.01)	16.19 (4.19)	15.28 (4.04)
Benefits	12.02 (2.03)	12.28 (2.39)	12.26 (2.04)	12.21 (2.36)	12.20 (2.07)	12.24 (2.44)
Severity	15.95 (3.65)	16.87 (4.17)	17.67 (3.79)	16.37 (4.08)	16.82 (3.92)	16.50 (4.14)
Self Regulatory Model						
Identity	3.53 (1.35)	3.73 (1.32)	3.95 (1.29)	3.59 (1.36)	3.76 (1.33)	3.59 (1.36)
Chronic timeline	22.34 (2.38)	21.79 (4.00)	22.50 (2.78)	21.78 (3.81)	22.32 (2.58)	21.66 (4.18)
Cyclical timeline	13.07 (3.19)	13.58 (3.58)	14.24 (3.30)	13.24 (3.49)	13.72 (3.31)	13.25 (3.57)
Consequences	19.45** (3.86)	22.23 (4.81)	22.00 (4.81)	21.37 (4.73)	20.89 (4.39)	21.90 (4.94)
Personal control	20.10* (3.80)	18.53 (4.62)	19.55 (3.34)	18.74 (4.77)	19.89* (3.57)	18.23 (4.98)
Treatment control	20.50 (2.48)	20.12 (3.24)	19.81 (3.51)	20.25 (3.09)	20.06 (2.87)	20.23 (3.37)
Cohesion	11.50 (3.60)	12.70 (4.68)	12.93 (4.01)	12.29 (4.58)	12.09 (3.97)	12.63 (4.78)
Emotional effect	16.98 (5.47)	18.57 (5.24)	19.52 (6.15)	17.84 (5.10)	18.07 (5.76)	18.24 (5.08)
Beliefs about Medications Questionnaire						
General harm	8.78 (2.58)	8.99 (2.49)	8.71 (2.91)	8.98 (2.41)	8.90 (2.76)	8.95 (2.34)
General overuse	10.64 (2.23)	10.36 (2.97)	10.15 (3.42)	10.54 (2.65)	10.55 (2.81)	10.41 (2.82)
Specific concern	12.74 (3.99)	13.76 (3.83)	13.98 (4.10)	13.41 (3.87)	13.35 (4.23)	13.63 (3.71)
Specific necessity	18.88 (3.30)	19.64 (3.73)	18.80 (4.01)	19.59 (3.51)	18.86 (3.62)	19.81 (3.58)
Necessity-concerns differential	6.14 (0.64)	5.88 (0.38)	6.23 (0.37)	4.83 (0.73)	6.23 (0.37)	4.83 (0.73)
Depression, Anxiety and Positive Outlook						
Depression	9.21 (4.53)	8.42 (4.33)	11.02**(5.67)	8.12 (3.89)	9.58* (5.03)	8.09 (3.89)
Anxiety	5.58 (2.97)	5.37 (3.22)	6.73* (3.73)	5.16 (2.97)	5.84 (3.36)	5.22 (3.05)
Positive outlook	10.93 (2.92)	10.36 (3.22)	10.20 (3.57)	10.55 (3.07)	10.67 (3.09)	10.36 (3.22)
Disease outcomes						
HAQ	1.01* (0.84)	1.38 (0.82)	1.25 (0.80)	1.29 (0.85)	1.17 (0.82)	1.35 (0.85)
DAS	3.19 (1.39)	3.57 (1.54)	4.03* (1.49)	3.33 (1.48)	3.54 (1.48)	3.43 (1.53)
EQ5D VAS	67.47* (21.41)	59.60 (19.75)	56.29 (22.78)	63.02 (19.65)	62.21 (22.19)	61.33 (19.26)
EQ5D utility	0.67* (0.26)	0.53 (0.29)	0.53 (0.30)	0.58 (0.28)	0.60 (0.29)	0.55 (0.29)
Treatment groups						
Newly diagnosed	9 (19.6%)	35 (76.1%)	10 (21.7%)	34 (73.9%)	16 (34.8%)	28 (60.9%)
Established	29 (30.9%)	64 (68.1%)	16 (17.0%)	78 (83.0%)	38 (40.4%)	56 (59.6%)
Biologic	20 (23.8%)	58 (69.0%)	16 (19.0%)	62 (73.8%)	31 (36.9%)	47 (56.0%)

*p<0.05, **p<0.001

7.3.4.1: Overall non-adherence

7.3.4.1.1: Univariate analysis

If a patient is classified as a high intentional adherer *and* does not forget then they are classified as high overall adherence. If they have low intentional adherence *or* they forget *or* both then they are classified as low overall adherence. Table 7.6 shows that 37.4% of patients had sub-optimal adherence. Low adherers were ten years younger on average at 51.47 (SD=14.97) than high overall adherers at 61.76 (SD=13.45) years (t(195) =-5.00 p<0.001) and had a shorter disease duration (t(209) = -2.22, p=0.03).

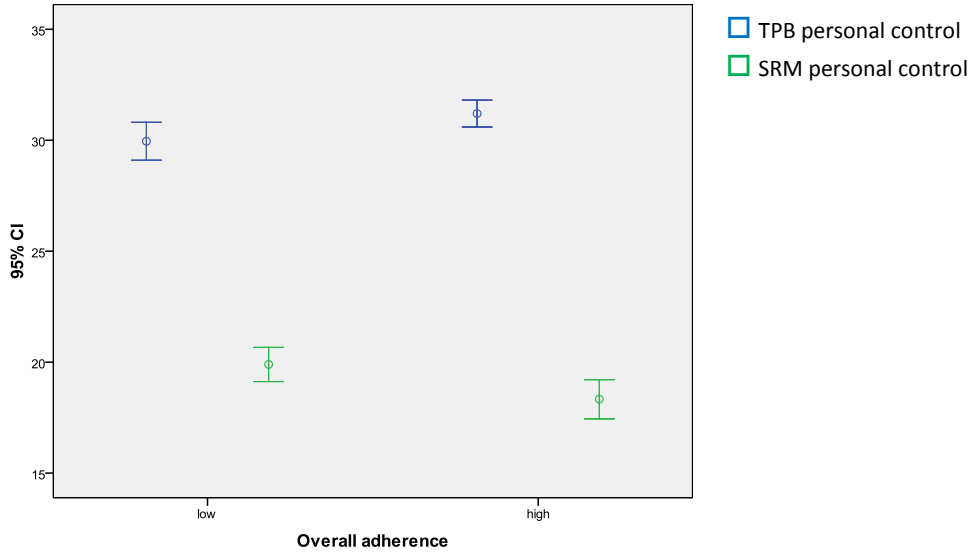


Figure 7.5: Mean differences for model factors between *overall* high and low adherence

As Figure 7.5 shows, the only factors that showed a significant difference between overall high and low adherence were personal control. The different models measure slightly different aspects of control with the TPB concentrating on the ability to take medication *as prescribed* whereas the SRM refers to the *"power to influence the course of rheumatoid arthritis"*. Low adherers perceive themselves to have more influence over RA (p=0.01) but less confidence in being able to take DMARDs as directed (p=0.02). This demonstrates that when taking adherence as a whole, it is the patients' perceptions of their own ability to self-manage their illness that is most related to medication adherence.

7.3.4.1.2: Bivariate analysis

Few variables correlated with overall adherence (Table 7.3). Higher perceptions of TPB behavioural control were related to higher adherence (r=0.16) and lower levels of SRM personal control were

related to lower adherence (r=-0.18). Age was also strongly correlated with older age related to higher adherence (r=0.34).

7.3.4.1.3: Multivariate analysis

Stepwise logistic regression analysis was employed to determine if the social cognition models of illness could predict overall adherence. For logistic regression, it is recommended that there are 5 cases per predictor (Tabachnick & Fidell, 2007). There are a total of fifteen predictors and 212 cases used meaning there is adequate power to undertake logistic regression in the sample.

Each of the social cognition models were tested separately, along with beliefs about medications and are presented in separate columns of Table 7.7. For all models, age was entered as the first step as a continuous variable and in all cases was significantly related to adherence with Nagelkerke R^2 showing it explained between 13.5% (in the HBM model) and 15.5% (in the BMQ model) of the variance in adherence alone.

Table 7.7: Stepwise logistic regression of social cognition models on *overall* adherence

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications	
Variable	Wald's β	OR	Wald's β	OR	Wald's β	OR	Wald's β	OR
Step 1								
Age	16.02	1.05**	15.10	1.05**	15.42	1.05**	22.08	1.06**
Step 2								
TPB important others	2.40	0.82						
TPB perceived control	6.18	1.14*						
HBM barriers			1.43	0.95				
HBM benefits			0.71	1.09				
HBM severity			0.07	1.02				
SRM identity					0.001	0.996		
SRM chronicity					1.48	0.94		
SRM cyclical					2.10	0.93		
SRM consequences					3.36	1.09		
SRM personal control					4.05	0.92*		
SRM treatment control					4.27	1.14*		
SRM coherence					0	1		
SRM emotion					0.81	1.04		
BMQ harmful							0.13	0.97
BMQ overuse							1.15	0.93
BMQ necessity							2.57	1.08
BMQ concern							1.97	1.08
Model	$\Delta\chi^2$ (2) = 7.05, p=0.03		$\Delta\chi^2$ (3) = 2.43, p=0.49		$\Delta\chi^2$ (8) = 14.43, p=0.07		$\Delta\chi^2$ (4) = 6.35, p=0.18	
	Model χ^2 (3) = 27.33, p<0.001		Model χ^2 (4) = 22.89, p<0.001		Model χ^2 (9) = 36.58, p<0.001		Model χ^2 (5) = 29.44, p<0.001	
	ΔNagelkerke R^2=0.180		ΔNagelkerke R^2=0.150		ΔNagelkerke R^2=0.234		ΔNagelkerke R^2=0.194	
	69.6% correct (47.4% low)		68.3% correct (46.1% low)		70.5% correct (50.0% low)		71.7% correct (50.0% low)	

*p<0.05, **p<0.001

The only psychological model that was shown to improve the fit of the data to predict overall adherence was the Theory of Planned Behaviour; $\Delta\chi2$ (2) = 7.05, p=0.03, although the Self Regulation Model was close as $\Delta\chi2(8)$ = 14.43, p=0.07. The Theory of Planned Behaviour variables explained an additional 18% of the variance in overall adherence and this model as a whole was able to correctly classify 47.4% of low adherers. The only significant predictors for this model were; age (Wald's

β=16.02, p<0.001) where a one point increase led to a 5% *increase* in the odds of high overall adherence and TPB Perceived Behavioural Control (Wald's β=6.18, p=0.013) where a one point increase in perceived control over taking medications led to a 14% *increase* in the odds of higher adherence.

7.3.4.2: Intentional non-adherence

7.3.4.2.1: Univariate analysis

In order to more clearly investigate adherence, patients were identified as "high" or "low" intentional adherers based on answers to the CQR5 (see Chapter 6 for a description of how intentional adherence in classified). Twenty-five percent of patients were categorised as low intentional adherers (Table 7.6). They were significantly younger at 51.86 (SD=16.08) years than high intentional adherers at 59.92 (SD=13.96) years; t(194) = -3.41, p=0.001. Interestingly, the low adherence group showed better functioning and better quality of life demonstrated by higher EQ5D utility and VAS values (Table 7.6). Figure 7.6 clearly shows that there is an interaction between age and intentional adherence on DAS28 and EQ5D VAS score. There is a much stronger effect of intentional adherence on both of these variable for younger patients (<58 years) than older patients.

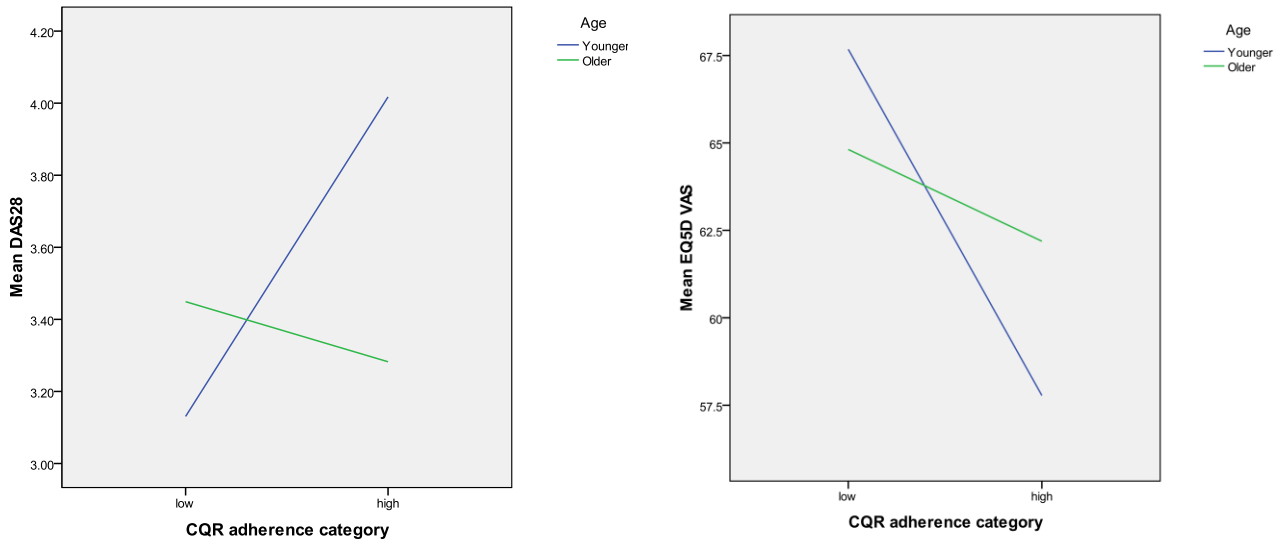


Figure 7.6: Interaction of age and *intentional* adherence for i) DAS28 and ii) EQ5D VAS score

There were few differences between model factor scales; however the low adherence group demonstrated interesting mean differences on some key factors, shown in Figure 7.7. Importantly, the low adherence group had higher HBM barrier scores (p=0.049) which refer directly to issues surrounding taking medications for RA. They also perceived lower consequences of having RA (p<0.001) and higher personal control over influencing the course of their RA (p=0.021). Although the

differences were not significant, there was also a trend towards lower negative emotional response to RA by low adherers and a lower perception of the necessity of DMARDs.

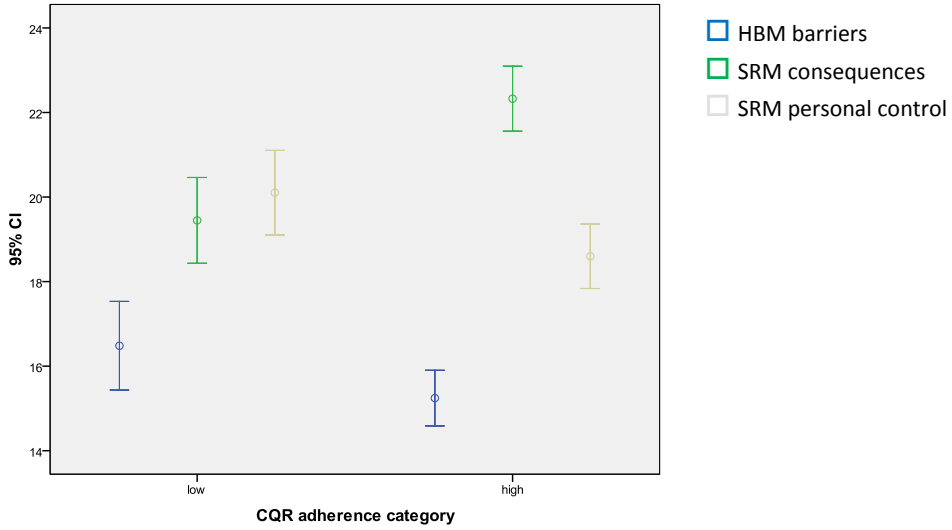


Figure 7.7: Mean sumscore differences for model factors between *intentional* adherence groups

7.3.4.2.2: Bivariate analysis

Table 7.3 shows the correlations between intentional adherence and the model factors. There was a strong correlation between SRM consequences and adherence (r=0.26) whereas there were negative correlations with HBM barriers (r=-0.14) and SRM personal control (-0.16) indicating that if patients perceive there to be more barriers to medication taking and that they have less control over the course of their RA then they have lower intentional adherence.

The correlations between intentional adherence and age, HAQ and EQ5D mirror the univariate analyses as patients with better intentional adherence were older (r=0.24), had higher functional disability (r=0.20) and better quality of life (-0.22).

7.3.4.2.3: Multivariate analysis

Stepwise logistic regression analysis was employed to determine if the social cognition models of illness could predict intentional adherence, shown in Table 7.8. Separate regressions were carried out for each of the models and then with all models combined (shown in the last column of Table 7.8) with the overall model fit shown at the bottom of the table. For all models, age was entered as the first step as a continuous variable and in all cases was significantly related to intentional adherence. Adding the Theory of Planned Behaviour variables did not improve the fit of the data as $\Delta\chi^2$ (2) = 2.03, p=0.36. The three other models however did improve the fit over and above age with the Self Regulatory Model proving to be the best as $\Delta\chi^2$ (8) = 21.67, p=0.01 and Nagelkerke R^2 = 0.225

showing that the addition of Illness Perceptions increased the fit of the data by 22.5%. This model also proved to be the best at correctly classifying the adherence of patients as 27.5% of low adherers were correctly classified. However, on further inspection of the model, only SRM consequences proved to be significant with Wald's β = 7.60 showing that a one point increase in the perception of consequences *increased* the odds of high adherence by 16%.

As three of the models; the Health Belief Model, Self Regulatory Model and Beliefs about Medications were significantly related to intentional adherence in the logistic regressions, these models were combined in an effort to improve the explained variance in intentional adherence and is shown in the final two columns of Table 7.8. Combining the models proved to explain the most variance as Naglekerke R^2 for the second step only was 0.358 indicating that the social cognition models explained 35.8% of the variance over and above age. By combining the models, 42.0% of low intentional adherers were correctly classified using the predictors, which is better than any of the models alone. This combined model showed that one standard deviation increase in age led to 4% *increase* in the odds of intentional adherence (Wald's β=5.97, p=0.02), one point increase in HBM barriers led to 21% *decrease* in odds of adherence (Wald's β=9.63, p=0.002), one point increase in SRM chronicity led to 14% *decrease* in odds of adherence (Wald's β=4.27, p=0.04), one point increase in SRM consequences led to 25% *increase* in odds of adherence (Wald's β=10.48, p=0.001) and one point increase in BMQ concerns led to 23% *increase* in odds of intentional adherence (Wald's β=4.81, p=0.03).

Table 7.8: Stepwise logistic regression of social cognition models on *intentional* adherence

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications		Combined	
Variable	Wald	OR	Wald	OR	Wald	OR	Wald	OR	Wald	OR
Step 1										
Age	8.15	1.03*	7.69	1.04*	9.37	1.04*	14.60	1.05**	5.97	1.04*
Step 2										
TPB important others	1.49	0.84								
TPB perceived control	1.20	1.06								
HBM barriers			6.98	0.86*					9.63	0.79*
HBM benefits			0.14	0.96					0.11	0.96
HBM severity			6.85	1.19*					1.11	0.90
SRM identity					0.14	1.07			0.07	1.05
SRM chronicity					3.28	0.89			4.27	0.86*
SRM cyclical					0.03	0.99			0.01	1.01
SRM consequences					7.60	1.16*			10.48	1.25**
SRM personal control					1.08	0.95			0.93	0.95
SRM treatment control					1.30	1.08			0.17	1.03
SRM coherence					0.05	1.01			0.12	1.02
SRM emotion					0.97	1.05			1.62	1.08
BMQ harmful							0.18	0.96	0.36	0.94
BMQ overuse							3.83	0.86*	2.66	0.86
BMQ necessity							1.33	1.06	0.63	1.06
BMQ concern							5.75	1.15*	4.81	1.23*
Model	$\Delta\chi^2$ (2) = 2.03, p=0.36		$\Delta\chi^2$ (3) = 12.53, p=0.006		$\Delta\chi^2$ (8) = 21.67, p=0.006		$\Delta\chi^2$ (4) = 11.22, p=0.024		$\Delta\chi^2$ (15) = 41.67, p<0.001	
	Model χ^2 (3) = 11.58, p=0.009		Model χ^2 (4) = 21.85, p<0.001		Model χ^2 (9) = 32.17, p<0.001		Model χ^2 (5) = 22.44, p<0.001		Model χ^2 (16) = 51.69, p<0.001	
	ΔNagelkerke R^2 = 0.086		ΔNagelkerke R^2 = 0.159		ΔNagelkerke R^2 = 0.225		ΔNagelkerke R^2 = 0.163		ΔNagelkerke R^2 = 0.358	
	75.3% correct (9.8% low)		72.9% correct (15.7% low)		74.5% correct (27.5% low)		75.8% correct (16% low)		77.5% correct (42.0% low)	

*p<0.05, **p<0.001

7.3.4.3: Unintentional non-adherence (forgetting)

7.3.4.3.1: Univariate analysis

Patients were dichotomised based on their answer to the statement "*I sometimes forget to take my medicines*" with those that agreed being classified as forgetters and those that disagreed classified as not forgetting. Table 7.6 shows that 18.5% of the sample sometimes forget their medicines. Again, patients that forget their medication were significantly younger at 49.18 (SD=13.44) years compared to 59.85 (SD=14.52) years for those that do not forget; $t(195) = 4.13$, $p<0.001$. They also had a shorter mean disease duration at 9 years compared to 13 years ($p=0.03$). The functional status and quality of life scores were all similar for those that do and do not forget, although there was a trend for the forgetting group to have a lower EQ5D VAS score. However, the DAS28 score for forgetters was significantly higher at 4.03 indicating moderate disease activity.

There were very few differences between the forgetters and non-forgetters for the psychological factors. The only scale on which there was a significant difference was for TPB personal control which refers directly to the patients' perceived ability to take their medication as prescribed. The forgetting group had a lower mean score at 29.14 than the non-forgetters at 31.04 ($t(211) = 3.06$, $p=0.003$) indicating that these patients do not feel confident in their ability to take DMARDs correctly. The forgetting group also showed higher levels of depression ($p<0.001$) and anxiety ($p=0.004$) than the non-forgetting group. There were no other differences for the social cognition models between the forgetting and non-forgetting group.

7.3.4.3.2: Bivariate analysis

In line with the univariate analysis, only one of the psychological factors correlated with forgetting (Table 7.3). Patients who had higher perceptions of TPB Perceived Behavioural Control were less likely to forget ($r=-0.21$). Forgetting also correlated negatively with age ($r=-0.28$) so younger people were more likely to forget and forgetters also had higher DAS28 scores ($r=0.18$).

7.3.4.3.3: Multivariate analysis

Stepwise logistic regression was carried out to determine the predictive ability of the social cognition models to identify patients that forget their medications. Again, age was entered as a continuous variable at the first step and was significant in each model shown in Table 7.9 explaining approximately 12% of the variance alone. Conversely to intentional adherence, the only psychological model which was significantly related to forgetting was the Theory of Planned Behaviour; $\Delta\chi^2$ (2) = 11.27, $p=0.004$ which improved the fit of the model by an additional 20% over

and above age. However, only Perceived Behavioural Control was significant showing that a one point increase in TPB Perceived Behavioural Control led to 17% *decrease* in the odds of forgetting (Wald's β=9.75, p=0.002). As the other social cognition models were not significantly related to forgetting, a combined model was not tested.

As age and working status were highly correlated (Pearson's R=-0.55, p<0.001), the effect of working status mediating the effect of age on forgetting was investigated. However, only 23.5% of the effect of age on forgetting was mediated by working, with Sobel's test = -1.46, p=0.14, making the mediation non-significant. Also, when working status and the interaction were entered into the logistic regression model with the Theory of Planned Behaviour, they did not significantly improve the fit of the model (final column of Table 7.9).

Table 7.9: Stepwise logistic regression of social cognition models on *unintentional* adherence (forgetting)

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medication		Working	
Variable	Wald's β	OR	Wald's β	OR	Wald's β	OR	Wald's β	OR	Wald's β	OR
Step 1										
Age	10.28	0.96**	11.55	0.95**	9.27	0.95*	11.32	0.95**	3.12	0.97
Working									0.23	1.29
Age-working interaction									0.15	1.01
Step 2										
TPB important others	3.61	1.42							4.31	1.49*
TPB perceived control	9.75	0.83*							10.91	0.81**
HBM barriers			0.14	0.98						
HBM benefits			2.60	0.82						
HBM severity			3.10	1.14						
SRM identity					0	1				
SRM chronicity					0.39	1.04				
SRM cyclical					2.37	1.10				
SRM consequences					0.003	0.98				
SRM personal control					1.68	1.07				
SRM treatment control					0.75	0.94				
SRM coherence					0.20	1.02				
SRM emotion					0.01	1.00				
BMQ harmful							0.44	0.94		
BMQ overuse							0.69	0.93		
BMQ necessity							1.32	0.94		
BMQ concern							1.08	1.07		
Model	Step χ^2 (2) = 11.27, p=0.004 Model χ^2 (3) = 25.73, p<0.001 Nagelkerke R^2 = 0.200 79.6% correct (13.2 forget)		Step χ^2 (3) = 3.56, p=0.31 Model χ^2 (4) = 17.76, p=0.001 Nagelkerke R^2 = 0.142 80.4% correct (7.9% forget)		Step χ^2 (8) = 5.91, p=0.66 Model χ^2 (9) = 21.29, p=0.011 Nagelkerke R^2 = 0.166 79.3% correct (0% of forget)		Step χ^2 (4) = 2.99, p=0.56 Model χ^2 (5) = 18.53, p=0.002 Nagelkerke R^2 = 0.148 79.6% correct (2.7% forget)		Δ χ^2 (2) = 13.04, p=0.001 Model χ^2 (5) = 29.7, p<0.001 Nagelkerke R^2 = 0.229 80.6% correct (18.4% forget)	

*p<0.05, **p<0.001

7.3.5: Using adherence and social cognition models to predict functional status

A hierarchical regression analysis was used to predict functional status (HAQ) using age, intentional adherence and the psychological factors. Table 7.10 shows that 48.2% of the variance in HAQ was explained by the final model. However, once the psychological factors are added to the model, adherence is no longer a significant predictor of HAQ. A very large percentage of the variance is explained by the psychological models (43.6%), however as this is cross-sectional, the direction of causality is not clear. This is highlighted by the fact that the consequences of having RA is the strongest predictor, which itself is likely to be influenced by functional status.

Table 7.10: Hierarchical regression of age, *intentional* adherence and social cognition models on functional status

Variable	B	SE B	β	p	Variance
Step 1					
Age	0.016	0.004	0.271	0.001	7.3%
Step 2					
Age	0.014	0.004	0240	0.001	5.5%
Intentional adherence	0.275	0.137	0.145	0.047	2.0%
Step 3					
Age	0.018	0.004	0.315	<0.001	7.0%
Intentional adherence	-0.105	0.119	-0.055	0.197	
SRM identity	0.090	0.044	0.139	0.043	1.3%
SRM chronicity	-0.023	0.016	-0.091	0.141	
SRM cyclical	-0.004	0.015	-0.019	0.762	
SRM consequences	0.098	0.015	0.533	<0.001	13.0%
SRM personal control	-0.015	0.012	-0.077	0.230	
SRM treatment control	<0.001	0.019	-0.001	0.985	
SRM coherence	-0.007	0.013	-0.039	0.564	
SRM emotion	0.015	0.013	0.097	0.259	
HBM barriers	-0.015	0.015	-0.067	0.337	
HBM benefits	0.036	0.030	0.098	0.224	
HBM severity	-0.017	0.021	-0.083	0.405	
TPB important others	0.023	0.030	0.048	0.447	
TPB personal control	-0.031	0.015	-0.130	0.045	1.3%
Note $R^2 = 0.074$ ($p<0.001$), $\Delta R^2 = 0.094$ ($p=0.047$), $\Delta R^2 = 0.436$ ($p<0.001$)					

7.3.6: Correlations between the model factors

Table 7.11 shows the correlations between the psychological factors. A number of factors from each model correlate highly with other model factors, suggesting that the models themselves are measuring the same psychological processes. This is particularly evident when an element of

consequence or negative emotion is included as these seem to underlie and inform other factors related to rheumatoid arthritis and medication taking. These correlations are in line with other studies using these models (Chilcot et al., 2010; Orbell et al., 2006) and indicate that there is a large amount of overlap, suggesting that they could be more usefully combined to create a more parsimonious model of health behaviour.

Table 7.11: Correlations between the model factors

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
Self Regulatory Model																		
1)	SRM identity	1																
2)	SRM chronicity	.142*	1															
3)	SRM cyclical	.235**		1														
4)	SRM consequences	.458**	.249**	.212**	1													
5)	SRM personal control				-.212*	1												
6)	SRM treatment control	-.236**	-.150*		-.353**	.425**	1											
7)	SRM cohesion		-.144*	.199*		-.267**	-.232**	1										
8)	SRM emotion	.364**		.219**	.510**	-.206*	-.297**	.348**	1									
Theory of Planned Behaviour																		
9)	TPB important others		.186*				.134*			1								
10)	TPB personal control		.153*					-.301**	-.241**	.412**	1							
Health Belief Model																		
11)	HBM barriers	.176*		.173*	.261**		-.256**	.255**	.389**	-.159*	-.312**	1						
12)	HBM benefits	.240**		.153*	.442**		-.139*		.453**		-.138*	.349**	1					
13)	HBM severity	.346**		.248**	.595**	-.157*	-.224**	.210*	.633**		-.226**	.433**	.695**	1				
Beliefs about Medications																		
14)	BMQ harmful		-.162*				-.148*	.330**	.222**	-.227**	-.248**	.299**	.181*	.193*	1			
15)	BMQ overuse		-.188*				-.245**	.306**	.204*	-.249**	-.211*	.347**	.178*	.151*	.529**	1		
16)	BMQ concern	.135*		.299**	.270**		-.150*	.396**	.544**	-.209*	-.438**	.531**	.400**	.536**	.512**	.432*	1	
17)	BMQ necessity	.215*	-.183*		.389**				.300**				.385**	.419**			.206*	1
18)	Necessity-concerns		.215*	-.153*				-.346**	-.206*	.238**	.413**	-.348**			-.401*	-.336*	-.650**	.609**

*p<0.05, **p<0.001

7.4: Discussion

There were a number of relationships between the social cognition models and the treatment groups, adherence types and disease factors.

7.4.1: Treatment groups

The fact that the mean sumscores for each of the variables did not differ between patients diagnosed with RA six months previously and two years previously is surprising as it was expected that the social cognition models would be more variable until the patient has had more experience of having rheumatoid arthritis. However, as this was not the case but there were differences between the newly diagnosed and established group, it could be possible that the changeable and unpredictable course of disease and treatment that patients experience before remission is successfully established generally takes a couple of years which informs the social cognition models of illness. Although previous research does not appear to have objectively tested this period, most assume a cut-off period of two years to be "early" RA (Emery, Breedveld, Dougados, Kalden, Schiff & Smolen, 2002; NICE, 2009).

The mean differences that were found between the treatment groups for each of the psychological factors support the hypothesis that the patient's experience is influencing their social cognition models. For factors relating to serious consequences of the illness, the biologic group generally had higher mean sumscores than both the new and established group, reflecting their worse experience of RA. Similarly, perceptions of chronicity and necessity of medications were lower in the new group which could indicate that they are not yet aware or have come to terms with the fact that their illness is progressive and chronic. However, even those with a longer disease duration do not score very well on the SRM coherence scale which measures their perception of their understanding of RA, implying that none of the patients feel that they are particularly well informed.

It was interesting to note that the biologic patients did not differ on their scores for SRM treatment control which asks them to evaluate the ability of DMARDs to successfully control their RA. As these patients have previously failed standard DMARD therapy in order to receive biologics, it was expected that these patients would have a lower treatment control score. This could be due to patients incorrectly answering these questions in relation to their current biologic medication, rather than the DMARD which was asked.

The discriminant function analysis showed that the social cognition models differed between the illness groups and did so in a way that is likely to be related to their experience of having had RA and

taking DMARDs. This supports the hypothesis that the social cognition models will change as patients "self regulate" based on their experiences and knowledge. There was variability in the function means for each group and the discriminant functions were only able to correctly classify 56.1% of patients, however as this is better than by change alone, these results add validity to the models and the assumption that they will change during the course of the disease.

7.4.1.1: Adherence in treatment groups

The rate of non-adherence did not differ significantly between any of the treatment groups, which does not support the hypothesis that the experience of the patient would affect adherence. However, the rates of forgetting were highest for the new patients whereas their rate of intentional non-adherence was lowest. This suggests that these patients are keen to follow instructions to improve the symptoms that they are having, but have yet to form a habit for taking their medication, leading to forgetting. More of the new patients were working which may have an effect on forgetting as a busy, non-structured day away from the home can lead to forgetting (Chesney, 2000; Garcia-Gonzalez et al., 2008). However, the mediation of working on the effect of age on adherence was not significant. This may be because the majority of people who were not working were either retired (due to age) or were homemakers and therefore generally younger women. It would be beneficial in the future to determine some of the reasons why people think that they forget their medications to determine whether working status has a true effect.

The established group had the highest rates of intentional and overall non-adherence. This could be due to the fact that they have learnt to cope with having RA but as their disease activity is remaining relatively low (i.e. they do not yet require biologic therapy), they are less concerned with keeping to medication regimens than biologic patients who have experienced worse flare ups.

It is important to consider the different treatment groups separately, particularly those that have been newly diagnosed or who are also prescribed biologic medication as these results show that the different experiences that these patients have had has a strong effect on their social cognition model of illness which can impact on interpretation of interventions in RA. Little previous research has investigated these groups separately or adequately separated their results for analysis and so little is known about the differing perceptions that these patients have. As these results indicate that there are clear differences in levels of adherence for different treatment regimens, future research should try to quantify exactly why these differences are occurring and what effect it has on the disease.

7.4.2: Adherence groups

There were a number of differences between the different adherence types, most notably the fact that there was a higher rate of intentional non-adherence than forgetting. This is contrary to other researchers who have found higher unintentional than intentional non-adherence (Atkins & Fallowfield, 2006; Garcia-Gonzalez et al., 2008; Lowry et al., 2005). They were both relatively low at less than 25%, however when considering both, the overall non-adherence rate was 37.4%. This is in line with published adherence rates (Barber et al., 2004; Haynes, 2001), however most previous research has not specifically focussed on the differences between intentional and unintentional non-adherence and so individually, the rates appear quite low.

7.4.2.1: Overall non-adherence

A number of hypotheses concerning adherence were generated based on previous research. Notably, it has been found previously that demographics cannot reliably predict adherence (DiMatteo, 2004; Elliott, 2008; McDonald, Garz & Haynes, 2002; Treharne et al., 2004; Vermeire, Hearnshaw, van Royen & Denekens, 2001), which was also the case in this sample, other than age. Non-adherers were significantly younger and had shorter disease duration.

The focus of this study was to determine the differences between intentional and unintentional adherence as it was hypothesised that they would have different underlying processes. The results highlight this important difference as there was little difference in the psychological process of overall adherence/non-adherence.

7.4.2.2: Intentional non-adherence

Low adherers were approximately eight years younger than high adherers and had shorter disease duration, although this was not statistically significant. Contrary to the hypothesis, the low adherers showed better functioning and quality of life than high adherers. This could be related to adherence in that patients that find themselves functioning well whilst not taking DMARDs may continue to be non-adherent to lessen the burden of medication taking, although as this study is cross-sectional it is not possible to determine causality. There was a strong interaction between age and adherence for both DAS28 and quality of life with age. It would appear that for younger patients, their decision to adhere is strongly related to disease activity and those that are not taking their medications having less pill burden and also less disease activity. However, those that have high adherence tend to have high disease activity and worse quality of life, possibly because they are not seeing an improvement in their symptoms despite taking the medication. The effect is much less pronounced for older

patients whose disease activity is more in line with what would be expected so that those with low adherence have worse disease activity and quality of life. It may be that the decision to take medications by older patients is not as reactive to disease activity.

The psychological factors that differed between the high and low adherers suggest that low adherers perceive themselves more able to control their RA via means other than medication and that they perceive DMARDs to be less necessary and have more barriers to taking them than high adherers. This is reinforced with the logistic regression analysis as in the combined model HBM Barriers, SRM Consequences and SRM Chronicity were significant. The regression also shows that the Theory of Planned Behaviour is not related to intentional adherence at all, which is surprising as this theory claims to predict the intention a person has to perform a health behaviour, however Perceived Behavioural Control was only related to forgetting which is contrary to most research using the Theory of Planned Behaviour (Ajzen, 2005). This could be due to the fact that the Attitude factor had to be excluded from the analysis because of missing data as Albarracin et al. (2001) and Armitage & Conner (2001) found Attitudes to be good predictors of behaviour.

Although the Health Belief Model, Self Regulatory Model and Beliefs about Medications were all separately related to intentional adherence, a model combining all of these factors proved to be the best with 42% of low adherers correctly classified. This supports the fact that each of these models is useful in explaining adherence behaviour, which has been found in previous research (Orbell et al., 2006). However on combining the models, some previously significant factors became non-significant. As logistic regression enhances shared variance between the variables, this provides evidence that there is considerable collinearity between the models, indicating that they are measuring the same psychological processes. This is also supported by the high correlations between some factors in Table 7.11. This study provides evidence that there is a need to identify the most predictive factors and combine some elements of the models to provide a coherent, parsimonious model of intentional medication adherence, particularly as most previous research using these models individually have not been able to explain a lot of the variance in adherence (Armitage & Conner, 2001; DiMatteo, Haskard & Williams, 2007; Groarke et al., 2004; Hagger & Orbell, 2003; Harrison et al., 1992; Hurkmans et al., 2010).

7.4.2.3: Unintentional non-adherence (forgetting)

As with intentional adherence, patients that forget their medication were generally younger and had shorter disease duration. Unlike for intentional non-adherence, the forgetters had worse disease activity and quality of life, which would be expected if DMARDs were not being taken correctly and supports the hypothesis.

The only social cognition model associated with forgetting was the Theory of Planned Behaviour and the patient's confidence in being able to take their medication correctly "as prescribed" which explained 20% of the variance in forgetting. Patients that forget were also 3.75 times more likely to be working than non-forgetters. This suggests that the effect of age on adherence was mediated by working, however only 23.5% of the direct effect of age on forgetting was mediated which was non-significant.

The lack of association between the social cognition models and forgetting supports the hypothesis that intentional non-adherence is based on a deliberate decision whereas forgetting is completely unintentional, reiterating the importance of addressing these different types of non-adherence differently. The only factor that appears to be related is the patient's confidence to take their DMARDs, however this could be as a result of the patient's realisation that they often forget to take their medication. It is not possible to determine the direction of this relationship in a cross-sectional study.

7.4.3: Beliefs about medications

Both the general and specific aspects of beliefs about medications were measured in this sample. However, contrary to previous research (de Thurah et al., 2010; Horne, 1999; Treharne et al., 2004), perceptions of necessity were not related to either intentional or unintentional non-adherence. This is surprising as this has been found to explain approximately 15-20% of the variance in medication adherence previously (Horne, 1999), however univariate analyses showed that there was no difference between necessity scores for any of the adherence groups. The means were reasonably high for all groups indicating that all patients, regardless of their adherence perceived their DMARDs to be necessary for their treatment which could explain why there was no effect in multivariate analysis. However, this is at odds with other research looking at adherence to DMARDs by RA patients (de Thurah et al., 2010; Treharne et al., 2006) and removes a potential avenue for intervention through education about DMARD treatment.

7.5: Conclusions

Overall, the differing relationships between the social cognition models and intentional and unintentional adherence provide evidence for the fact that patients use information and experience to develop a model of illness to make a logical decision to take medication. Patients that have more disease activity and have longer to develop a model are more likely to decide to take their DMARDs than patients who have not had to endure the negative consequences of RA for as long. As only confidence in taking DMARDs as prescribed was related to forgetting, it can be assumed that

forgetting is in fact unintentional and not related specifically to treatment or illness perceptions. This suggests that interventions to tackle each type of adherence would be necessary in order to improve prognosis. A reminder or cue to action to prompt patients who forget might be sufficient for them to take their medication whereas information regarding possible effects and consequences of non-adherence would be needed to inform those patients who have chosen not to take their DMARDs. These results demonstrate that it is imperative for the different types of adherence to be investigated separately in order to determine exactly why patients are non-adherent and the best ways to address this as they have very different underlying mechanisms that will not respond to a "one size fits all" approach. All future research must take this into account when measuring non-adherence in chronic illness.

Chapter 8

Stability and change in social cognition models of illness in rheumatoid arthritis patients over six months: Longitudinal analysis

8.1: Introduction

From a theoretical perspective, the social cognition models of illness posit that a patient's experience and knowledge of their illness will influence the expression of various factors such as perceived severity and attitudes towards self-management behaviours. For example, Leventhal, Nerenz & Steele (1984) argued that a patient's representation of their illness is constantly updated with new knowledge and experience and so it would be expected that there would be changes in perceptions over time. Given the unpredictable and changeable nature of RA progression, patients from a rheumatology clinic would be expected to have very different experiences of disease activity and treatment regimens from which they draw knowledge of their illness. Changes in illness perceptions over a relatively short period of time would be expected for newly diagnosed patients who may have many contacts with a Rheumatologist and adjustments to treatment directly after diagnosis. In addition, patients who have experienced a changeable disease leading to biologic therapy would also be required to adjust to a different routine. A literature search revealed a paucity of research that has specifically identified which factors are more susceptible to change and at what point in a chronic illness stability is likely to occur with only three studies that had investigated any of the social cognitive models of illness longitudinally in chronic illness. However, the empirical studies suggest that Leventhal's theory is not supported as Rutter & Rutter (2007) found that illness perceptions were stable over 12 months for patients with Irritable Bowel Syndrome. Stability of medication necessity beliefs have also been found over nine months in RA (de Thurah et al., 2010) and 12 months in ischemic heart disease (Allen LaPointe et al., 2010), although concerns about medication increased in both studies.

However, these studies had small sample sizes and all patients had established disease. It is likely that these patients had already incorporated the new knowledge and experience gathered rapidly after diagnosis into an illness representation that remained stable at the point of measurement. For this reason, it is important to establish at what point in the disease illness representations become stable and which factors are most susceptible to initial change which has not been carried out previously. Although Leventhal's theory that patients subject to a changeable illness would have

changes in illness perceptions is not supported by these studies, this could be due to methodological issues within the current literature.

The baseline results shown in Chapter 7 showed that newly diagnosed rheumatoid arthritis patients had significantly different psychological sumscores than more experienced patients suggesting that there could be more change in these patients' representations as they become more accustomed to the disease and its treatment. To test the stability of the social cognition models over time, the patients were followed-up over six months and asked to complete the psychological questionnaires again. The aim of this prospective longitudinal study is to test Leventhal's theory that new knowledge and experience leads to changes in illness representations.

8.1.1: Hypotheses

Based on Leventhal's assumption, a number of hypotheses were generated:

1) Patients with long-term disease (the established group), will have stable Self Regulatory Model and Beliefs about Medications sumscores over six months (Allen LaPointe et al., 2010; Rutter & Rutter, 2007).
2) Newly diagnosed patients will have significantly different psychological sumscores at six months than at baseline (Berry et al., 2004), specifically those concerning the potential severity of RA and the treatment requirements as they gather more experience and knowledge.
3) There will be similar changes in Health Belief Model sumscores as Self Regulatory Model sumscores (based on cross-sectional results, Chapter 7).
4) Patients with concurrent biologic treatment will demonstrate some changes in psychological sumscores due to fluctuating disease experience but they will be mostly stable.

8.2: Methodology

8.2.1: Materials and procedure

Patients were required to complete a follow-up questionnaire six months after initial recruitment, as detailed in the information sheet and consent form that they received at baseline. The questionnaire was identical to that at baseline (Appendix 7.1) except for the omission of demographic questions such as age and gender.

Follow-up questionnaires were sent by post to patients along with an explanatory letter and stamped addressed envelope in order to return it to the researcher. Questionnaires were sent approximately

one week prior to the date required. If a questionnaire had not been returned within 18 days of it being sent, and there were no other reasons for non-response (e.g. death) then a reminder letter with another copy of the questionnaire and stamped addressed envelope was sent. Clinical data including changes in RA prescription, number of outpatient appointments since baseline, number of inpatient days since baseline, number of Accident and Emergency contacts since baseline, latest DAS28 score and latest inflammatory blood markers were recorded from patients' notes.

8.2.2: Patients

Figure 8.1 shows the response rate for the follow-up questionnaires at six months. After reminders were sent there was an excellent follow-up rate of 75.3% (N=171). Successful follow-up was highest for the new patients with 82.9%, although the established and biologic groups did not differ very much at 71.4% and 76.25% respectively. There was some variation between the six different hospitals from which patients were recruited with the lowest successful follow-up being 60% and the highest at 90.6%, although on average it was good at 72.4%.

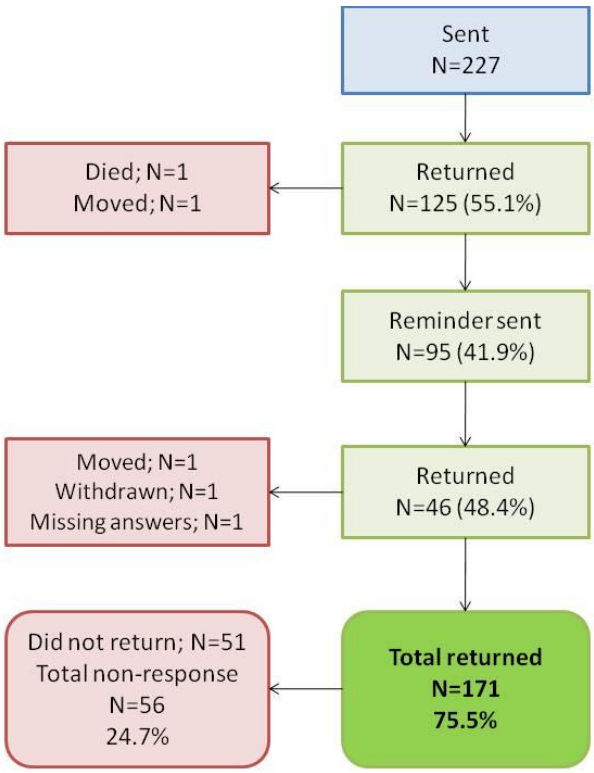


Figure 8.1: Follow-up response rates

Demographic variables for all patients are shown in Table 8.1. A total of 171 patients responded at six months and there were very few differences between responders and non-responders. Non-responders tended to be younger at 53.3 (16.3) years than responders at 59.1 (14.3); t(222) = 2.56, p=0.01 and were more likely to be working; χ^2 (1) = 7.59, p=0.01, although this may be because they were younger. Non-responders were also more likely at baseline to report unintentional non-adherence at 35% compared to just 15% of the responders reporting forgetting; χ^2 (1) = 10.20, p=0.001. This may impact on the results as the prevalence of unintentional non-adherence is likely to be underestimated in the follow-up analysis, although the number of non-responders that report low intentional adherence did not differ.

Table 8.1: Demographic variables for responders and non-responders

	Total (N=227)		Responders at six months (N=171)		Non-responders at six months (N=56)		Bivariate analysis		
	N (%)	Mean (SD)	N	Mean	N	Mean	Statistic	df	p
Age	224	57.7 (15.0)	168	59.1 (14.3)	56	53.3 (16.3)	2.56	222	0.011*
Gender									
Male	55 (24%)		45 (26%)		10 (18%)		1.01	1	0.315
Female	172 (76%)		126 (74%)		46 (82%)				
Education									
Secondary school	110 (50%)		86 (50%)		24 (45%)		0.45	3	0.930
College	61 (27%)		46 (28%)		15 (28%)				
University	32 (14%)		23 (13%)		9 (17%)				
Postgraduate	19 (9%)		14 (9%)		5 (9%)				
Working									
No	131 (58%)		107 (63%)		24 (43%)		7.59	1	0.006*
Yes	96 (42%)		64 (37%)		32 (57%)				
Disease duration	222	12.6 (10.8)	165	13.1 (11.4)	57	11.3 (8.8)	1.05	220	0.295
DAS28	175	3.6 (1.5)	137	3.49 (1.47)	38	3.9 (1.7)	1.49	173	0.139
HAQ	227	1.1 (0.8)	170	1.04 (0.76)	57	1.1 (0.8)	0.63	225	0.527
Intentional adherence									
Low	58 (25.7%)		44 (27%)		14 (27%)		NA		
High	157 (69.2%)		120 (73%)		38 (73%)				
Unintentional adherence									
Forget	42 (18.6%)		24 (15%)		18 (35%)		10.20	1	0.001*
Do not forget	174 (76.7%)		141 (85%)		34 (65%)				

Note: statistics for the bivariate analysis are student's t test for continuous variables and χ^2 for categorical variables.
*p<0.05

8.2.3: Statistical analyses

Patients' adherence and treatment groups were classified in the same way as at baseline. Univariate analyses were carried out in the same way as at baseline with ANOVA with Bonferroni correction for continuous variables and χ^2 for categorical. Repeated measures student's t tests were used to assess differences between baseline and six month sumscores for the same variable.

8.3: Results

8.3.1: Missing data

Missing data at six month follow-up was very similar as at baseline with between 5.5% and 23% for individual questions with the exception of the Theory of Planned Behaviour Attitudes questions and DAS28 score. Inspection of the missing data suggested that other than TPB Attitudes and DAS28, the data was *missing at random* and so other than for these variables, missing data was imputed using the same methodology as at baseline.

8.3.2: Reliability of scales used

The scales were tested for internal reliability using Cronbach's α for six month follow-up. Very similar values were found for most scales indicating that the majority remained above 0.70. All of the Cronbach's α values are shown in Appendix 8.1. In summary the BMQ overuse scale had better internal consistency at six months with Cronbach's α = 0.71 compared to 0.67 at baseline. However, two scales had worse internal consistency at six months; HBM benefits (Cronbach's α = 0.52) and SRM treatment control (Cronbach's α = 0.55), although this has also been found by other researchers (Menckeberg et al., 2008; Treharne et al., 2004). To retain consistency between baseline and follow-up, no changes to the scales were made.

8.3.3: Social cognition models in treatment groups

As there was a very good response rate at six months, the number of patients for each treatment group remains high. The established and biologic groups retained 72.3% and 72.6% of patients respectively and there was very little attrition in the new group with 85.7% of patients successfully followed-up. The actual sample size for each treatment group is shown in Table 8.2 and indicates that there were still sufficient numbers of cases per variable in order to carry out logistic regression, indicating that there remains sufficient power at six month follow-up.

8.3.3.1: Stability of social cognition models within treatment groups

Table 8.2 shows the mean *differences* in sumscores from baseline to 6 month follow-up to identify whether factors of the social cognition models changed over time. The sample as a whole had very little variation, however, the scores for the different treatment groups varied greatly as the newly diagnosed patients had statistically significant changes on five factors whereas the established patients' psychological scores were stable. At six months, the newly diagnosed patients perceived their RA to have significantly higher consequences (repeated measures $t(37) = -2.37$, $p=0.02$) and

that they have lower personal control ($t(37) = 2.11$, $p=0.04$) and lower treatment control ($t(37) = 2.87$, $p=0.01$) than at baseline. They also perceived their DMARD medication to be more necessary with an increase of 1.14 points ($t(35) = -2.06$, $p=0.047$). The biologic group showed statistically significant differences from baseline on only two factors; they perceived there to be more barriers to taking medication ($t(60) = -4.10$, $p<0.001$) and that their RA had fewer cyclical symptoms ($t(61) = 3.26$, $p=0.002$). In contrast, the established group showed no statistically significant changes from baseline in their sumscores.

Table 8.2: Mean changes in sumscores from baseline to 6 months for each treatment group

	Whole sample	Newly diagnosed	Established	Biologic
Total N	171	42	68	61
Theory of Planned Behaviour				
Important others	-0.10 (1.50)	0.19 (1.43)	-0.19 (1.31)	-0.18 (1.72)
Personal control	0.09 (3.58)	0.72 (3.47)	0.30 (3.49)	-0.49 (3.71)
Health Belief Model				
Barriers	0.88 (3.09)	-0.06 (3.16)	0.68 (2.91)	**1.62 (3.09)***
Benefits	0.23 (1.90)	0.44 (1.87)	0.10 (2.07)	0.25 (1.74)
Severity	0.14 (2.68)	0.06 (2.71)	0.53 (3.16)	-0.20 (2.05)
Self Regulation Model				
Identity	0.27 (2.12)	0.18 (2.35)	0.32 (1.71)	0.29 (2.39)
Chronic timeline	0.26 (3.86)	0.68 (5.16)	0.13 (3.93)	0.17 (2.89)
Cyclical timeline	-0.54 (3.14)	-0.68 (3.67)	0.27 (2.70)	**-1.27 (3.08)***
Consequences	-0.02 (2.89)	**1.0 (2.60)***	-0.42 (3.35)	-0.25 (2.44)
Personal control	-0.05 (3.98)	**-1.42 (4.14)***	0.63 (3.94)	0.10 (3.77)
Treatment control	-0.75 (3.31)	**-1.97 (4.23)***	-0.18 (2.60)	-0.59 (3.16)
Cohesion	0.15 (3.14)	0.32 (3.73)	0.02 (3.05)	0.19 (2.89)
Emotional effect	-0.35 (3.39)	-0.21 (3.11)	-0.03 (3.69)	-0.73 (3.27)
Beliefs about medications				
General harm	0.27 (2.13)	0.03 (2.20)	0.20 (2.03)	0.50 (2.20)
General overuse	0.36 (2.49)	0.18 (2.90)	0.16 (2.26)	0.68 (2.45)
Specific concern	0.33 (3.03)	-0.03 (3.03)	0.36 (2.88)	0.51 (3.21)
Specific necessity	-0.03 (2.90)	**1.14 (3.31)***	-0.42 (3.02)	-0.31 (2.30)
Necessity-concerns differential	-0.35 (4.27)	1.17 (4.60)	-0.78 (3.95)	-0.81 (4.26)
Depression, Anxiety and Positive Outlook				
Depression	0.02 (3.20)	0.76 (2.83)	-0.38 (3.48)	0.00 (3.07)
Anxiety	0.19 (2.26)	0.29 (2.30)	0.14 (2.57)	0.18 (1.89)
Positive outlook	0.07 (2.78)	0.13 (2.80)	-0.17 (3.31)	0.28 (2.10)
Disease outcomes				
HAQ	0.01 (0.43)	0.06 (0.51)	-0.06 (0.45)	0.04 (0.34)
DAS	-0.66 (1.57)	**-1.62 (0.59)***	-0.09 (1.39)	-0.66 (1.70)
EQ5D VAS	0.27 (21.12)	0.92 (21.57)	-2.80 (22.32)	2.97 (19.46)
EQ5D utility	0.01 (0.25)	0.002 (0.24)	0.01 (0.24)	0.01 (0.26)

*p<0.05

The changes between baseline and follow-up *within* treatment groups resulted in different relationships *between* treatment groups. At six months, new patients had significantly lower SRM timeline scores at 20.86 than biologic patients at 22.69; F(2, 161) = 3.25, p=0.04, Bonferroni p=0.04 (see Appendix 8.2). This mimics the relationship at baseline; however the scores of the newly diagnosed patients had risen so that at follow-up they did not differ from the established patients. Similarly, the SRM consequences sumscore for the new patients had risen so that at six months it did

not differ from the biologic group, whereas the established group was significantly lower at 19.52 than both the new patients at 21.90 (Bonferroni p=0.04) and biologic patients at 22.69 (Bonferroni p=0.001).

Similar changes were seen for the Beliefs about Medications variables as the necessity scores for new patients had risen so that there was no difference to established patients (Figure 8.2). At six months, the new patients had significantly lower BMQ necessity scores (Bonferroni p=0.046) and necessity-concerns differential (Bonferroni p=0.02) than the biologic patients.

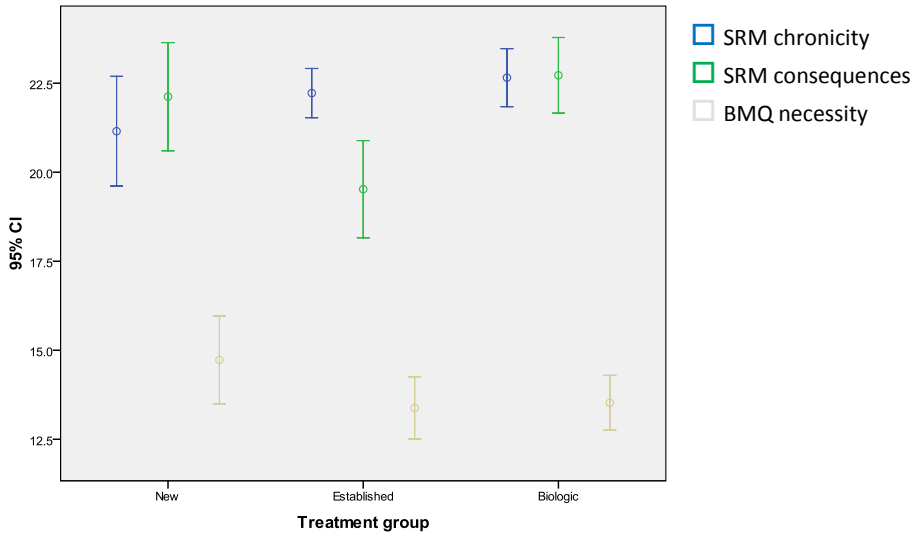


Figure 8.2: Follow-up mean sumscores for the model factors for each treatment group

8.4: Discussion

8.4.1: Responders versus non-responders

A very high proportion of patients were successfully followed up over six months with completed questionnaires received for 76.3% of the sample. The only differences found between patients who responded and those who failed to respond were age, working status and unintentional non-adherence. This suggests that patients who were younger, working and forgetful found it more difficult to remain in the study. The fact that more of the non-responders self-reported forgetting their medication at baseline than responders could impact on the longitudinal results by underestimating the prevalence of forgetting. Overall, the sample of 171 patients available at six months appeared to be a good representation of the sample as a whole.

8.4.2: Social cognition models in treatment groups

The small amount of previous research that has assessed psychological factors of chronic illness previously had varying results with regards to the potential changes in psychological measures over time (Allen LaPointe et al., 2010; de Thurah et al., 2010; Rutter & Rutter, 2007). Therefore, in line with the concept of appraisal and self regulation proposed by Leventhal, hypothesis 1 stated that the social cognition models would be stable for the established patients but that there would be changes in illness and treatment beliefs (SRM and BMQ) for the newly diagnosed patients in response to their growing knowledge and experience of RA. It was also hypothesised that the biologic patients would show some changes in the social cognition models as they have less stable disease but to a lesser extent than the newly diagnosed patients. These hypotheses was supported to a large extent as the newly diagnosed patients had a number of significantly different sumscores, namely increased SRM consequences and BMQ necessity but decreased SRM personal and treatment control. These changes brought the new patients' sumscores to be more in-line with the established and biologic patients meaning there were fewer differences *between* the treatment groups than at baseline. Although these results support the underlying theory of the Self Regulation Model, previous longitudinal studies have shown mixed results as Allen-LaPointe et al. (2010) demonstrated a very small effect of increased BMQ necessity perceptions over one year whereas Rutter & Rutter (2007) found no changes in illness perceptions for patients with Irritable Bowel Syndrome over one year. This discrepancy may be due to methodological issues in these studies including small sample sizes and the fact that the patients recruited had established disease and it would therefore be expected that they have a stable illness representation. The lack of adaptation found later in the disease course for both RA and Irritable Bowel Syndrome suggests that interventions that aim to modify illness or treatment beliefs should be aimed at newly diagnosed patients who may be more open to information that challenges their illness representation than patients with a lot of experience and persistent beliefs.

As there was no previous research which demonstrated a longitudinal analysis of the Theory of Planned Behaviour or Health Belief Model in health behaviours in chronic illness, the aim of this study was to establish whether these concepts are stable over time or subject to similar processes as the Self Regulatory Model and Beliefs about Medications model. Based on the cross-sectional results (Chapter 7), it was hypothesised that the HBM factors would also be variable in newly diagnosed patients but not in more established patients. However, none of the HBM factors changed significantly for the new patients and only the biologic patients scored significantly higher on HBM barriers at six months. It would appear that these factors remain stable over time, although it is

possible that more time is required for the newly diagnosed patients to score differently on these scales, which was not possible to determine from this study.

Overall, it seems that the social cognition models perform differently over time. In line with Goodacre & Goodacre (2004), answers to the Health Belief Model were mostly stable whereas the Self Regulatory Model was more subject to change, particularly for newly diagnosed patients. As Leventhal et al. (1992) claimed that the illness representations of patients would change as they acquire new knowledge and experience, the expected change in illness perceptions was supported by these data.

8.5: Conclusions

The theoretical assumptions that patients' perceptions of their illness are influenced by knowledge and experience are supported by these data as newly diagnosed patients showed changes in the psychological sumscores whereas the established patients had stable representations over time. This demonstrates the importance of acknowledging the likely heterogeneity of a clinic population and therefore separating newly diagnosed patients both for research into illness perceptions and in any intervention relating to the social cognition models of illness.

Chapter 9

Using social cognition models of illness to predict adherence to DMARDs by rheumatoid arthritis patients over six months: Longitudinal analysis

9.1: Introduction

In order to understand the effects that social cognition models of illness have on medication adherence over and above other aspects such as demographics and what effect adherence has on wellbeing in patients with a chronic illness, longitudinal studies must be carried out in order to establish causality. Although there have been a number of studies that have investigated this cross-sectionally (e.g. Chilcot et al., 2010; Horne & Weinman, 2002; Llewellyn et al., 2003; Niklas et al., 2010; Ross et al., 2004) including in rheumatoid arthritis (Carlisle, John, Fife-Shaw & Lloyd, 2005; Goodacre & Goodacre, 2004; Scharloo et al., 1998; Treharne, Lyons, Kitas & Booth, 2005), there is currently a scarcity of prospective, longitudinal studies with large sample sizes in order to effectively model the causal impact of the social cognition models on adherence.

A literature search found only three studies that had used any of the four social cognition models being studied in longitudinal analysis. Ediger et al. (2007) investigated the effects of beliefs about medications on adherence in Inflammatory Bowell Disease. The two studies that included RA patients had psychological (Scharloo et al., 2000) and functional outcomes (Frostholme et al., 2007) and did not investigate adherence. There is therefore little known about how adherence changes in chronic illness or the best ways to predict non-adherence. In order to establish influences on adherence to medication, how this changes over time and the best ways to intervene to improve illness, more evidence is required, particularly in an unpredictable and progressively disabling disease such as rheumatoid arthritis.

Three studies have specifically used the social cognition models in this study to predict adherence to treatment in a prospective study. Orbell et al. (2006) compared the Theory of Planned Behaviour and Self Regulatory Model in predicting attendance to treatment for abnormal cervical smear tests over a period of 15 months. Although a number of factors from both models significantly predicted the *intention* to attend the follow-up appointments, only Perceived Behavioural Control (TPB) was a significant predictor of actual attendance, although perception of treatment control (SRM) was also

successful in discriminating between attenders and non-attenders. Although attendance at follow-up treatment appointments is a different health behaviour that may have different underlying psychology than medication adherence, this study does provide some evidence that some psychological factors, namely perceived efficacy of the treatment and confidence to carry out the behaviour can successfully predict adherence to follow-up colposcopy treatment.

Allen LaPointe et al. (2010) measured Beliefs about Medications in 812 patients with ischemic heart disease over 12 months. As has been found cross-sectionally (Ross et al., 2004; Treharne et al., 2005), only necessity scores were related to medication adherence. In a study investigating adherence to Methotrexate by rheumatoid arthritis patients, de Thurah et al. (2010) measured Beliefs about Medications and adherence by patients who were newly diagnosed and nine months later. They found very little variation in the *prevalence* of low adherence; however they do not report intra-individual variation. Like Allen LaPointe et al. (2010), higher necessity scores were associated with higher adherence but there was little change in necessity or concern scores over nine months. Although BMQ and adherence were measured at two time points, de Thurah et al. (2010) do not use baseline scores to predict adherence and so this study only provides information on the variability of psychological factors and adherence, not any causal effects.

An interesting effect that has been demonstrated cross-sectionally is the fact that some illness perceptions have been shown to impact on beliefs about medications which in turn have an effect on treatment adherence. Horne & Weinman (2002) found that perception of the likely length of the illness (SRM chronicity) and the potential seriousness of the outcomes (SRM consequences) are mediated by the perceived necessity of the medication (BMQ necessity) which impacts on adherence to asthma preventer medication. Similarly, Niklas et al. (2010) found again that SRM consequences impacted on BMQ necessity and also that the emotional effects (SRM emotions) influenced the level of concern about the medication (BMQ concerns) which in turn explained variance in adherence to pharmacological treatment for non-malignant pain. These studies clearly demonstrate that the social cognition models are strongly related and that by modelling potential mediators it is possible to understand more of the nuances of the psychology behind medication adherence. However, as these studies were cross-sectional, the effects of illness and treatment beliefs on adherence over time are not clear.

The studies mentioned above start to provide some knowledge and evidence of which psychological factors are predictive of treatment adherence over time, although only the Self Regulatory Model and Beliefs about Medications have been investigated longitudinally in chronic illnesses. However, these studies have involved patients with chronic illnesses other than RA and there are a number of

issues that prevent applicability to rheumatoid arthritis. Firstly, as illness perceptions are expected to differ for different illnesses (Hagger & Orbell, 2003) studies in asthma and heart disease are not directly comparable to adherence to DMARDs by RA patients. The longitudinal studies also tended to have very small sample sizes with adherence measured and analysed in different ways. For example, de Thurah et al. (2010) measured Beliefs about Medications at baseline but did not use this to predict adherence to DMARDs at nine months. Although establishing how these beliefs change over time and the corresponding changes in adherence is desirable, being able to predict which patients will be non-adherent through baseline psychological measures is more clinically useful as a means of targeting interventions in the future. For this reason, this study will investigate adherence to DMARDs prospectively over six months by patients with rheumatoid arthritis in an attempt to identify which social cognition models at baseline best predict non-adherence at six months.

9.1.1: Aims and hypotheses

The cross-sectional results shown in Chapter 7 indicate that the Self Regulatory Model and Beliefs about Medications perform better than the other models at predicting intentional non-adherence to DMARDs. None of the models reliably explained unintentional adherence. The primary aim of this prospective longitudinal study is to test how well the social cognition models at baseline predict adherence six months later. The secondary aim is to establish the changes in adherence over six months; particularly for the newly diagnosed patients who are expected to differ more than the experienced patients. This will provide the evidence upon which future interventions could be based as identifying "negative" illness representations allows for more targeted development of effective interventions to improve adherence.

As discussed, there has been little previous research using the social cognition models to predict medication adherence longitudinally and none of these studies have separated intentional and unintentional adherence. Therefore, many of the aims of this study are exploratory; however a number of hypotheses were generated for overall adherence:

1) There will be little variation in adherence over six months for the established and biologic patients (de Thurah et al., 2010).
    a. Contrary to de Thurah et al. (2010), it is hypothesised that patients newly prescribed DMARDs *will* have variability in their adherence from baseline as they become accustomed to the regimen.
2) Higher baseline SRM identity, SRM consequences, SRM timeline and BMQ necessity will predict better adherence at six month follow-up (Hagger & Orbell, 2003; Hampson, Glasgow & Ziess, 1994, Horne & Weinman, 2002; Wallston, 1993).

3) Treatment beliefs (BMQ) will mediate the relationship between illness perceptions (SRM) and adherence (Horne & Weinman, 2002; Nicklas et al., 2010).

As there has been no previous research investigating adherence over time for patients with high or low adherence, or using the Theory of Planned Behaviour and Health Belief Model to predict adherence over time, a number of exploratory aims will also be tested:

1) Determine whether the Theory of Planned Behaviour and Health Belief Model predict adherence status at six months.
2) Determine whether adherence is more likely to improve or worsen over time.
3) Determine which social cognition models best predict *changes* in adherence over six months to identify potential areas for intervention.

9.2: Methodology

9.2.1: Materials and procedure

The follow-up procedure for this study is described in Chapter 8, section 8.2.2.

9.2.2: Patients

After one reminder, a total of 171 (75.3%) patients were successfully followed-up after six months. Demographic information for all patients is shown in Table 8.1.

9.2.3: Statistical analyses

The variability in adherence over six months was examined for each of the treatment groups. Patients were categorised based on whether their adherence status did or did not change for intentional, unintentional and overall adherence groups. Differences in baseline psychological sumscores and the odds ratio of changing adherence were calculated.

Logistic regression was used to assess the predictive power of the psychological factors of each model to predict adherence. To establish the best predictors of adherence, the analysis was split into three for each adherence type creating six regression tables. These included; i) using baseline psychological sumscores to predict six month adherence status, ii) using baseline psychological factors sumscores to predict *change* in adherence status and iii) using *changes* in psychological scores to predict *change* in adherence. Changes in adherence were from high to low and low to high intentional adherence and from forgetting to not forgetting and from not forgetting to forgetting.

The χ^2 test, percentage of correctly classified cases and Nagelkerke's R^2 were used to assess the suitability of each of the social cognition models to predict the dependent variable.

In order to test causal pathways and the hypothesised mediating relationship of treatment beliefs on illness perceptions, structural equation modelling (SEM) was carried out which allows for multiple regression analyses to be carried out simultaneously. Multiple independent variables, labelled "exogenous variables" can be used to predict multiple dependent variables ("endogenous variables") which can either be directly observed or latent variables. SEM is also particularly useful for testing mediating and moderating relationships which were expected in relation to treatment and illness beliefs and the effects on adherence. Variables can also be set to correlate with each other which allows for more sophisticated models that more accurately represent the likely complex decision making involved in health behaviours. The method of estimation was maximum likelihood which assumes that the observed variables are representative of the population. Standard goodness-of-fit indices were used to assess the suitability of the models tested including χ^2, CFI, RMSEA, and SRMR which are discussed in Chapter 6, section 6.6.3. Standard thresholds are used except for χ^2 which is often significant in SEM simply due to a large sample size and is therefore interpreted with caution. Initially, two models of medication adherence developed in other chronic illnesses (Horne & Weinman, 2002; Nicklas, Dunbar & Wild, 2010) were tested for model fit in the current sample. Two models based on the correlations and regression analysis of the current samples were then tested to determine the best model of medication adherence for rheumatoid arthritis.

9.3: Results

At six months, a total of 23.4% (N=40) patients self-reported low intentional adherence and 21.6% (N=37) reported forgetting. Using the same categorisation methodology as described in Chapter 3, 36.3% of the total sample were classified as overall low adherers. There were some differences between treatment groups as newly diagnosed patients had the highest rates of forgetting and overall low adherence at 29.3% and 39% respectively but the lowest rates of intentional low adherence at 17.1%. In contrast, the established patients had the highest rates of intentional low adherence (27.3%) but the lowest self-reported forgetting at 16.7%.

9.3.1: Variability in adherence over six months

Figure 9.1 shows that there was some variation in adherence from baseline to 6 month follow-up and that the amount of variation differed both for the type of adherence (intentional/unintentional) and for treatment groups. The biggest changes were for unintentional non-adherence with an increased proportion of patients forgetting at six months relative to baseline rates. There was less of a change

for intentional adherence although at follow-up, the established patients had a slightly lower percentage of patients with low intentional adherence (27.3%) than at baseline (34.8%).

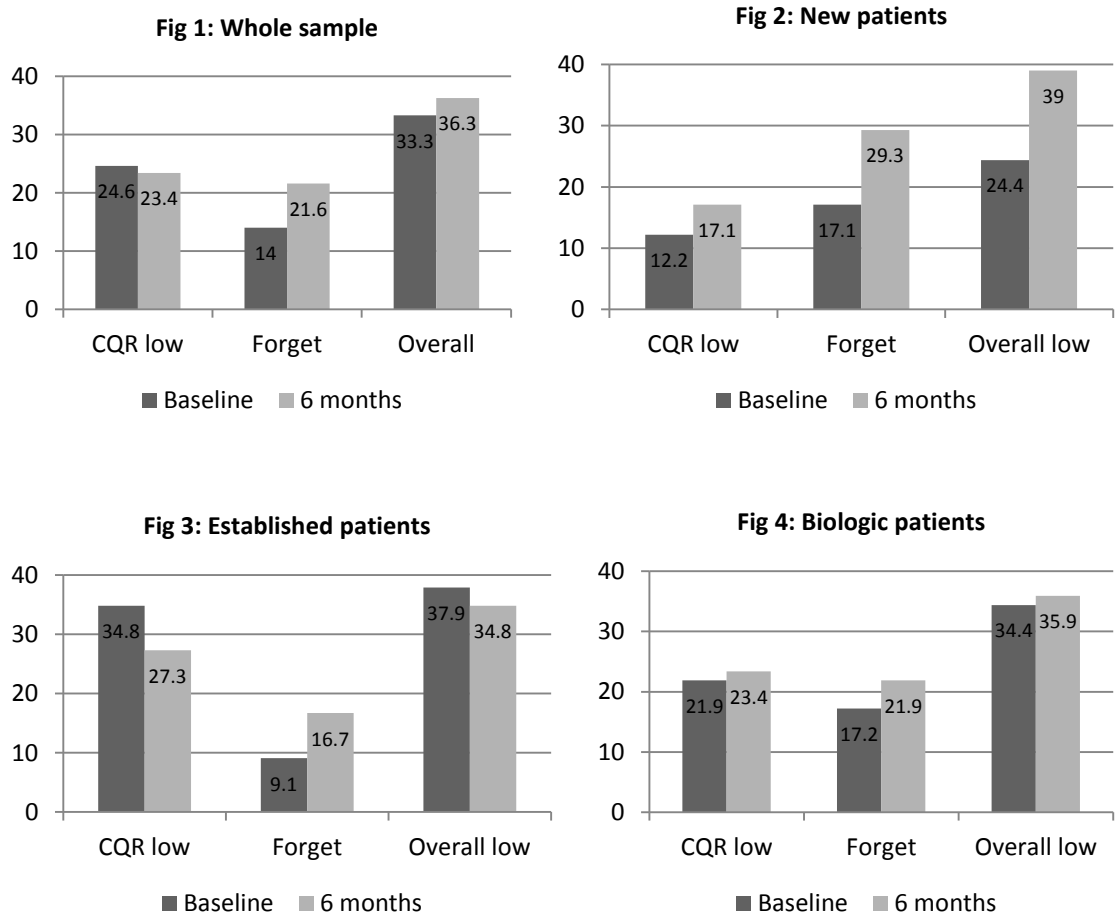


Figure 9.1: Percentage of patients with low adherence at baseline and six month follow-up for each treatment group

Although the total proportion of patients with low intentional adherence remained similar at baseline and six months, approximately 30% of patients' scores changed. As a similar number of patients changed in both directions, the net effect was low. In contrast, more patients who did not forget at baseline started forgetting at six months than vice versa.

9.3.2: Variability in social cognition models within adherence groups

Table 9.1 shows that there were significant mean psychological sumscore changes from baseline to follow-up for the low intentional adherence group only. The significant changes shown in Table 9.1 are an increase of 1.10 (2.87) points for HBM barriers ($t(39) = -2.42$, $p=0.02$) and a decrease of 1.20 (3.14) points for SRM treatment control ($t(39) = 2.42$, $p=0.02$) for the low intentional group showing

that at six months, they perceive there to be even more barriers to their medication taking and have less confidence in the ability of their DMARDs to control their RA.

The mean changes over six months have resulted in a number of changes in the differences *between* adherence groups from baseline (see Appendix 9.1 for six month mean sumscores). There is now only a significant difference for HBM severity with low intentional adherers having a sumscore of 15.73 (3.71) compared to 17.19 (3.82) for high intentional adherers; $t(161) = -2.12$, $p=0.04$. This difference was not apparent at baseline, however at 6 months there is no longer a difference between sumscores for HBM barriers, SRM consequences, and SRM personal control as there was at baseline. Overall high adherers also perceive their medications to be more necessary than low adherers ($t(161) = -3.09$, $p=0.002$). The only difference for unintentional adherence is for TPB Perceived Behavioural Control as forgetters have significantly lower scores (29.92) than those who do not forget (31.17).

Table 9.1: Mean changes in sumscores for adherence groups from baseline to six month follow-up

	Intentional low	Intentional high	Forget	Do not forget	Overall low	Overall high
Total N	40 (24.25%)	125 (75.75%)	37 (22.7%)	126 (77.3%)	62 (37.6%)	103 (62.4%)
Theory of Planned Behaviour						
Important others	-0.13 (1.36)	-0.9 (1.56)	<0.01 (1.94)	-0.13 (1.37)	-0.03 (1.72)	-0.15 (1.37)
Personal control	0.30 (3.52)	0.04 (3.64)	-0.14 (4.31)	0.14 (3.39)	0.02 (3.66)	0.16 (3.58)
Health Belief Model						
Barriers	**1.10 (2.87)***	0.74 (3.19)	0.46 (2.83)	0.94 (3.18)	0.73 (3.04)	0.89 (3.16)
Benefits	0.03 (1.49)	0.32 (2.01)	0.09 (2.03)	0.29 (1.85)	0.13 (1.85)	0.32 (1.91)
Severity	-0.65 (2.59)	0.33 (2.66)	-0.40 (2.71)	0.22 (2.65)	-0.52 (2.64)	0.45 (2.64)
Self Regulation Model						
Identity	0.40 (2.30)	0.24 (2.10)	0.08 (2.16)	0.36 (2.15)	0.05 (2.19)	0.42 (2.11)
Chronic timeline	-0.38 (3.06)	0.56 (4.07)	0.18 (3.31)	0.36 (4.01)	-0.22 (2.95)	0.64 (4.27)
Cyclical timeline	-0.35 (3.39)	-0.65 (3.09)	-0.34 (3.42)	-0.65 (3.11)	-0.70 (3.30)	-0.50 (3.09)
Consequences	0.30 (2.77)	-0.22 (2.92)	0.64 (2.64)	-0.26 (2.91)	0.30 (2.89)	-0.33 (2.86)
Personal control	-1.03 (3.68)	0.37 (4.03)	-1.06 (3.89)	0.36 (3.95)	-0.87 (3.79)	0.57 (4.02)
Treatment control	**-1.20 (3.14)***	-0.55 (3.39)	-0.47 (4.01)	-0.79 (3.14)	-0.92 (3.77)	-0.59 (3.04)
Cohesion	0.10 (3.30)	0.24 (3.09)	0.22 (2.77)	0.20 (3.26)	0.10 (2.94)	0.28 (3.26)
Emotional effect	-0.45 (3.34)	-0.29 (3.47)	-0.43 (3.19)	-0.31 (3.52)	-0.58 (3.21)	-0.18 (3.56)
Beliefs about Medications Questionnaire						
General harm	0.73 (2.22)	0.14 (2.09)	0.40 (2.51)	0.26 (2.02)	0.42 (2.37)	0.21 (1.99)
General overuse	0.38 (2.55)	0.31 (2.50)	0.83 (2.49)	0.19 (2.50)	0.62 (2.58)	0.15 (2.46)
Specific concern	-0.62 (2.28)	0.62 (3.19)	0.44 (3.46)	0.28 (2.92)	0.08 (3.05)	0.45 (3.03)
Specific necessity	0.08 (2.99)	-0.05 (2.89)	<0.01 (3.47)	-0.02 (2.75)	-0.02 (2.94)	-0.02 (2.90)
Necessity-concerns differential	0.69 (3.71)	-0.67 (4.41)	-0.44 (4.97)	-0.31 (4.09)	-0.10 (4.33)	-0.47 (4.26)
Depression, Anxiety and Positive Outlook						
Depression	-0.13 (3.56)	0.06 (3.15)	-0.14 (3.58)	0.02 (3.14)	0.03 (3.34)	<0.01 (3.20)
Anxiety	-0.03 (2.44)	0.25 (2.24)	0.20 (2.95)	0.16 (2.09)	0.12 (2.59)	0.22 (2.10)
Positive outlook	-0.05 (3.33)	0.08 (2.60)	-0.24 (2.57)	0.14 (2.86)	-0.03 (3.06)	0.09 (2.63)

*p<0.05

9.3.3: Predicting adherence status at six month follow-up

Logistic regression was employed to determine if baseline psychological sumscores were able to reliably predict intentional adherence at six month follow-up. As collinearity was expected within each model (Petrie & Weinman, 2006) all of the factors for each model were included to extract the variance common to all factors. Each of the three social cognition models were tested separately and then combined to determine the best predictor of adherence (Table 9.2). Both the Self Regulatory Model and the Beliefs about Medications Questionnaire performed well with Nagelkerke R^2 being 20.5% and 13.1% respectively. However, neither the Theory of Planned Behaviour nor the Health Belief Model were able to reliably predict adherence at six months (χ^2 for both >0.05) and fared particularly badly for low adherers with less than 9% correctly identified.

The most accurate way of predicting six month intentional adherence was to use a combination of all of the models and add the baseline intentional adherence category (shown in the final column of Table 9.2). For this model, χ^2 (17) = 33.53, p=0.01 and 81.6% of cases were correctly identified, including 35.5% of low adherers. The odds ratios for each of the model factors are shown in Table 9.2. The trends for an increase in TPB important others scores leading to an *increased* odds of adherence whilst an increase in BMQ concern scores leading to a *decrease* in the odds of adherence were expected. Unsurprisingly, the most useful predictor of adherence at follow-up was adherence at baseline with patients who had high adherence at baseline being 3.84 times more likely to have high adherence at 6 months.

Although some factors included in the social cognition models at baseline adequately predicted intentional adherence at six months, they were not able to reliably predict forgetting at six months. Table 9.3 shows that none of the models separately were able to predict those who forgot their medication at six months. Combining the models with age and baseline forgetting status was significant; χ^2 (19) = 62.06, p<0.001 with Nagelkerke R^2 = 54.7%. Using this model, 96.1% of cases were correctly identified including 72.7% of forgetters. However, on closer inspection it is mostly age (Wald's β = 9.48) and baseline forgetting (Wald's β = 17.07) that were significant with only baseline SRM personal control significantly predicting forgetting at six months as a 1 point increase in personal control led to a 17% *increase* in the odds of forgetting.

Table 9.2: Logistic regression using baseline model factor sumscores to predict *intentional* adherence at six month follow-up

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications		Combined	
Variable	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR
TPB important others	4.13	1.03*							3.13	1.37 (p=0.077)
TPB perceived control	1.89	1.21							0.004	1.01
HBM barriers			2.09	0.92					0.001	1.00
HBM benefits			1.22	1.15					1.74	1.25
HBM severity			0.17	1.03					0.38	0.93
SRM identity					3.45	1.40			1.56	1.39
SRM chronicity					4.18	0.86*			4.74	0.78*
SRM cyclical					0.59	0.95			0.12	0.97
SRM consequences					0.43	1.04			0.12	1.03
SRM personal control					0.63	0.96			1.39	0.93
SRM treatment control					4.46	1.17*			2.38	1.19
SRM coherence					0.24	0.97			0.11	0.98
SRM emotion					3.27	1.10			2.71	1.13
BMQ harmful							5.81	1.30*	5.25	1.40*
BMQ overuse							0.42	0.95	0.27	1.06
BMQ necessity							1.34	0.92	0.02	1.01
BMQ concern							2.38	1.09	3.35	0.81 (p=0.067)
Age									1.77	1.03
Baseline adherence									4.48	3.84*
Model	χ^2 (3) = 7.36, p=0.061 Nagelkerke R^2 = 0.073 77.4% correct (8.3% of low)		χ^2 (4) = 8.26, p=0.083 Nagelkerke R^2 =0.083 75.5% correct (2.8% of low)		χ^2 (9) = 21.95, p=0.009 Nagelkerke R^2 = 0.205 81.2% correct (25% of low)		χ^2 (5) = 13.30, p=0.021 Nagelkerke R^2 = 0.131 77.9% correct (20% low)		χ^2 (19) = 36.33, p=0.01 Nagelkerke R^2 = 0.358 81.5% correct (35.5% low)	

*p<0.05

Table 9.3: Logistic regression using baseline model factor sumscores to predict *unintentional* adherence at six month follow-up

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications		Demographics		Combined	
Variable	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR
TPB important others	0.30	0.93									1.78	0.75
TPB perceived control	1.16	0.94									0.23	1.05
HBM barriers			3.73	1.11*							0.70	1.09
HBM benefits			0.04	0.97							0.29	0.89
HBM severity			0.50	0.95							1.94	1.25
SRM identity					0.39	0.90					1.34	0.75
SRM chronicity					1.38	0.94					0.18	0.96
SRM cyclical					0.41	1.04					0.24	0.96
SRM consequences					0.60	0.96					0.08	1.02
SRM personal control					6.04	1.14*					3.62	1.17*
SRM treatment control					4.06	0.86*					0.71	0.91
SRM coherence					0.03	0.99					0.001	1.00
SRM emotion					0.95	1.05					1.61	0.90
BMQ harmful							1.10	0.90			0.07	0.96
BMQ overuse							1.96	1.13			3.08	1.29
BMQ necessity							3.22	0.91			2.56	0.84
BMQ concern							0.13	1.02			2.10	0.83
Age									6.54	0.96*	9.48	0.93*
Baseline adherence									19.14	11.09**	17.07	27.20**
Model	χ^2 (2) = 2.19, p=0.334		χ^2 (3) = 3.91, p=0.27		χ^2 (8) = 10.20, p=0.252		χ^2 (4) = 5.21, p=0.266		χ^2 (2) = 36.41, p<0.001		χ^2 (19) = 62.06, p<0.001	
	Nagelkerke R^2 = 0.021		Nagelkerke R^2=0.038		Nagelkerke R^2 = 0.093		Nagelkerke R^2 = 0.050		Nagelkerke R^2 = 0.326		Nagelkerke R^2 = 0.547	
	77.4% correct (0% of forget)		77.7% correct (0% of forget)		77.6% correct (2.7% of forget)		78.6% correct (0% of low)		82.2% correct (45.9% of forget)		96.1% correct (72.7% of forget)	

*p<0.05, **p<0.001

9.3.4: Predicting change in intentional adherence

9.3.4.1: Predicting change in intentional adherence at six month follow-up using baseline sumscores

Equally as important as being able to predict adherence after six months, is the ability to predict and explain *changes* in adherence that may occur, as detailed in the exploratory aims. In section 9.3.1 it was clear that a significant proportion of patients changed over six months from high to low intentional adherence (and vice versa) and from not forgetting to forgetting (and vice versa) and so it would be advantageous to be able to predict these changes.

Logistic regression analysis was used to identify the best psychological predictors of patients whose adherence status changed over six months. Two regressions using baseline social cognition models scores were carried out to predict; i) baseline high intentional adherence changing to low and ii) baseline low intentional adherence changing to high.

Using baseline psychological scores to predict patients who changed from high to low intentional adherence was not successful as none of the social cognition models could reliably predict change (see Appendix 9.2 for details). Similarly, the social cognition models could not reliably predict change in adherence from low intentional at baseline to high intentional adherence at six months (Appendix 9.3).

9.3.4.2: Predicting change in intentional adherence at six month follow-up using change in sumscores

As well as using the baseline psychological sumscores, the *change* in sumscores over the six month follow-up period was also investigated to predict *change* in adherence because it was found in section 9.3.2 that there were significant changes in psychological sumscores for low intentional adherers only. Again, logistic regression was used to test each social cognition model as well as all of them combined to predict change in adherence from high to low and from low to high. For those with high baseline intentional adherence, it was not possible to reliably predict change to low intentional adherence; χ^2 (17) = 21.43, p=0.21 (Table 9.4).

Two of the logistic regression models predicting change in adherence from low at baseline to high at six months produced significant results (Table 9.5). The Health Belief Model correctly identified 68.3% of cases including 71.4% of those who changed from low to high intentional adherence. In this model, a 1 point increase in the change in HBM barriers led to a 41% *increase* in the odds of remaining a low adherer. Combining the psychological models also led to a marginally significant

regression model; χ^2 (17) = 27.54, p=0.051. The combined model correctly identified 86.8 % of cases including 89.5% of those whose adherence changed. Nagelkerke's R^2 is also very high at 68.7%. Although none of the individual variables are significant by themselves, there was a trend for an increase in the change of scores for HBM barriers (Wald's β = 2.64) to lead to an *increase* in the odds of remaining a low adherer and an increased change in SRM personal control (Wald's β = 2.60) and BMQ concern (Wald's β = 3.40) to lead to a *decrease* in the odds of remaining a low adherer. However although there appears to be an association between a change on some of the psychological factors and change in adherence, the *direction* of the change and the direction of the association (i.e. the change in psychological factors could impact on change in adherence or vice versa) is not available.

Table 9.4: Logistic regression using *change* in model factor sumscores to predict change in *intentional* adherence from high at baseline to low at follow-up

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications		Combined	
Variable	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR
TPB important others	1.27	0.84							1.79	0.76
TPB perceived control	0.18	0.97							0.03	1.02
HBM barriers			0.05	0.98					1.89	0.83
HBM benefits			1.90	0.80					2.39	0.74
HBM severity			4.12	1.28*					4.13	1.39*
SRM identity					0.004	1.01			0.38	1.11
SRM chronicity					2.90	1.13			3.16	1.20
SRM cyclical					0.65	1.08			1.63	1.16
SRM consequences					0.30	0.94			0.73	0.88
SRM personal control					2.17	1.12			2.31	1.15
SRM treatment control					0.03	0.98			0.12	0.96
SRM coherence					0.98	0.92			0.82	0.91
SRM emotion					0.93	1.09			0.56	1.09
BMQ harmful							0.03	0.97	0.003	0.99
BMQ overuse							0.42	0.93	0.34	1.10
BMQ necessity							0.62	0.93	1.08	0.88
BMQ concern							4.63	1.28*	2.44	1.24
Model	χ^2 (2) = 1.46, p=0.482 Nagelkerke R^2=0.024 85.3% correct (0% of changers)		χ^2 (3) = 5.56, p=0.14 Nagelkerke R^2=0.088 84.4% correct (0% of changers)		χ^2 (8) = 7.88, p=0.45 Nagelkerke R^2=0.125 84.1% correct (6.3% of changers)		χ^2 (4) = 5.95, p=0.20 Nagelkerke R^2=0.092 85.8% correct (0% of changers)		χ^2 (17) = 21.43, p=0.21 Nagelkerke R^2=0.333 83.7% correct (12.5% of changers)	

*p<0.05

Table 9.5: Logistic regression using *change* in model factor sumscores to predict *change* in intentional adherence from low at baseline to high at follow-up

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications		Combined	
Variable	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR
TPB important others	0.44	0.85							0.19	0.74
TPB perceived control	0.38	0.95							1.79	0.51
HBM barriers			4.33	1.41*					2.64	1.89
HBM benefits			2.20	0.70					0.25	0.75
HBM severity			1.10	0.87					0.11	0.78
SRM identity					0.59	1.18			0.62	0.39
SRM chronicity					1.38	0.81			0.46	0.55
SRM cyclical					1.21	1.16			1.63	2.28
SRM consequences					0.10	0.95			0.12	1.13
SRM personal control					0.35	0.93			2.60	0.35
SRM treatment control					3.40	0.75			1.95	0.37
SRM coherence					0.06	0.96			0.15	1.21
SRM emotion					0.17	0.96			0.37	1.19
BMQ harmful							3.36	1.40	0.29	1.35
BMQ overuse							0.03	0.98	0.33	0.75
BMQ necessity							0.49	0.90	0.30	1.33
BMQ concern							1.18	0.88	3.40	0.19
Model	χ^2 (2) = 0.84, p=0.66 Nagelkerke R^2=0.026 47.6% correct (68.2% of changers)		χ^2 (3) = 8.21, p=0.042 Nagelkerke R^2=0.242 68.3% correct (71.4% of changers)		χ^2 (8) = 7.47, p=0.49 Nagelkerke R^2=0.227 65% correct (65% of changers)		χ^2 (4) = 5.61, p=0.23 Nagelkerke R^2=0.171 63.4% correct (72.7% of changers)		χ^2 (17) = 27.54, p=0.051 Nagelkerke R^2=0.687 86.8% correct (89.5% of changers)	

*p<0.05

9.3.5: Predicting change in unintentional adherence (forgetting)

9.3.5.1: Predicting change in unintentional adherence at six month follow-up using baseline sumscores

One of the exploratory aims was to determine if the Theory of Planned Behaviour or Health Belief Model explained adherence. An interesting finding showed that those who did *not* forget at baseline and also had low TPB important others scores were 10.5 times more likely to become forgetters than those with high baseline TPB important others scores (χ^2 (1) = 8.87, p=0.003). These patients also perceived significantly higher HBM barriers to medication taking (F(1, 128) = 4.15, p=0.04).

To test the models more fully, using the same regression method as for intentional adherence, the baseline psychological model sumscores were used to predict change in *unintentional* adherence from i) those who became forgetful at six month follow-up and ii) those who forgot at baseline but ceased to forget at six month follow-up. For patients who at baseline did not forget, it was not possible to reliably predict change in adherence; χ^2 (17) = 26.02, p=0.07 (Table 9.6). However, there was a trend for a 1 point increase in TPB important others scores led to a 50% *increase* in the odds of a patient continuing to remember their medication.

The Self Regulatory Model produced a significant regression model (χ^2 (6) = 14.40, p=0.03) with Nagelkerke R^2 = 64.4% to successfully predict change from baseline forgetting to not forgetting (Table 9.7). This model correctly identified 87.5% of cases including 57.1% of those who changed from forgetting at baseline to not forgetting at 6 months. More specifically, a 1 point increase in baseline SRM personal control scores led to the odds of remaining a forgetter being 2.08 times higher. Also, a 1 point increase in SRM treatment control scores led to a 36% *decrease* in the odds of remaining a forgetter. Based on the associations found cross-sectionally between personal and treatment control and forgetting (see Chapter 7), the relationship of these variables to change in unintentional adherence are in the expected direction.

9.3.5.2: Predicting change in unintentional adherence at six month follow-up using change in sumscores

In contrast to the intentional adherence, the change in psychological scores was not predictive of change in unintentional forgetting in either direction. None of the social cognition models alone or combined were able to reliably predict patients whose unintentional adherence status changed with Nagelkerke R^2 being less than 15% for all of the models tested. The logistic regressions are summarised in Appendices 9.4 and 9.5.

Table 9.6: Logistic regression using baseline model factor sumscores to predict change in unintentional adherence when at baseline patients do *not* forget

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications		Combined	
Variable	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR
TPB important others	3.30	1.33							3.73	1.50*
TPB perceived control	0.08	0.98							0.85	0.91
HBM barriers			4.19	0.86*					4.76	0.74*
HBM benefits			0.01	1.02					0.29	1.14
HBM severity			0.26	1.05					4.23	0.71*
SRM identity					1.67	1.31			4.02	1.76*
SRM chronicity					5.65	1.16*			1.23	1.10
SRM cyclical					1.96	0.88			1.80	0.85
SRM consequences					0.01	0.99			0.80	1.10
SRM personal control					2.25	0.91			2.11	0.89
SRM treatment control					3.61	1.21*			0.17	1.06
SRM coherence					0.48	1.05			0.14	1.04
SRM emotion					0.35	1.04			3.13	1.19
BMQ harmful							0.25	1.07	1.18	1.21
BMQ overuse							1.51	0.87	0.42	0.89
BMQ necessity							0.01	1.01	0.04	1.02
BMQ concern							1.45	1.09	2.33	1.30
HAQ										
EQ5D utility										
Model	χ^2 (2) = 3.32 p=0.19 Nagelkerke R^2=0.044 86.4% correct (5.3% of changers)		χ^2 (3) = 4.58, p=0.21 Nagelkerke R^2=0.063 86.2% correct (0% changers)		χ^2 (8) = 11.39, p=0.18 Nagelkerke R^2=0.143 86.6% correct (15% of changers)		χ^2 (4) = 2.84, p=0.59 Nagelkerke R^2=0.039 86.5% correct (0% of changers)		χ^2 (17) = 26.02, p=0.074 Nagelkerke R^2=0.340 90.6% correct (29.4% of changers)	

*p<0.05

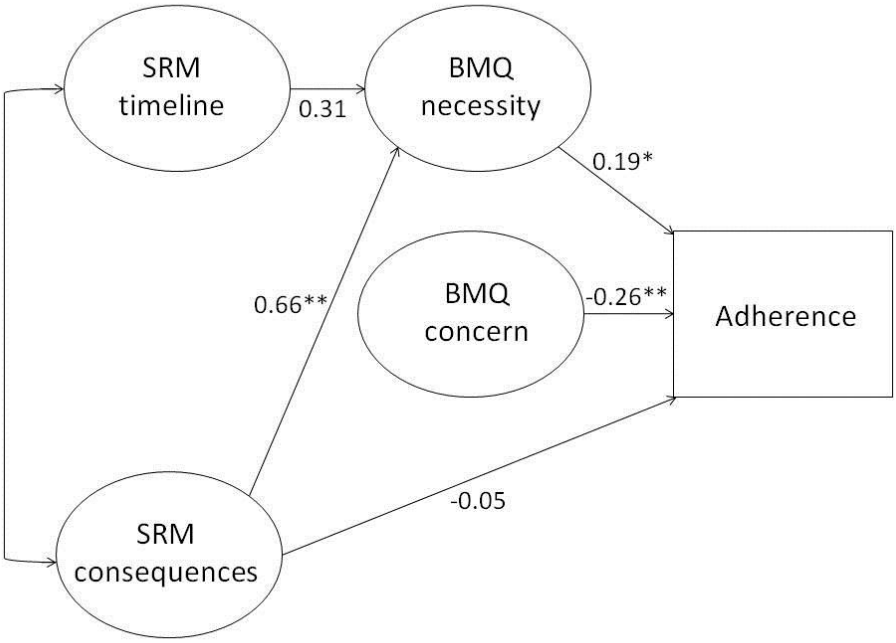
Table 9.7: Logistic regression using baseline model factor sumscores to predict change in unintentional adherence when at baseline patients *do* forget

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications	
Variable	Wald β	OR	Wald β	OR	Wald β	OR	Wald β	OR
TPB important others	0.18	1.24						
TPB perceived control	0.12	0.95						
HBM barriers			0.53	1.09				
HBM benefits			0.13	1.14				
HBM severity			1.46	0.82				
SRM identity					Not entered			
SRM chronicity					1.15	1.44		
SRM cyclical					0.88	0.79		
SRM consequences					1.81	0.77		
SRM personal control					2.62	2.08		
SRM treatment control					2.54	0.64		
SRM coherence					Not entered			
SRM emotion					1.54	1.24		
BMQ harmful							0.02	1.05
BMQ overuse							1.34	1.30
BMQ necessity							2.34	0.78
BMQ concern							0.17	0.93
HAQ								
EQ5D utility								
Model	χ^2 (2) = 0.24 p=0.89 Nagelkerke R^2 = 0.014 70.8% correct (0% of changers)		χ^2 (3) = 1.94, p=0.58 Nagelkerke R^2 = 0.111 70.8% correct (14.3% of changers)		χ^2 (6) = 14.40, p=0.025 Nagelkerke R^2 = 0.644 87.5% correct (57.1% of changers)		χ^2 (4) = 5.16, p=0.27 Nagelkerke R^2 = 0.284 82.6% correct (57.1% of changers)	

9.3.6: Structural equation modelling of social cognition models and adherence

Structural Equation Modelling (SEM) allows for more of the effects of multiple exogenous variables on multiple endogenous variables to be tested with multiple regressions being carried out simultaneously. SEM also allows for the hypothesised mediated effect of illness perceptions through treatment beliefs on adherence to be tested whilst controlling for multiple testing. As opposed to logistic regression, the endogenous variable can also be an unobserved latent variable which is more sensitive than a dichotomised outcome. Goodness-of-fit indices with standard cut-off thresholds are used, as detailed in Chapter 6, section 6.3.3. The thresholds recommended by Hu & Bentler (1999) are; CFI ≥ 0.95, RMSEA ≤ 0.06, SRMR ≤ 0.08. To take into account the hypothesised predictors of adherence as well as the results of the exploratory aims, a number of SEMs were carried out.

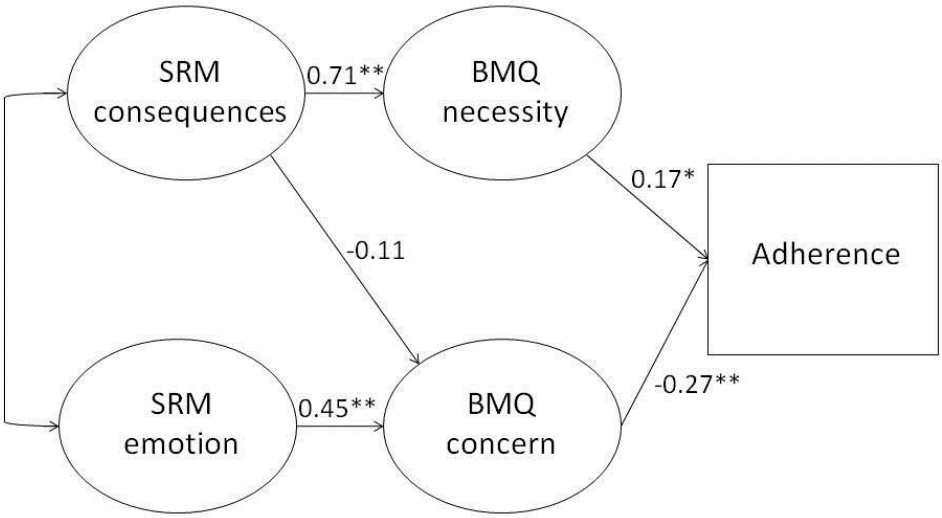
Firstly, two *a priori* models developed by Horne & Weinman (2002) and Nicklas et al. (2010) were tested for model fit in the current dataset. The first model, originally developed by Horne & Weinman (2002) in an asthma patient group is shown in Figure 9.2 with the parameter estimates generated for the current dataset. Although the direction of the paths are all the same as those found by Horne & Weinman (2002), the strength of the associations are not the same and two paths are not statistically significant. In the current dataset, SRM consequences does not directly impact on adherence, although there is a significant mediation through BMQ necessity for both datasets. The fit of the model for the current dataset is not satisfactory as CFI = 0.85, RMSEA = 0.075 and SRMR = 0.075. However, although Horne & Weinman (2002) report a good fit to their data for the model shown in Figure 9.2, the RMSEA was 0.14 which indicates that the fit of that model could also have been improved in their sample.



χ^2 (291) = 548.69, p<0.001.
CFI = 0.85
RMSEA = 0.075
SRMR = 0.075

Figure 9.2: Structural equation model of illness perceptions and treatment beliefs explaining adherence based on Horne & Weinman (2002)

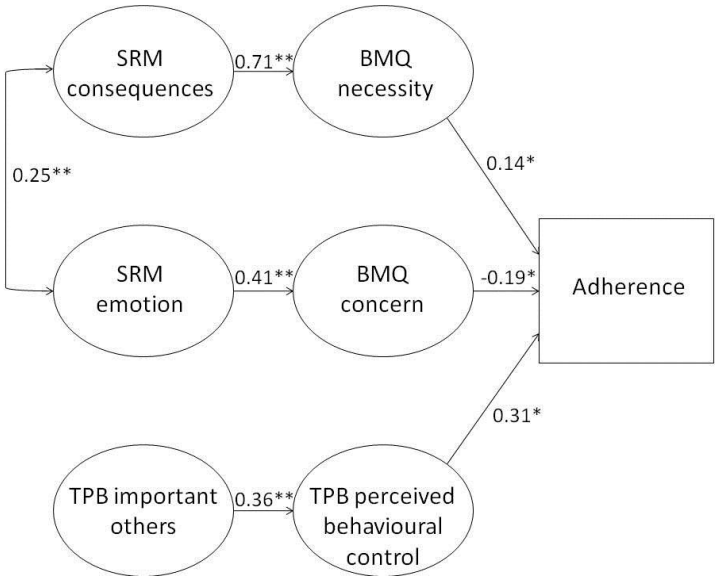
The second model by Nicklas, Dunbar & Wild (2010) was carried out in a chronic non-malignant pain sample and was based on the model by Horne & Weinman (2002). This model was tested in the current dataset and is shown with parameter estimates in Figure 9.3. As with the model shown in Figure 9.2, the current dataset does not match all of the paths identified by Nicklas et al. (2010). Most notably, SRM consequences does not impact on BMQ treatment concerns in the current dataset as it does in the chronic pain sample. The relationship between SRM consequences and adherence is also not mediated by treatment concerns although it is mediated by treatment necessity. These non-significant pathways contribute to the lack of fit shown in the dataset as CFI = 0.87, RMSEA = 0.071 and SRMR = 0.074 compared to CFI = 0.97 and RMSEA = 0.058 found by Nicklas et al. (2010).



χ^2 (318) = 574.61, p<0.001
CFI = 0.87
RMSEA = 0.071
SRMR = 0.074

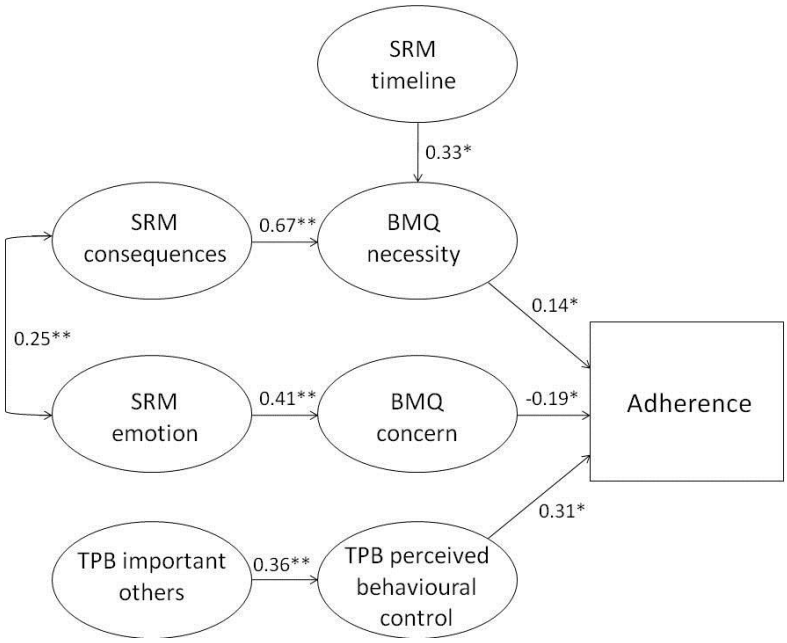
Figure 9.3: Structural equation model of illness perceptions and treatment beliefs explaining adherence based on Nicklas et al. (2010)

Although the *a priori* models were not developed in rheumatoid arthritis patients, they included factors from the Self Regulatory Model and Beliefs about Medications model that were shown cross-sectionally to be predictors of adherence in this study. The fit of these models was not ideal, however there were common elements such as increased perceptions of consequences and treatment necessity leading to better adherence. As these factors were shown in the correlations and logistic regressions to be predictive of adherence, further models were tested that included factors of the Theory of Planned Behaviour in order to improve the fit of the data to explain adherence in this RA sample. Two models were found to have reasonable fit and are shown in Figures 9.4 and 9.5.



χ^2 (585) = 924.44, p<0.001
CFI = 0.86
RMSEA = 0.06
SRMR = 0.09

Figure 9.4: Structural equation model of illness perceptions, treatment beliefs and Theory of Planned Behaviour variables explaining adherence



χ^2 (766) = 1166.75, p<0.001
CFI = 0.86
RMSEA = 0.06
SRMR = 0.09

Figure 9.5: Structural equation model of illness perceptions including chronic timeline, beliefs about medications and Theory of Planned Behaviour variables to explain adherence.

Both of these models which use baseline psychological factors to predict intentional adherence six months later show a reasonable fit to the data. For both, the CFI is above 0.85, although is below the accepted threshold for good fit (Hu & Bentler, 1999). Similarly, the RMSEA and SRMR are just above the thresholds for a good fit indicating overall that these models show a reasonable fit to predict adherence and are the best fitting models for this data. This is supported by the fact that these baseline predictors explain 24.7% of the variance in adherence at six months. The models incorporate pathways between the same illness perceptions and treatment beliefs as Horne & Weinman (2002) and Nicklas et al. (2010) and support the hypothesis that illness consequences are fully mediated by perceptions of treatment necessity which predict adherence (Horne & Weinman, 1998; Horne & Weinman, 2002; Nicklas et al., 2010; Ross et al., 2004). As with Nicklas et al. (2010), higher illness related emotions impact on higher treatment concerns which create lower adherence. The relationship between illness emotions and adherence are fully mediated by treatment concerns. As was found by Horne & Weinman (2002) but not by Nicklas et al. (2010), higher perceptions of the illness duration create higher perceptions of treatment necessity, although there is no mediating effect on adherence.

The addition of the Theory of Planned Behaviour variables increased the explained variance in adherence by 4.4% with both a direct effect of higher TPB Perceived Behavioural Control leading to higher adherence and a mediation of TPB important others on adherence through Perceived Behavioural Control. Although the inclusion of behavioural control would be expected to increase the likelihood of the behaviour being performed (Armitage & Conner, 2001), this relationship was not evident in the logistic regression. Overall, the best fitting models using baseline psychological variables to predict adherence at six months include SRM consequences, SRM emotion, SRM timeline, BMQ necessity, BMQ concern, TPB important others and TPB Perceived Behavioural Control. These models contain factors that have been shown by previous studies to be predictive of adherence, but were not statistically significant in the logistic regressions. This is likely due to the fact that the structural equation model used the 5 items of the Compliance Questionnaire for Rheumatology to estimate the latent variable of adherence whereas the logistic regressions relied on a dichotomised variable of high/low adherence therefore reducing the sensitivity to detect change.

9.4: Discussion

A number of interesting results were found both for the hypotheses that were identified as well as the exploratory associations predicted for the longitudinal relationship of psychological factors on adherence to disease modifying medication in rheumatoid arthritis.

9.4.1: Social cognition models in adherence groups

Contrary to the baseline results, there were no statistically significant differences between any of the SRM factors for the adherence groups at six months as the scores for non-adherers had moved towards adherers for all three types. However, high overall adherers had significantly higher BMQ necessity scores than low adherers indicating that these patients perceived their medication to be more necessary at follow-up, a relationship which was not found at baseline. It would be expected that high adherers would have higher BMQ necessity scores based on research in hypertension (Ross et al., 2004), severe haemophilia (Llewellyn et al., 2003) and asthma (Horne & Weinman, 2002). The fact that this was not found in the cross-sectional analysis is surprising but most likely due to the fact that all patients had high necessity scores with high overall adherers increasing further at six months whilst low adherer's perception of necessity remained stable over time.

The combination of the sumscore changes for each group as well as the sumscore differences *between* groups provides an interesting insight into the relationship between social cognition models and adherence over time. Although the magnitude of change was only large enough to be statistically significant for two factors for the low intentional adherers only, a number of relationships between adherence groups had changed indicating that the combination of smaller changes for each group narrowed the differences, warranting them insignificant. As very few previous studies have demonstrated this variability, this is a very important step towards understanding how social cognition models and adherence interact over time which could present opportunities to develop interventions. For example, low intentional adherers perceive significantly higher barriers to medication taking and lower confidence in DMARDs to control their RA at six months, both of which could reassert low adherence. Addressing these perceptions could go some way to improving medication taking in these patients.

9.4.2: Variability in adherence

Very little previous research has measured adherence over time, although de Thurah et al. (2010) reported no change in adherence to Methotrexate over a nine month period. However, it was hypothesised that the newly diagnosed patients would have more variability as they become more experienced in taking a new medication.

As approximately 30% of patients in this study changed on at least one type of adherence, there was more variation in this sample of RA patients than was found by de Thurah et al. (2010). On closer inspection, the new patients had the most variation, across all adherence types. A concerning result is that at six months the new patients reported higher proportions of low intentional adherence,

more forgetting and more overall low adherence showing that as time progresses, these new patients are demonstrating worse adherence to DMARDs. This is particularly worrying given that NICE (2009) guidelines recommend aggressive treatment of RA within the first three months of symptom onset to prevent irreversible joint damage (see Chapter 1) which will not be effective if patients are not adhering to the regimen.

There was a relatively large increase in forgetting for all treatment groups from baseline to six months, which could be underestimated given that non-responders to the follow-up questionnaire were more likely to be forgetters. Although this may be expected for the new patients who would still be adapting to a new medication regimen, given the length of time that the established and biologic patients would have been prescribed DMARDs, it would be expected that they would be less prone to forgetting. However, as there is no previous research looking at patients forgetting DMARDs over time, these results give some insight into the behaviour of patients which appears to be more variable than was expected. However, as adherence was measured solely through self-report, some of the variation seen in this sample may be due to a lack of validity of the measures. It is not possible to test this in the current sample as there was no objective measure of adherence, but the nature of dichotomising patients as high/low adherers may lead to error over six months.

9.4.3: Predicting adherence to medication at six month follow-up

9.4.3.1: Predicting intentional adherence at six month follow-up

It was hypothesised that SRM identity, consequences and timeline would be associated with adherence as well as BMQ necessity based on cross-sectional studies. None of the individual social cognition models at baseline predicted intentional adherence at six months. When the models were combined, only SRM chronicity and BMQ harmful were significant which only partly supports the hypothesis. It was expected that BMQ necessity would be predictive of intentional adherence as this has been found consistently cross-sectionally (de Thurah et al., 2010; Horne, 1999; Treharne et al., 2004) and longitudinally in ischemic heart disease (Allen LaPoint et al., 2010) and in chronic illness including RA (Clifford et al., 2008), however DMARD necessity was not predictive of adherence in this sample. This is most likely due to the very high necessity scores for all patients indicating that all of these patients believe in the necessity of DMARDs but that this is not sufficient for adherence. Clinically, it would be more desirable to be able to predict low adherence, however the relatively small amount of variance explained by the social cognition models shows that improvements could be made to more effectively predict low adherence.

Within clinical practice, it would be equally as useful to be able to predict which patients change from high to low adherence, particularly given that a substantial proportion of patients in this sample did change over the six month period. None of the models proved to effectively predict change in intentional adherence. Although the Beliefs about Medications model correctly identified 86.4% of patients who changed from low to high adherence, this is likely due to the fact that more of the sample were high adherers and that the model was not performing better than chance.

Although the regression analyses could not reliably predict adherence, there were some interesting baseline differences for the psychological factors. For example, patients with high adherence at baseline who changed to low adherence had significantly lower SRM chronicity scores than those who remained high adherers. This suggests that although the difference was not strong enough to predict change in adherence, perceptions of a chronic illness may be related to patients' adherence over time, providing a possible insight into an area for intervention and supporting the results of successful interventions in other patients groups (Broadbent, Ellis, Thomas, Gamble & Petrie, 2009; Petrie et al., 2002; Petrie et al., 2011).

9.4.3.2: Predicting unintentional adherence at six month follow-up

As a large proportion of patients who did not forget at baseline subsequently started forgetting at six months, it would be particularly advantageous to be able to identify these patients and the reasons behind the change.

As there has been no previous research looking specifically at forgetting over time in RA or other chronic illnesses, these analyses were exploratory with an aim of providing some of the first insights into this area of adherence. Simply using the baseline psychological scores to predict forgetting status at six months was not successful. When adding age and baseline forgetting status, 96.1% of cases were correctly identified; however only SRM personal control added any explained variance indicating that the social cognition models did not reliably predict forgetting.

The logistic regressions used to predict *change* in forgetting scores produced interesting results. For patients who did not forget at baseline, a combination of all of the models performed the best with a number of factors being significant. These results support some previous less specific studies into adherence as Berry et al. (2004) found that RA patients perceived there to be risks to taking DMARDs with adherence being lower if the risks outweighed the benefits. Similarly, quality inter-personal relationships seem to aid medication taking (DiMatteo, 2004; Owen et al., 1985).

9.4.4: Using structural equation models to predict adherence

Structural equation modelling allows for multiple regression analyses to be carried out simultaneously in order to test for causal pathways and mediation between variables. To test the fit of baseline social cognition models to predict adherence at six months, a number of models were tested included two *a priori* models developed by Horne & Weinman (2002) and Nicklas et al. (2010) as well as two models based on the correlation matrices of the current dataset.

Although the *a priori* models were not developed in rheumatoid arthritis patients, as they contained factors from the Self Regulatory Model and Beliefs about Medications model that were shown cross-sectionally to be predictors of adherence they were tested in the current sample. The overall fit of these models was reasonable, however not all of the pathways were significant indicating that the fit could be improved. The final model, shown in Figure 9.5 showed quite a good fit to the data, although it explained only 24.7% of the variance in adherence. Interestingly, it contains factors from the SRM and BMQ that have been shown by previous studies to be predictive of adherence, although were not significant in the logistic regressions. This is likely due to the fact that the structural equation model used the 5 items of the Compliance Questionnaire for Rheumatology to estimate the latent variable of adherence whereas the logistic regressions relied on a dichotomised variable of high/low adherence therefore reducing the sensitivity to detect change.

The pathways are in the expected directions and support the claims that the effects of illness perceptions on adherence are medicated by treatment beliefs (Horne & Weinman, 1998; Horne & Weinman, 2002; Nicklas et al., 2010; Ross et al., 2004). Higher consequences and chronic timeline perceptions lead to higher BMQ necessity scores which in turn result in higher adherence. The addition of the Theory of Planned Behaviour factors in the SEM adds only 4.4% to the explained variance in adherence, although the pathways are highly significant. This is again a slightly surprising relationship as these variables were not able to reliably predict intentional adherence through logistic regression, although the SEM shows that higher scores on TPB important others results in higher perception of control over taking medications which contributes towards higher adherence. This supports previous research that has shown that the amount of confidence a person has in performing the behaviour increases the likelihood of that behaviour being performed (Armitage & Conner, 2001).

9.4.5: Summary of predicting adherence to medication

It is interesting to note that the relationships between the social cognition models and intentional and unintentional adherence changed over the six month period. In Chapter 7, it was shown that

cross-sectionally, the Self Regulatory Model, Beliefs about Medications and to a certain extent the Health Belief Model were significantly related to intentional adherence whereas the Theory of Planned Behaviour was only related to forgetting. However longitudinally, the only factors that were predictive of intentional adherence in logistic regression were the SRM chronic timeline and BMQ harmful scales. Based on previous research in arthritis (Carlisle et al., 2005; Scharloo et al., 1998) and other chronic illnesses (Llewellyn et al., 2003; Ross et al., 2004; Rutter & Rutter, 2007), it would be expected that SRM consequences would also be predictive of adherence at six months, although this wasn't found in the logistic regression. However, SRM consequences were found to be predictive of forgetting at six months, a relationship that was not apparent cross-sectionally. Equally, the Theory of Planned Behaviour factors that were predictive of forgetting cross-sectionally were not related to forgetting six months later.

Despite the lack of good models to predict changes in intentional adherence using a dichotomised high/low adherence outcomes, the structural equation modelling that used adherence as a latent continuous model did provide strong evidence for some of the associations between social cognition models and adherence over time that were hypothesised. In particular, SRM consequences became a significant predictor along with SRM chronicity, as did BMQ necessity. BMQ concern also had a significant negative impact on adherence showing that the full cost-benefit analysis of medication adherence that is suggested by these social cognition models is involved in the decision to undertake the behaviour. Although the structural equation model that best fit this dataset was not identical to that found by Horne & Weinman (2002) or Nicklas et al. (2010) there were a number of common variables which is to be expected as they were generated for different chronic illness patients. Following a large amount of research into illness and treatment beliefs in various chronic illnesses, it has been suggested that as the experience and aetiology will differ substantially, it is important to test these theories independently in each illness type (Hagger & Orbell, 2003). Although higher perceived chronicity and consequences have been found to be related to worse outcomes in some illnesses such as hypertension (Ross et al., 2004), for patients with RA, a more realistic representation of the chronic and progressive nature of the illness appears to be related to better adherence to medications.

The effects of the Health Belief Model and Theory of Planned Behaviour have not been evaluated with regards to medication adherence in chronic illness, and so most of the analyses involving these models were exploratory. However, Orbell et al. (2006) compared the Self Regulatory Model and the Theory of Planned Behaviour to explain attendance at follow-up colposcopy treatment. Upon combining the models, they found that SRM consequences and TPB Perceived Behavioural Control significantly predicted attendance to treatment, two factors that were also found to be predictive of

medication adherence in the structural equation model. This study has made the first step in advancing the utility of the current models of illness by combining a number of models to predict medication adherence. The best fitting structural equation model included factors from each of the models tested other than the Health Belief Model and provides an insight into the multidimensional process that is involved in the decision to take medications and the way mediations of these factors are evident.

9.5: Conclusions

Although the social cognition models as a whole did not explain a very large amount of variance in adherence at six months, there were a number of associations that were able to reliably distinguish between high and low adherers and which were expected based on previous research in rheumatoid arthritis and other chronic illnesses. Higher perceived consequences in particular appear to be related to intentional adherence, although treatment necessities did not have as large an effect as was expected. This longitudinal analysis of the effects of social cognition models on adherence to DMARDs adds a considerable amount of information to the literature by supporting previous research that combines social cognition models of health to explain behaviour as well as indicating which areas could potentially be targeted for intervention to improve adherence to DMARDs in rheumatoid arthritis.

Chapter 10

Health economic analysis of adherence to disease modifying medication by rheumatoid arthritis patients

10.1: Introduction

The progressive nature of rheumatoid arthritis and the need for aggressive and expensive treatment means that although only approximately 1% of the population in the United Kingdom are diagnosed with RA, the total costs associated with the disease are very high. The National Audit Office (NAO; National Audit Office, 2009) and the National Rheumatoid Arthritis Society (NRAS, 2010) have estimated the cost to the NHS of treating RA to be £689 million per year for the UK. An inception cohort of early inflammatory polyarthritis in Norfolk, UK found that the NHS costs were approximately £392 per person for the six months post symptom onset (Cooper et al., 2002). However this is likely to rise with the increased disease activity expected over time.

Cost of Illness (COI) studies aim to describe the total cost of a particular illness by itemising, valuing and summing the costs involved and then applying them to prevalence rates to determine the overall cost to the economy. Cost of Illness studies should include direct and indirect costs in order to be accurate. Direct costs are borne by the health care system, patient and community when dealing directly with the problem. These would include medication costs (to both the healthcare system and the patient), hospital costs and travel costs to appointments. Direct costs can either be from the service provider, patient or societal perspective depending on the focus of the analysis. For example, direct costs from the service provider perspective would include only medication production costs, and all costs associated with primary and secondary care. Direct costs from the patient perspective would include only prescription costs and out-of-pocket costs associated with treatment such as travel to appointments, but inpatient and outpatient costs (in the UK) would not be included as they are free at the point of access. Indirect costs mostly relate to loss of productivity through sickness and early retirement and would be viewed mostly from the patient and societal perspective.

A number of COI studies have been carried out for rheumatoid arthritis across different countries. Zhu, Tam & Li (2011) calculated that the average total cost of RA in Hong Kong is US$9286 per patient year with US$2051-13,349 being direct costs and $1426-43,012 being indirect costs. In the US in 1998 the estimates of total direct costs per patient were $1342-7244 and $1454-21,273 for

indirect costs (Cooper, 2000; Pugner, Scott, Holmes & Hieke, 2000). More recently in the UK, the total direct costs were estimated at £689 million per year with an additional £7.9 billion per year lost through lack of productivity (NRAS, 2010). Indirect costs are significantly higher than direct (NAO, 2009; NRAS, 2010; Zhu et al., 2011) with a review of COI studies in rheumatoid arthritis by Fautrel & Guillemon (2002) reporting that indirect costs account for 50-70% of the total costs (Birnbaum et al., 2000; Cooper, 2000; Pugner et al., 2000) and can be up to 90% (Jonsson & Husberg, 2000). The largest cause of indirect costs is loss of productivity (NRAS, 2010; Zhu et al., 2011) as work disability is high among RA patients with 45% of all UK patients being unemployed (NRAS, 2007) and approximately one third of those stopping work within the first two years (Barrett et al., 2000; Young et al., 2002). In addition to this, those RA patients who are employed have an average of forty sick days per year in the UK compared to 6.5 days per year for the average worker (NRAS, 2007). In contrast, direct costs account for less than half of the total costs with approximately 75% accounted for by inpatient hospital costs and medication costs accounting for less than 20% (Cooper, 2000; Cooper et al., 2002; Jonsson & Husberg, 2000; Pugner et al., 2000). However, the proportion of medication costs may change in the future as expensive anti-TNF α treatments become more widespread resulting in fewer hospitalisations. With the exception of the very recent costs calculated by the National Audit Office and the National Rheumatoid Arthritis Society, other Cost of Illness studies have often not included the effects of anti-TNF α and so may underestimate at least the direct costs, although the overall benefit in productivity may compensate for the increased treatment costs.

Adherence to medications can have a big effect on the total costs of a condition as non-adherence can lead to less symptom control and more disability (Grijalva et al., 2007). This can also have a societal effect as these patients are more likely to require frequent hospital and GP visits and escalation to more aggressive and expensive treatments such as anti-TNF α (Hughes et al., 2001). Despite this high impact, the effect of adherence on costs has been largely neglected in the literature, particularly in health psychology. Although a review by Hughes et al. (2001) found a number of studies that demonstrated that as adherence decreased, costs increased, there were also some studies that found the opposite effect. Part of this incongruity may be due to the fact that the majority of these studies made assumptions and estimates based on clinical opinion to derive costs and benefits rather than measuring costs directly. Two studies have attempted to more robustly measure the costs associated with adherence to medication in chronic illness. Balkrishnan et al. (2003) used MediCare records in the US to determine the Medication Possession Ratio (MPR) for elderly patients with Type II Diabetes using the number of days a prescription is intended for, divided by the number of days between refills (perfect adherence = 1). The mean MPR across five years was

0.71-0.78 with mean total healthcare costs being US$5043.14-8305.89 per patient across five years. The level of adherence and costs remained relatively stable over the five years, however there was a significant reduction in costs for high (>90%) adherers compared with low (<50%) adherers. In multivariate regression analysis, the authors found that a 10% increase in adherence led to an 8.6% *decrease* in total costs. Very similar results were found for elderly patients with diagnosed urinary incontinence as Balkrishnan, Bhosle, Camacho & Anderson (2006) found using the same methodology that high adherers had significantly lower costs than low adherers and that a 10% increase in adherence led to a 5.6% *decrease* in costs. There are limitations to these studies, particularly concerning the method of measuring adherence and the fact that these patients were enrolled in a private health insurance scheme meaning that costs were measured retrospectively without applying standard discounting rates. However, they are unique in attempting to quantify the costs associated with non-adherence longitudinally in chronic illnesses affecting elderly patients.

As well as the costs associated with the treatment of an illness, the Health Related Quality of Life (HRQoL) of a patient should also be considered and is required by NICE to evaluate health technology assessments (Whitehead & Ali, 2010). The common unit of measurement is the Quality Adjusted Life Year (QALY) which combines the quantity of life (years) with the quality of life. NICE recommend that the EQ5D (EuroQol group, 1990) or an equivalent that can be mapped onto the utility index is used to compare across illness types (NICE, 2008). The Health Assessment Questionnaire (HAQ) has been found to be highly correlated with both costs and quality of life (Bansback, Ara, Karnon & Anis, 2008; Kobelt, Jonsson, Lindgren, Young & Eberhardt, 2002) with higher HAQ being associated with higher costs and lower HRQoL. Although HAQ and HRQoL are often measured when evaluating new treatments for RA, HRQoL in particular is rarely assessed in relation to adherence to treatment. There is therefore little known about the effects of medication adherence on HRQoL or the associated costs in rheumatoid arthritis or other chronic illnesses.

Although rheumatoid arthritis costs the UK economy billions of pounds per year, very little is known about the economic impacts of treatment non-adherence in this patient group. Two studies carried out in other chronic illnesses have indicated that reduced adherence leads to increased healthcare costs (Balkrishnan et al., 2003; Balkrishnan et al., 2006), but this has so far remained unexplored in rheumatoid arthritis. For that reason, this prospective longitudinal study takes the health service provider perspective and aims to calculate the direct costs associated with low intentional and unintentional adherence to DMARDs over a six month period by rheumatoid arthritis patients. In addition to this, HRQoL will also be investigated via the EQ5D to determine whether adherence also impacts on *quality* of life, by calculating the QALY associated with medication adherence, which has

not been carried out before. The aim of this study is to establish robust costs and benefits of medication adherence in rheumatoid arthritis.

10.1.1: Aims and Hypotheses

Based on previous research by Balkrishnan et al. (2003) and Balkrishnan et al. (2006), it is hypothesised that:

1) Healthcare costs will be higher for patients with low medication adherence.

As there is no previous research that has investigated quality of life in relation to adherence to DMARDs, an additional aim of this study is to:

2) Determine if there is a difference between EQ5D scores for high and low medication adherers.

10.2: Methodology

10.2.1: Patients

This study formed part of the larger study investigating social cognition models of health and medication adherence. The patient demographics are described in Chapter 7, section 7.2.1. In summary, a total of 227 patients were recruited (75.7% female) at baseline with a mean age of 57.39 years and mean disease duration of 12.54 years. Eligible patients had received a diagnosis of rheumatoid arthritis and were prescribed at least one DMARD. Eighty-four patients were also prescribed an anti-TNF α medication. Patients completed a questionnaire including the five itemed Compliance Questionnaire for Rheumatology and the Reported Adherence to Medication questionnaire to assess adherence to DMARDs and the EQ5D to assess quality of life. Their current prescription was recorded from medical notes by the researcher.

Patients were followed-up six months after baseline to complete the questionnaire again. A total of 171 patients were successfully followed-up (75.3%). Non-responders were more likely to self-report forgetting their DMARDs at baseline but no other differences were found. Adherence, quality of life and current prescription were again recorded to calculate the costs of medications for each adherence group and the EQ5D utility index. In addition, the number of outpatient appointments, "did not attend" (DNA) outpatient appointments, inpatient days and Accident and Emergency contacts was recorded prospectively over the six month follow-up period for all patients.

10.2.2: Procedure

Patients were categorised as high or low adherers for intentional, unintentional and overall medication adherence using the method described in Chapter 3. Current prescriptions for RA specific medications were recorded from patient notes and separated into the following categories; DMARDs (Methotrexate, Sulfasalazine, Hydroxychloroquine and Leflunamide), anti-TNF α (Enbrel, Humira & Remicade) and steroids (Prednisolone). To determine differences in DMARD costs, each of the four DMARDs were analysed individually for the proportion of patients that were prescribed them and the mean dose. This COI study took the NHS perspective and so the cost for NHS service use, disease modifying medication and all medication was calculated for each patient with mean costs for each adherence group being used for analysis.

The EQ5D (EuroQol Group, 1990; Dolan, 1997) consists of five components of quality of life scored on a three point scale *(none – some – extreme)* including; mobility, self care, usual activities, pain/discomfort and anxiety/depression. Using a weighted formula developed by the authors, a continuous index is generated ranging from 0 (death) to 1 (perfect health). The formula chosen for this study is generated from population Time Trade Off (TTO) measures in which participants are asked on the basis of the answers given in the EQ5D to decide how many years of remaining life expectancy they would exchange for perfect health (Jefferson, DeMicheli & Mugford, 2000).

The EQ5D utility scores are used to calculate Quality Adjusted Life Years (QALYs) which combines the quantity of life years with the quality to provide a standard unit of health gain against which treatments for different ailments can be compared. QALYs are measured on an interval scale so 1 QALY can represent one year of perfect health or two years at "half" of perfect health.

QALYs are calculated by multiplying the length of time spent in a health state by the utility score associated with that health state (Whitehead & Ali, 2010). The EQ5D scores were measured at baseline and six months and so the change in QALY can be determined for these patients over time. To calculate the mean QALY for each adherence group and the incremental difference in utility, the EQ5D utility index at baseline was determined for a period of six months (utility score * 0.5) and the follow up utility score determined for the following six months.

10.2.3: Costs

The costs for each drug were taken from the British National Formulary 60 (BNF, 2010). The total cost per patient for the three medication types above was then calculated. The cost of a GP visit,

outpatient appointment, inpatient day and Accident and Emergency contact was taken from the Heath Unit Costs of Health and Social Care (PSSRU, 2010).

10.3: Results

10.3.1: Cross-sectional results

Cross-sectional results were based on the responses of 227 patients with rheumatoid arthritis who completed questionnaires assessing adherence to DMARDs, quality of life and their current RA prescription.

10.3.1.1: Adherence

The CQR5 resulted in 25.5% of patients being classified as “low” intentional adherers, 19% as “forgetting” and 37.7% as “overall non-adherent”, which are consistent with published rates of non-adherence (Haynes, 2001). There were no differences between gender or anti-TNF α status for any of the adherence types and so all subsequent analyses focused on the differences between adherence groups only.

10.3.1.2: NHS service costs

The mean, median, minimum and maximum GP costs for each adherence group are shown in Table 10.1. There was a trend towards higher GP costs in the previous four weeks for self-reported *high* adherers, however this was not statistically significant.

Table 10.1: Mean (median, range) cost of medication for adherence groups (in 2010 GBP £)

Group	GP cost past 4 weeks	DMARD cost per year	All medication cost per year	DMARD cost per year excluding Leflunamide
Intentional adherence				
Low	15.25 (0, 0-72.00)	142.37 (22.41, 0.33-944.22)	2530.40 (116.65, 0-9921.29)	83.12 (21.74, 0.33-341.07)
High	21.28 (0, 0-144.00)	77.15 (18.25, 0.33-781.51)*	2347.96 (58.24, 0-9632.06)	63.12 (17.90, 0.33-449.54)
Unintentional adherence				
Forget	20.45 (0, 0-144.00)	160.58 (108.47, 0.66-928.20)	2420.68 (138.01, 0-9914.32)	92.78 (50.94, 0.66-330.98)
Do not forget	19.45 (0, 0-144.00)	76.40 (17.73, 0.33-944.22)*	2393.18 (23.82, 0-9921.29)	62.04 (17.73, 0.33-449.54)
Overall adherence				
Not adhering	17.56 (0, 0-144.00)	139.25 (25.90, 0.33-944.22)	2451.42 (122.56, 0-9921.29)	83.46 (23.82, 0.33-341.07)
Adhering	21.00 (0, 0-144.00)	63.87 (17.73, 0.33-626.42)*	2342.98 (22.94, 0-9632.06)	58.53 (17.73, 0.33-449.54)

*p<0.05

10.3.1.3: DMARD and all medication costs

When all medication costs are considered, including DMARDs, biologics and steroids, the mean cost is higher in self-reported low adherence although this is not statistically significant. However, Table 10.1 indicates that the mean cost of DMARDs only for self-reported low adherence was approximately twice as much as for self-reported high adherence. One way ANOVAs showed that the mean DMARD costs were significantly higher for self-reported low adherence for *intentional adherence*; $F(1, 214) = 4.95$, $p=0.03$, *unintentional adherence*; $F(1, 216) = 10.22$, $p=0.002$ and *overall adherence*; $F(1, 215) = 10.41$, $p=0.001$.

To identify the reason behind the increased DMARD costs for low adherers, the prescriptions were investigated in more detail. The number of patients prescribed each DMARD and the mean dose for *those prescribed the drug only* is shown in Table 10.2. There were no differences between the rates of prescription or the mean dose for Methotrexate or Hydroxychloroquine for any of the adherence types. However, patients who forget were 2.1 (1.5 : 2.7) times more likely and those with overall low adherence were 1.9 (1.3 : 2.5) times more likely to be prescribed Sulfasalazine. However, there was no significant difference between the mean doses.

Table 10.2: Mean dose of DMARDs for each adherence group

	MTX (mg)	N (%)	SASP (mg)	N (%)	HCQ (mg)	N (%)	LFM (mg)	N (%)
Intentional adherence								
Low	15.14	37 (64.4)	1722.22	18 (30.5)	257.14	7 (11.9)	18.75	4 (6.8)*
High	15.39	114 (72.3)	1618.42	38 (23.9)	284.21	19 (11.9)	16.67	3 (1.9)
Unintentional adherence								
Forget	16.52	28 (65.9)	1447.37	19 (43.2)*	266.67	3 (6.8)	18.75	4 (9.1)*
Do not forget	15.06	123 (71.6)	1756.76	37 (21)	278.26	23 (13.1)	16.67	3 (1.7)
Overall adherence								
Not adherent	15.98	56 (66.7)	1564.52	31 (35.6)*	244.44	9 (10.3)	19.17*	6 (6.9)*
Adherent	14.95	95 (72.7)	1760.00	25(18.9)	294.12	17 (12.9)	10.00	1 (0.8)

*$p<0.05$

There were large differences between the prescribing patterns of Leflunamide. Intentionally low adherers were 3.6 (2.0 : 5.3) times more likely to be prescribed Leflunamide, those that forget were 5.6 (3.9 : 7.3) more likely and those with overall low adherence were 8.6 (6.3 : 10.9) times more likely to be prescribed Leflunamide. The dose was also significantly higher for overall low adherence at nearly twice as much; $t(5) = 4.16$, $p=0.01$. As Leflunamide is much more expensive at 170p per 20mg dose compared to 6.7p per 20mg dose of Methotrexate (British National Formulary 60), and there were few other differences in dosing between the high and low adherers, it was anticipated that Leflunamide prescribing may be causing the higher DMARD costs in low adherers. Therefore, to test the sensitivity of the DMARD costs, Leflunamide was omitted (shown in the last column of Table 10.1). In this case, although the mean DMARD costs were still higher for low adherers, the difference was no longer significant.

In an attempt to identify why patients with low adherence in particular were being prescribed Leflunamide, the clinical notes of these patients were reviewed. Most were prescribed Leflunamide because of a lack of efficacy of Methotrexate, although little is known as to why Methotrexate did not maintain remission in these patients. One patient experienced intolerable side-effects with Methotrexate and so was swapped to Leflunamide and Methotrexate was contra-indicated in one patient because of alcoholic fatty liver disease.

10.3.2: Longitudinal results

To determine the effects of medication adherence on medication and NHS service costs, a number of contacts were recorded prospectively over a six month period for all patients. Using baseline adherence scores, the costs were then calculated for all adherence groups with the aim of identifying disparities in NHS contact and costs for high and low medication adherers.

10.3.2.1: Adherence

A total of 56 patients were lost to follow-up at six months. See Chapter 8, section 8.2.2 for a full description of the patients at follow-up. In summary, there remained 42 patients with low intentional adherence, 121 with high intentional adherence, 24 who forget their medication, 140 who did not forget, 57 patients with overall low adherence and 107 with high overall adherence.

10.3.2.2: NHS service costs

The number of outpatient appointments, the number of "did not attend" (DNA) outpatient appointments, the number of inpatients days and the number of Accident and Emergency contacts for each patient was recorded from medical notes for the six months between recruitment into the study and follow-up. Using standardised costs from the PSSRU (2010), the total cost for each of these secondary care contacts was calculated for each of the baseline adherence groups and are shown in Table 10.3. To create an accurate representation of the groups as a whole, each patient was included when calculating the costs, regardless of whether they had had contact with the NHS or not.

There was a trend for low adherers to attend more outpatient appointments as well as to DNA more appointments. This is reflected in the costs as low adherers had higher outpatient costs, particularly for intentional adherence with outpatient costs being approximately £50 more over the six month follow-up period. Although there was a larger difference between those who forget their medication and those who do not forget for the frequency of DNA appointments, than for intentional adherence, there was a smaller difference in total outpatient costs, although those who forget still had a trend towards higher outpatient costs than those who do not forget. Although the mean differences between high and low adherence groups for the number of outpatient appointments and the associated costs were not significantly different, it appears that over the six month period low adherers had more outpatient contact than high adherers.

There was a different association for inpatient costs however as high adherers had more inpatient days resulting in higher costs, although the total number of inpatient days was very low for the entire sample at 175 days for 16 patients. The inpatient stays were a mixture of planned and emergency

with some being related to rheumatoid arthritis and some not. The increased Accident and Emergency and inpatient contacts generated by the high medication adherers mean that their total service use costs were higher than the low adherers, although the differences were not significant.

Table 10.3: Mean (median, range) cost of NHS service contacts over six months for baseline adherence groups (in 2010 GPB £)

Group	No. of outpatient appointments	Cost of outpatient appointments	No. of DNA outpatient appointments	Cost of outpatient including DNAs	No. of inpatient days	Cost of inpatient stays	No. of A&E contacts	Cost of A & E contacts	Total service use costs
Intentional adherence									
Low	1.83 (2, 0-5)	289.67 (316, 0-790)	0.14 (0, 0-2)	312.24 (316, 0-790)	0.57 (0, 0-15)	137.14 (0, 0-3600)	None	None	448.38 (316, 0-3600)
High	1.52 (1, 0-6)	240.26 (158, 0-948)	0.09 (0, 0-2)	254.63 (316, 0-1106)	1.25 (0, 0-60)	299.50 (0, 0-14400)	0.02 (0, 0-1)	1.60 (0, 0-97)	555.74 (316, 0-14716)
Unintentional adherence									
Forget	1.67 (2, 0-5)	251.21 (316, 0-948)	0.21 (0, 0-2)	296.25 (316, 0-790)	0.83 (0, 0-12)	200 (0, 0-2880)	None	None	496.25 (316, 0-3196)
Do not forget	1.59 (1, 0-6)	260.56 (316, 0-790)	0.09 (0, 0-2)	264.85 (316, 0-1106)	1.12 (0, 0-60)	267.63 (0, 0-14400)	0.01 (0, 0-1)	1.40 (0, 0-97)	533.87 (316, 0-14716)
Overall adherence									
Not adhering	1.65 (2, 0-5)	260.56 (316, 0-790)	0.14 (0, 0-2)	282.74 (316, 0-790)	0.77 (0, 0-15)	185.26 (0, 0-3600)	None	None	468 (316, 9-3600)
Adhering	1.58 (11, 1-6)	248.92(158, 0-948)	0.08 (0, 0-2)	262.34 (316, 0-1106)	1.24 (0, 0-60)	296.60 (0, 0-14400)	0.02 (0, 0-1)	1.83 (0, 0-97)	560.77 (316, 0-14716)

Table 10.4: Mean (median, range) cost of medication at six month follow-up for baseline adherence groups (in 2010 GBP £)

Group	DMARD cost per year	Biologic cost per year	All medication cost per year	DMARD cost per year excluding Leflunamide
Intentional adherence				
Low	165.89 (18.77, 0-3730.63)	2916.40 (0, 0-9295.52)	3082.76 (137.16, 0-9916.02)	62.30 (17.55, 0-337.96)
High	93.69 (19.81, 0-3893.46)	3238.57 (0, 0-9295.52)	3332.99 (186.97, 0-9922.47)	52.60 (19.81, 0-452.81)
Unintentional adherence				
Forget	366.71 (23.82, 0-3893.46)**	3941.80 (436.58, 0-9295.52)	4309.63 (3814.65, 0-9324.54)	55.85 (23.12, 0-337.96)
Do not forget	68.37 (18.25, 0-627.47)	3941.80 (436.58, 0-9295.52)	3088.75 (132.59, 0-9922.47)	54.97 (17.73, 0-452.81)
Overall adherence				
Not adhering	199.52 (93.15, 0-3893.46)*	3541.89 (0, 0-9295.52)	3742.21 (221.32, 0-9916.02)	57.74 (17.73, 0-337.96)
Adhering	65.39 (19.81, 0-627.47)	2947.81 (0, 0-9295.52)	3013.79 (155.32, 0-9922.47)	53.68 (19.03, 0-452.81)

*p<0.05, *p<0.001

10.3.2.3: DMARD and all medication costs

The same method to calculate the medication costs for patients using the prescription at six months as at baseline was used and is shown in Table 10.4. A similar pattern of prescribing and costs was found as at baseline with low adherers having significantly higher DMARD costs but that overall medication costs do not differ. Again, the increased incidence of Leflunamide prescribing for low adherers accounted for the significantly increased DMARD costs.

The dose of each DMARD decreased over the six months for all adherence groups with the exception of Leflunamide which increased by 2.50mg for patients who reported forgetting (see Appendix 10.1). There were also a number of changes with regards to which DMARD was prescribed with some patients starting and stopping each of the drugs in every adherence type (see Appendix 10.2). However, there remained a higher percentage of low adherers being newly prescribed Leflunamide.

10.3.2.4: Quality of life and adherence to DMARDs

Patients completed the EQ5D at baseline and six month follow-up and a utility score was calculated for each patient for both time-points. As shown in Chapters 7, 8 and 9, the EQ5D index ranges between approximately 0.55 and 0.65 for the different treatment and adherence groups. This demonstrated that the quality of life of these patients is not high, although it is in line with previous research of rheumatoid arthritis patients (Whitehead & Ali, 2010).

Chapters 7 and 8 demonstrate that the HRQoL of patients with low adherence was higher than those with high adherence. There was an interaction between HRQoL and both age and disease activity, both of which were shown to impact on adherence so that patients with low disease activity and low adherence had higher quality of life. The EQ5D scores were relatively stable over time for each adherence group showing little variation over six months.

10.3.2.4.1: Incremental difference in EQ5D utility scores

To investigate how the EQ5D utility score may be related to changing adherence, the baseline and six month scores were assessed for those whose adherence *changed* only. There was more variability in EQ5D scores for those whose adherence status changed than for those who stayed the same, however the change was very small at a magnitude of approximately 0.05. An exception to this was for patients who reported forgetting DMARDs at baseline but changed to not forgetting at six months with EQ5D scores of 0.38 and 0.54 respectively, showing a moderate increase in quality of life for those who started remembering to take their DMARDs.

To compare those who forgot their medication at baseline and then did or did not start remembering at six months, the incremental difference in utility was calculated for both groups of patients. The QALYs for the first and second six months were determined and the difference between them calculated. The calculations are shown in equations 10.1 and 10.2.

Patients who forget at baseline (EQ5D = 0.38) and did not forget at six months (EQ5D = 0.54)

QALY = (0.5*0.38) + (0.5*0.54)

QALY for patients who forget at baseline and do not forget at six months is 0.46

Equation 10.1

Assuming that EQ5D remains at 0.38 for patients who remain forgetting

QALY = (0.5*0.38) + (0.5*0.38)

QALY for patients who remain forgetting is 0.38

Equation 10.2

The incremental difference in utility for patients who forget to take DMARDs at baseline but did not forget at six months was 0.08 and is shown in graphical form in Figure 10.1. Area A represents the EQ5D index at 0.38 for all patients who forgot at baseline for half a year. Area B represents the continued EQ5D index at 0.38 for patients who remained forgetters for the following half a year. Area C represents the incremental increase in EQ5D index of 0.08 to 0.54 for patients who did not forget their DMARDs for the following half a year.

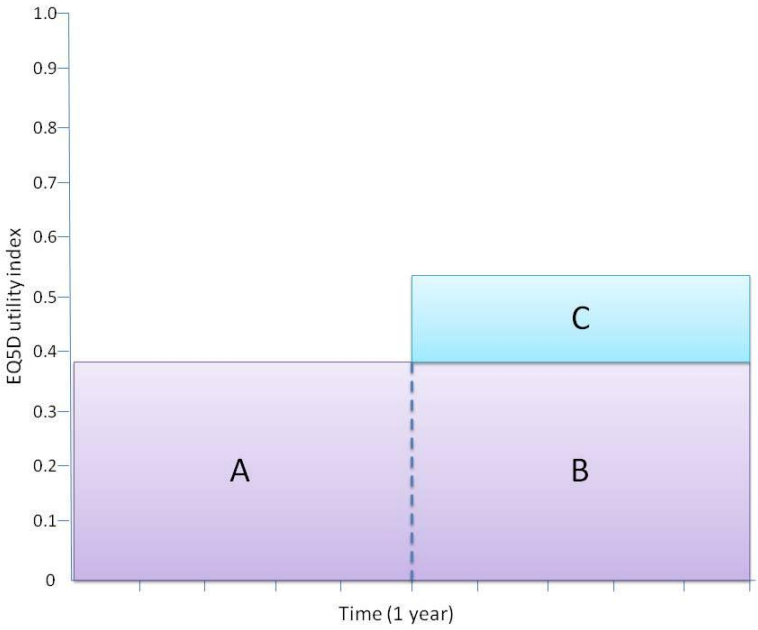


Figure 10.1: Incremental increase in QALY for patients who forget their DMARDs at baseline but do not forget at six month follow-up

For the current sample, seven patients who forgot their DMARDs at baseline subsequently did not forget at six months and so there was an overall gain of 0.56 QALYs. To gain 1 Quality Adjusted Life Year, it would be necessary for 13 patients to improve from forgetting their DMARDs to not forgetting.

10.4: Discussion

This study aimed to provide a health service provider perspective of the costs associated with adherence to DMARDs by patients with rheumatoid arthritis in a prospective longitudinal study. As this type of cost of illness study has not been previously carried out in rheumatoid arthritis, there was little previous research on which to base hypotheses, however it was anticipated that patients with low adherence would generate higher costs and that the health related quality of life would differ for high and low medication adherers.

10.4.1: Medication costs related to adherence to DMARDs

Although overall medication costs were higher for low adherers cross-sectionally, this was not significant. This is likely to be influenced by the fact that 37% of patients were prescribed a biologic medication which is very expensive, thus reducing the effect of small changes in other areas. This is supported by a study by Borah, Huang, Zarotsky & Globe (2009) who estimated adherence to

biologics by RA patients and found that high (>80%) adherers had significantly *higher* health care costs, mainly due to the high cost of biologic medication. To compensate for this, the cost of DMARDs only was calculated and it was found that low adherers, particularly those who forget had significantly higher DMARD costs. Further inspection found that this was directly due to increased prescribing of Leflunamide for these patients, a trend which continued longitudinally. Although not formally identified and recorded, a lack of Methotrexate efficacy or intolerable side-effects may have prompted patients to be non-adherent which could explain why these patients were more likely to be prescribed Leflunamide. Although Leflunamide has been shown to be efficacious where Methotrexate has previously failed (Kremer et al., 2002; Osiri et al., 2003; Strand et al., 1999), a cost-effectiveness modelling study by Schipper et al. (2011) demonstrated that starting patients on Methotrexate plus Leflunamide provided no additional benefits on either disease activity or HRQoL but had substantially higher costs with an incremental cost-effectiveness ratio of €437,930 compared to €133,000 for Methotrexate monotherapy. The results of the current study indicate that there appears to be a particular prescribing pattern for patients with low medication adherence which makes them more likely to be prescribed the more costly Leflunamide. It is beyond the scope of this study to speculate as to the reasons why this may be the case but given that there appears to be no additional benefit for patients (Schipper et al., 2011) this is an area that requires more investigation to determine how adherence and Leflunamide prescribing are related to make healthcare practitioners more aware of the impact that adherence has on the cost of medications.

10.4.2: NHS service costs related to adherence to DMARDs

Based on research into Type II Diabetes (Balkrishnan et al., 2003) and urinary incontinence (Balkrishnan et al., 2006), it was hypothesised that the total costs would be higher for patients with low adherence than high adherence. However, the costs obtained showed differing results. There were no significant differences for total direct costs for any of the adherence groups, although when including biologic medication, there was a tendency for high adherers to have higher costs except for overall low adherers who had higher costs than high adherers. With biologics excluded, overall low adherers and forgetters had higher total costs but the difference was very low. The increased costs were mainly due to a larger number of inpatient days for higher adherence, which is consistent with the make-up of direct costs (Zhu et al., 2011). Based on the cross-sectional and longitudinal results for the main study (see Chapters 7 and 9), it is not surprising that the high adherers had more inpatient days as they tended to have worse RA disease activity and more disability than low adherers. This suggests that adherence is a product of disease activity and associated NHS contacts, rather than adherence causing increased service use, which has been suggested by Balkrishnan et al. (2003) and Balkrishnan et al. (2006). This discrepancy could in part be due to the fact that the

average disease duration for these patients was 12 years, meaning the disease would be well developed which is influencing adherence more than in an illness that is less progressive. There was also a very short follow-up on which to base service use costs which may underestimate the causal effect of adherence on NHS contacts. It would therefore appear that more adherent patients are in fact more costly to the NHS; however a longer follow-up may provide more insight into the relationship between adherence and costs.

10.4.3: Quality of life related to adherence to DMARDs

As little research has investigated quality of life in relation to medication adherence, the aim of this study was to provide some of the first information to describe HRQoL for RA patients with high and low adherence to DMARDs. In general, the QALY scores were quite low at between 0.55 and 0.65; however this is not uncommon for RA patients (Staples, March, Lassere, Reid & Buchbinder, 2011; Suarez-Almazor & Conner-Spady, 2001). There was a difference in EQ5D scores, but unexpectedly, they were generally higher for *low* adherers. This is again likely to be due to the interaction with disease activity with patients with low activity and low adherence having particularly high QALY scores whereas those with high adherence and high activity having very low EQ5D scores. However, it was found that patients who forget their DMARDs at baseline but then start to remember had a 0.08 improvement in QALY scores. Although this gain seems very small, it nonetheless represents a desirable gain in quality of life. A study by Staples et al. (2011) showed that patients treated with biologic medication had an incremental QALY gain of 0.16 over six months whereas patients treated aggressively with DMARDs had a 0.19 incremental QALY gain over five years (NAO, 2009). The current study suggests that simply enabling patients to remember to take their medications could provide some improvement in quality of life. This should be further investigated with intervention studies that not only measure adherence but also HRQoL.

10.5: Conclusions

The results of this cost of illness study have provided valuable information relating to NHS service use and associated costs by RA patients that self-report high and low adherence to DMARDs. There was evidence that prescribing patterns differ for patients with low adherence, particularly those who self-report forgetting their medication with these patients more likely to be prescribed Leflunamide, resulting in significantly higher DMARD costs. This association was previously unknown and provides valuable information for prescribers to monitor and establish why this may be the case. These preliminary results demonstrate the need to more formally establish the prescribing patterns for high and low adherent patients and the reasons behind this in the future. However, these differences

did not affect the total direct costs for adherence groups and with more wide-spread use of biologic medication, these differences may not be apparent in the future. This study does provide evidence that adherence should be carefully monitored in relation to prescribing practices in the future, particularly as more biologic medication becomes self-administered and therefore vulnerable to the same possible sub-optimal self-management as traditional DMARDs.

Although the costs of adherence have been largely neglected in the literature, this study provides preliminary evidence that as well as being an outcome in itself, improved adherence could lead to a potential monetary saving as well as a gain in quality of life. More research should focus on this relationship over a longer follow-up period and incorporate more indirect costs through sick days and early retirement to create a fuller economic picture of the effects of non-adherence to DMARDs in rheumatoid arthritis to strengthen the argument for an increased awareness and clinical utility of addressing medication adherence in the clinic.

Chapter 11

Using an electronic reminder service to increase adherence to DMARDs and improve quality of life: Applying theory to practice in a simulated cost-utility study

11.1: Introduction

The ultimate aim of research into adherence to treatment in chronic illness is to understand which patients struggle to adhere to their regimen and why. This allows interventions to be designed and implemented based on this knowledge to improve adherence with the aim of improving prognosis and quality of life for patients. Although there has been a raft of research into the reasons behind non-adherence which has led to a number of systematic reviews (DiMatteo, 1994, 2004; Haynes, 2001; Haynes et al., 2007; WHO, 2003), there has been considerably less attention on evaluating interventions, with the overall comparability being poor due to heterogeneous samples and non-standard designs and outcomes (Nichol, Venturini, Sung, 1999). Systematic reviews by McDonald et al. (2002) and Kripalani et al. (2007) found varying degrees of success at improving adherence and clinical measures in chronic illness interventions. Simple behavioural measures such as reducing the dose burden generally improved adherence in the short-term although this was not always sustained (Baird et al., 1984; Brown et al., 1997; Girvin, McDermott & Johnston, 1999). Otherwise, the most effective interventions were multifaceted, involving behavioural, educational and communication strategies as well as reminders and psychological training (Bailey et al., 1990; Gallefoss & Bakke, 1999). Even with these complex and labour intensive interventions, the effect on adherence was not strong over time and clinical improvement was negligible (Berrien, Salazar, Reynolds & McKay, 2004; Tuldra et al., 2000). Although these interventions did not report the total cost of implementation; due to the complexity, it is likely that they would be very expensive with little benefit reducing their cost-effectiveness. It is therefore essential for researchers to start targeting interventions directly towards patients who require them and to acknowledge that different types of non-adherence (i.e. intentional and unintentional) are likely to require different methodologies (Lehane & McCarthy, 2007).

Chapter 9 showed that unintentional non-adherence is a substantial problem for patients with rheumatoid arthritis with 20 patients who did not report forgetting DMARDs at baseline

subsequently reporting forgetting at six months, in addition to the 17 patients who remained forgetters. Chapters 7 and 9 demonstrated that the social cognition models had little impact in explaining forgetting, with only factors measuring Perceived Behavioural Control and social support able to explain any of the variance. This suggests that a simple reminder could act not only as a cue to take the DMARDs but could increase confidence and self-efficacy as the patient becomes more able to successfully manage their medication. In addition to this, Chapter 10 showed that patients who improved from forgetting at baseline to not forgetting at six months had an incremental QALY gain of 0.08 suggesting that HRQoL could be improved in these patients simply by enabling them to remember to take their DMARDs. If this were possible, it could provide a very simple avenue to improve the quality of life of patients with a serious disease who generally have a lower QoL than the general public (Whitehead & Ali, 2010).

As discussed in Chapter 4, a simple SMS message reminder could act as the cue to help patients to remember to take their medications. A study by Villella et al. (2004) found that SMS reminders improved adherence to Hepatitis A and B vaccinations by between 13.7% and 17.2% in real terms. Similarly, a study by Petrie, Perry, Broadbent & Weinman (2011) improved adherence to asthma preventer medication by 15% by using SMS messages to address maladaptive illness perceptions in a sample of young asthma patients. As well as addressing perceptions of the illness and treatment, as the SMS messages were all related to asthma and preventer medication, they would also act as reminders to patients who had a tendency to forget. These studies suggest that an SMS reminder has the potential to improve adherence to medication by approximately 15%. Although it may be expected that patients with a generally older age would not be contactable via this relatively new technology, the results of the technology use survey of RA patients in Chapter 5 shows that up to age 65, the majority of patients are already regularly using mobile phones and SMS messaging. Based on the evidence presented in this programme of research, as well as previous studies by other researchers, this chapter aims to cost the potential of an SMS reminder in this patient sample and the cost per QALY gain in a simulated cost-utility analysis. The aim is to provide some preliminary evidence of putting the theory of medication non-adherence into practice using the evidence gathered from a number of previous chapters.

11.2: Methodology

11.2.1: Patients

The sample of patients on which this analysis is based is described in Chapter 8, and focuses specifically on 42 patients who self-reported forgetting DMARDs at baseline but self-reported *not*

forgetting at six months. The health related quality of life of these patients was measured at baseline and six months using the EQ5D and the incremental QALY gain was calculated to be 0.08 (see Chapter 10, section 10.3.2.4.1).

11.2.2: Procedure

The technology use survey in Chapter 5 asked similar patients about their usual use of information and communication technology including email and SMS messages. One of the questions asked patients how confident they are in reading text messages (Chapter 5, section 5.3.3) and the answer to this question was used to base the accessibility and acceptability of an SMS reminder service in this sample.

The likely success rate and cost of improving adherence to medications through an SMS reminder was based on previous research that is presented in the systematic review in Chapter 4. In addition, a recent study by Petrie et al. (2011) reported the success rate of an SMS based intervention to improve adherence to asthma preventer medication.

Using the combined information above, a simulated cost-utility analysis was carried out based on sending SMS message reminders to the 42 patients who reported forgetting DMARDs at baseline to increase their adherence and therefore HRQoL over a one year period. The total cost per year for this sample and the cost per QALY gained were calculated. To test the robustness of the cost per QALY gained, a sensitivity analysis was carried out by changing the assumptions of i) the number of messages sent over one year, and ii) the cost per SMS message.

11.3: Results

The average age of patients who self-reported forgetting DMARDs at baseline was 49 years (see Table 7.6). Based on the results of the survey in Chapter 5, 90% of patients aged 45-54 were confident in reading SMS messages and would therefore be contactable. In the current sample, 42 patients reported forgetting at baseline (Chapter 7) meaning that 38 patients would be contactable via SMS message. At an assumed improvement rate of 15% for unintentional non-adherence, as found by Petrie et al. (2011) and Villella et al. (2004), it could be assumed that six patients would experience the 0.08 increase in QALY scores that was calculated in Chapter 10. This would result in an overall QALY increase of 0.48 for the entire forgetting sample. To determine the cost per QALY gained, the total cost for sending the reminders should be divided by 0.48. In a study carried out by Koshy, Car & Majeed (2008) in the UK, the authors report the cost of an SMS reminder as 7.2p. Table 11.1 shows the results of a sensitivity analysis for the cost per QALY of sending SMS medication

reminders to the current sample. Two key elements of the reminder service were tested; firstly, the frequency of reminders was set at either daily (365 messages) or weekly (52 messages). Secondly, the cost per SMS message was set at 10p each to be conservative and at 7.2p each as reported by Koshy et al. (2008).

Table 11.1: Sensitivity analysis showing the cost per QALY gained (in GBP £) using a reminder service for patients who forget their medications

Assumed cost of SMS message	Total SMS cost for forgetting group (£)	Cost per QALY gained (£)
365*10p	1387	2889.58
365*7.2p	998.64	2080.50
52*10p	197.60	411.67
52*7.2p	142.27	296.40

Table 11.1 clearly demonstrates that the frequency of the SMS messages and the cost per message impacts strongly on the cost per QALY gained. The cheapest method would be to send a weekly message with an assumed cost of 7.2p per message which results in a cost per QALY gained of £296.40 which would demonstrate an incredibly cheap method to improve quality of life in rheumatoid arthritis patients. Sending a daily message at an assumed cost of 10p per message results in a cost per QALY gained of £2889.58 which is substantially more than a weekly message but still very cheap when compared to other methods to improve quality of life. As previous studies have demonstrated that daily messages are not well tolerated (Anhoj & Moldrup, 2004) and that some patients will only be prescribed weekly Methotrexate, an SMS reminder service that provides weekly medication reminders for the current sample of 38 eligible patients would cost between £197.60 and £142.27 per year and result in a cost of between £411.67 and £296.40 per QALY gained.

11.4: Discussion

The sensitivity analysis of the cost per QALY gain suggests that in this sample, the cost to gain one QALY would be between £296.40 and £2889.58 which is well below NICE's unofficial threshold of £20,000 per QALY gain (Devlin & Parkin, 2004) and considerably less than adding biologic medication to the regimen. Although a true cost-utility analysis could not be carried out because the incremental QALY gain was not directly derived by the proposed intervention, this simulation study provides some preliminary evidence for the likely cost of an electronic reminder service with the potential to improve adherence and HRQoL. A randomised controlled trial by Elliott, Barber, Clifford, Horne & Hartley (2008) calculated the cost-effectiveness of a telephone based pharmacist-delivered

intervention to increase adherence to new medications for patients with a chronic illness (including RA). The incremental cost-effectiveness ratio was -£2168 showing that the intervention was both more effective (at improving adherence) and less costly (reduced inpatient, outpatient and A&E contacts) than usual care. Studies by Elliott et al. (2008), Petrie et al. (2011), Villela et al. (2008) and the results from the current study provide some evidence that a tailored distance or electronic adherence intervention could prove to be both effective in reducing the costs associated with non-adherence to medication but also be cost-effective by providing cheap administration opportunities.

11.5: Conclusion

Although there is evidence suggesting that SMS reminders could provide a cheap and low-intensity method of improving medication adherence, neither this study nor those mentioned above have truly measured the potential for this type of service. Therefore it is imperative that future research implements a similar reminder service and robustly measures the costs and benefits (in adherence and quality of life) to provide a more accurate account of the cost-effectiveness and cost-utility to inform clinical practice.

Chapter 12

General Discussion

12.1: Summary of the aims of this programme of research

The psychology of medication non-adherence has been explored in other chronic illnesses; however the psychological predictors have not been effectively established in rheumatoid arthritis. As there are a number of social cognitive models of illness available, there is currently a lack of consensus of which factors are implicated in adherence to DMARDs.

The Self Regulatory Model and Beliefs about Medications have been investigated in rheumatoid arthritis with regards to psychological outcomes (Scharloo et al., 2000) and adherence (de Thurah et al., 2010; Goodacre & Goodacre, 2004; Treharne et al., 2005), however there is currently not enough evidence to establish which models provide the best explanation of adherence. The aim of this programme of research therefore was to establish the best ways to measure intentional and unintentional non-adherence to DMARDs, to measure a number of commonly used social cognition models of illness to establish which was the best predictor of non-adherence and to establish the monetary effects of non-adherence with respect to health service utilisation. Only one other study has measured more than one social cognitive model in adherence with Orbell et al. (2006) identifying that the Theory of Planned Behaviour explained a large amount of variation in *intention* to attend follow-up colposcopy treatment appointments but with neither the Theory of Planned Behaviour nor the Self Regulatory Model reliably predicting actual attendance. As adherence to medication in a chronic illness is expected to have a different psychological mechanism (Fishbein, 1993; Hagger & Orbell, 2003), a similar approach was used in this programme of research to identify the best predictors of adherence to DMARDs by RA patients.

There were four parts to this research with the aim of providing a coherent and complete analysis of the importance of adherence to treatment in RA. Firstly, the feasibility of using Information and Communication Technology (ICT) was assessed and tested through a simulation study as a potential administrator of a simple reminder service. Although it is beyond the scope of this research to have designed and tested an intervention because there was not enough evidence in the literature on which to base one, the information presented in Chapters 4 and 5 indicate that it would be possible and desirable to use SMS messages to implement reminders to patients up to 65 years old. The focus

was then on how to measure adherence in this patient group with an established self-report measure being reduced to increase the clinical utility and to remove the redundant items (Chapter 6). A large prospective longitudinal study was then carried out with 227 patients at baseline and 171 followed-up over 6 months specifically measuring both intentional and unintentional non-adherence. This allowed for the effects of social cognition models on adherence over time to be evaluated, which has not been previously done to a high standard in RA (Chapters 7, 8 and 9). This also allowed for all three of the most commonly used models of illness to be tested simultaneously to determine which aspects are most useful in predicting medication non-adherence and offering some evidence of psychological factors to target in future interventions. Finally, a health economic analysis was carried out to establish the cost of non-adherence which has been very rarely done in any chronic illness with no published work in RA. The aim of the economic analysis was to highlight the importance of non-adherence and to provide stronger evidence for clinicians and decision makers that adherence is an important area to tackle and that it can be done in a cost-effective way to improve QoL and prognosis for patients.

12.2: What this research has added to the current evidence base

A number of results and conclusions can be drawn from this programme of research that have added to the current literature around adherence to treatment in chronic illness.

1. The CQR5 is a shortened form of a self-report adherence measure that could be used in the rheumatology clinic to regularly screen for low medication adherence (Chapter 6).
2. It is important to consider newly diagnosed patients separately, particularly when investigating social cognition models of illness or adherence as they have a very different experience to more established patients (Chapters 7 and 8).
3. Adherence is a substantial problem in rheumatoid arthritis. However, it is important to measure intentional and unintentional non-adherence separately as they appear to have different psychological underpinnings (Chapters 7 and 9).
4. In order to understand the complexities and nuances of adherence to chronic medication, the mediating and moderating effects of psychological factors on adherence need to be investigated (Chapter 9).
5. An accurate representation of RA (i.e. higher perceptions of chronicity, consequences and the necessity of DMARDs) results in higher adherence (Chapter 9).
6. Aspects of the Theory of Planned Behaviour, Self Regulatory Model and Beliefs about Medications are predictive of adherence to DMARDs; however the Health Belief Model does not accurately predict adherence (Chapters 7 and 9).

7. The health economic analysis showed varying results with regards to adherence and health service costs. However, in order to justify interventions that improve the self-management of illness, researchers need to start evaluating and reporting the cost-effectiveness in order to compete for the finite resources that are available (Chapter 10).
8. ICT is a viable and underused method of engaging and communicating with patients which could provide a cheap and more acceptable method than face to face contact for patients up to 65 years old (Chapters 4, 5 and 11).

12.3: Social cognition models of illness in rheumatoid arthritis patients

The review of the commonly used social cognition models of illness in Chapter 2 demonstrated that they are based on the assumption that patients carry out a cost-benefit analysis of performing the health behaviour (in this case taking medication) and come to a logical conclusion based on the information available for the analysis. This means that as patients become more experienced with their illness and gather more information, the cost-benefit decision may be altered prompting changes in adherence to medication. Leventhal, Meyer & Nerenz (1980) explicitly state that the Self Regulatory Model is adaptive to patients' experience and therefore patients will "regulate" their illness representation accordingly. However, very little research has studied the regulation and adaptation over time, particularly for patients that have been newly diagnosed with a chronic illness in whom less stability would be expected given the rapid accumulation of knowledge and experience over a short period of time. The results shown in Chapters 7 and 8 support the regulation of social cognition models based on experience as newly diagnosed patients differed significantly on the psychological sumscores compared to established patients and had more variation over the six month study period. This was particularly true for the Self Regulatory Model and the Beliefs about Medications with perceptions of severity of RA, the chronicity and efficacy of treatment and the patient to control the illness being more subject to change than aspects of the Theory of Planned Behaviour or Health Belief Model.

The relative stability of the Theory of Planned Behaviour and Health Belief Model across all patients calls into question the applicability to explain behaviours in chronic illness as it would be expected that perceptions of severity, barriers, benefits and self-efficacy would change as the patient becomes more experienced. Although these models were primarily designed to explain preventive health behaviours such as exercise uptake (Ajzen, 1988, 1991; Rosenstock, 1966), they have been used separately to explain behaviours in chronic illness. The lack of sensitivity that they appear to display in detecting changes in patients' experience suggests that they are not suitable for use in chronic illness.

As well as providing evidence for the regulation proposed by Leventhal et al. (1980), the variability shown by the newly diagnosed patients but not the more established patients in both the psychological measures and adherence shows that these patients should be considered separately in future research, something which only a minority of previous research has considered (de Thurah et al., 2010; Goodacre & Goodacre, 2004). As well as separating them for informative research purposes, the lack of stability suggests that interventions to address adherence should be aimed at patients as they are starting a new treatment in order to guide them towards beneficial, adaptive perceptions that promote good adherence.

12.4: Predicting and explaining adherence to DMARDs in rheumatoid arthritis

Using a measure of intentional adherence that was refined in Chapter 6 (CQR5) along with a measure of unintentional adherence (RAM), the different types of adherence to DMARDs were evaluated. The overall non-adherence rate was 37.5% at both baseline and six months which is at the low end of published rates (Barber et al., 2004; DiMatteo, 1994; Dunbar-Jacob et al., 2000; Haynes, 2001). Rates of forgetting were quite low at 18.6% (baseline) and 21.6% (six months) compared to other illnesses (Atkins & Fallowfield, 2006; Lehane & McCarthy, 2007). This may be because there were a lot of older patients who have been shown previously to not forget because they use more cues and organisers than younger patients (Elliot et al., 2007; Hertzog et al., 2000; Kippen et al., 2005) but could also be related to the fact that non-responders at six months were more likely to report forgetting at baseline. The fact that some patients reported either intentional *or* unintentional non-adherence highlights the importance of measuring the two types of adherence separately in order to gather a more accurate picture of medication taking behaviour. Unintentional non-adherence also appears to effect different patients as those that are younger, newly diagnosed and working are more likely to report forgetting their DMARDs than older, more experienced patients, which supports previous research (Elliot et al., 2007; Hertzog et al., 2000; Johnson, 2002). There also appears to be different underlying psychological mechanisms related to forgetting which will therefore require different interventions to improve. It was hypothesised that the social cognition models would not explain a large amount of variance in unintentional non-adherence because it is assumed to not be related to a deliberate decision to not take medication. This was mostly supported in the data as only TPB Perceived Behavioural Control was significantly associated with forgetting which could be as a result of patients being aware that they struggle with remembering their medication and so are acknowledging their difficulties upon questioning.

This was the first study in rheumatoid arthritis to specifically separate intentional and unintentional adherence. As the social cognition models were not adequate in predicting or explaining forgetting

DMARDs, it appears that a reminder or cue could provide a simple way of reducing this type of non-adherence. As changing perceptions to improve intentional non-adherence would be a complex and expensive procedure, the possibility of improving quality of life and prognosis with a simple intervention is highly desirable. The results of the simulated cost-utility analysis in Chapter 11 suggest that SMS reminders sent to patients could provide an immediate, portable, cheap method of reminding patients about not only their medications but also other treatment requirements such as blood tests and outpatient appointments. As discussed in Chapter 1, there are a number of demands placed on patients, particularly in the first months following diagnosis that continue throughout the course of the disease, regardless of disease activity, such as twice-annual outpatient appointments and eight-weekly blood tests for most DMARDs. As the results from the cross-sectional (Chapter 7) and longitudinal studies (Chapter 9) into medication adherence suggest that these omissions are unrelated to perceptions about the illness or treatment and are therefore genuine memory lapses, patients may be receptive and appreciative for this type of reminder. This would have even more impact as the penetration of this media increases in the older generation and more patients are able to remain working following improved treatment, causing more conflict with hospital appointments. The popularity of using ICT for interventions is becoming more apparent (see Chapter 4), however more research is required to establish the optimum regimen as well as the latency of the effect after the messages are stopped. In order to justify these simple reminders, there is also a requirement of researchers to calculate the cost-effectiveness and cost-utility of these interventions in order to justify the expenditure compared to other methods.

Using the Theory of Planned Behaviour, Health Belief Model and Self Regulatory Model as well as Beliefs about Medications allowed for all of these models to be evaluated and compared for their ability to explain and predict non-adherence to DMARDs. This is the first study that has used all of these models in rheumatoid arthritis and one of a minority that has explored adherence and social cognition models in a prospective longitudinal study with a large sample of patients. The rationale behind using all of these models was that they are all commonly used to explain health behaviour but there is a certain degree of assumed collinearity as they measure similar latent factors. There is currently a lack of good quality intervention studies addressing adherence (Kripalani et al., 2007; McDonald et al., 2002; Peterson, Takiya & Finley, 2003; Roter et al., 1998) and by establishing exactly which factors of which models are associated with adherence would enable more targeted and effective interventions to be designed and tested. It was found both cross-sectionally and longitudinally that the Health Belief Model did not effectively predict non-adherence. This may be due to the fact that similar concepts are measured by the SRM in a way that is more appropriate for chronic illness. Therefore, although the HBM directly measures concepts that are inherent in the

cost-benefit decision of health behaviours, it would appear that it is not a suitable model to use to explain medication adherence in rheumatoid arthritis.

As has been found previously, perceptions of the illness and the treatment were best able to predict non-adherence to DMARDs in this study. This was true both for the logistic regression analyses and the structural equation modelling (SEM). The benefit of the current study is that baseline psychological models were used to predict adherence six months later. This starts to provide evidence for a causal relationship and indicates which areas may be best targeted for intervention. A more powerful method of evaluating causal paths is to use SEM, a method which has been previously employed by very few researchers (Horne & Weinman, 2002; Nicklas et al., 2010) and not at all in rheumatoid arthritis. As the SEM was much better at explaining adherence longitudinally than each of the models separately or combined in simple regression analyses, it is clear that this type of causal analysis is necessary for researchers to carry out in the future to determine the mediators and moderators of adherence. For example, it was shown that higher perceptions of DMARD necessity were directly related to higher adherence, but in the univariate analysis in Chapter 7, it was shown that *all* of the patients had high necessity perceptions; including those with low intentional adherence. Therefore, knowing that higher perceptions of consequences, chronicity and emotional response influence DMARD necessity, allows for manipulation of them to either raise perceptions of necessity further or make it a more prominent part of the cost-benefit analysis. This has been carried out with some success with asthma patients (Petrie et al., 2011), but as illness perceptions in particular are unique to each illness (Hagger & Orbell, 2003), this type of analysis that identifies the predictive factors is necessary for future interventions in RA.

However, the results reported here need to be carefully considered in relation to both the illness in question and the desired outcome. For example, many previous studies have suggested that perceptions related to increased severity and chronicity result in worse psychological outcomes (Hagger & Orbell, 2003; Schiaffino & Revenson, 1992), however the opposite was found in relation to DMARD adherence in these RA patients. Part of this is likely to be related to the fact that illness perceptions are expected to differ depending on the aetiology of the illness (Hagger & Orbell, 2003) as a perception of a chronic, potentially serious illness with a number of symptoms that is not necessarily easily controlled through conventional DMARDs is a more accurate representation than a less serious, acute perception. This has also been shown in asthma as patients with a more chronic illness perception had better adherence to preventer medication when they were asymptomatic than patients who had an acute representation dictated solely by symptoms (Horne & Weinman, 1998). Leventhal et al. (1980) propose that the symmetrical relationship between symptoms and disease labels are at the core of the regulation process, meaning that it would be expected that

patients would only be aware of their illness when they are experiencing symptoms. The presence of symptoms would therefore stimulate performance of the appropriate health behaviours; however, it is possible that this is maladaptive within a chronic, progressive illness such as RA where medication adherence during remission to prevent joint erosion is imperative. By accepting the reality of the illness, these patients may be more aware of the "benefit" part of the cost-benefit decision to take medications than others. This is also likely to be somewhat specific to medication taking as it has been shown that rates of depression are higher in patients with the more serious illness perceptions (Schiaffino & Revenson, 1992) which may be as a result of a realistic assessment of the likely outcomes through progressive disease activity (Young, 1992) and work disability (Barrett et al., 2000; Wolfe & Hawley, 1998; Young et al., 2002).

The model that was found to be the best fit to the data in Chapter 9 (Figure 9.5) also included the Important Others and Perceived Behavioural Control factors of the Theory of Planned Behaviour, which have not been included in SEM analyses previously with regards to medication adherence. Given that Perceived Behavioural Control measured self-efficacy which is an important component of all models of health behaviour (Bandura, 1977; Azjen, 1988), the inclusion of this to explain adherence has strong face validity. As well as perceptions about the necessity of DMARDs and addressing any concerns patients may have, increasing patients' efficacy at being able to take their DMARDs appropriately would also provide a succinct way of improving adherence not only to DMARDs but possibly also to other self-management behaviours.

As well as differences in the social cognition models themselves, there were differences in adherence between the three treatment groups. Both cross-sectionally and longitudinally the new patients had the highest rates of forgetting but lowest rates of intentional non-adherence, despite the fact that they generally had the lowest sumscores on the psychological factors that were related to adherence such as BMQ necessity and SRM consequences and chronicity. This suggests that they are relatively happy with adhering to the regimen but struggle to fit it into their routine. This seems to be the most obvious time to target an intervention to prevent both types of non-adherence. Reminders to reduce rates of forgetting and psychological and behavioural training to maintain low levels of intentional non-adherence based on promoting adaptive illness perceptions could be beneficial. The longitudinal results suggest that focussing on illness and treatment perceptions, self-efficacy in taking the DMARDs in particular and engaging family, friends and co-workers could aid adherence as patients become more accustomed to their illness. However, more research is required to monitor adherence specifically by newly diagnosed patients as it is likely that their motivations would change over time.

It was found that there was variance in adherence over six months. Although there is very little previous research on which to base hypotheses because most do not measure adherence at more than one time point, de Thurah et al. (2010) found no variance in the proportion of low adherers to DMARDs over nine months. This was also true in the current dataset, but the intra-individual variability was quite high at 30% (Chapter 9). This was expected for the newly diagnosed patients as they become more accustomed to their treatment regimen but there were also changes in the other two treatment groups which were not expected. This may be due to the fact that treatment "holidays" are common (de Klerk et al., 2003; Kruse et al., 1992; Osterberg & Blaschke, 2005), that taking medications during remission is often difficult (Garcia-Gonzalez et al., 2008; Kane et al., 2001; Kane et al., 2003) and/or that a lack of treatment efficacy has caused patients to stop taking their DMARDs, however this was not measured in this study. There may also be some lack of validity for the adherence questionnaires, as test-retest was not carried out for the reduced Compliance Questionnaire for Rheumatology (Chapter 6). However, it is important that clinicians are aware of this potential variability and not to assume that a patient remains a good adherer over a long period of time. Regular measurement of adherence in the clinic would be preferred in order to address any problems, which would be more achievable with the reduced CQR produced in Chapter 6 as it is short and easily interpretable to give an indication to clinicians of potentially sub-optimal adherence.

Although the social cognition models went some way to predicting and explaining adherence, none of the models were an ideal fit, indicating that there are other variables that are not currently included in the models and should be explored in the future. This could be related to the fact that patients who had a more "realistic" representation of RA (i.e. had higher consequences and chronicity scores) had better adherence but that other researchers have found that high scores on these factors are associated with higher levels of depression (Carlisle et al., 2005; Murphy et al., 1999; Petrie et al., 2007; Treharne et al., 2005). Therefore although patients realise the need to take their DMARDs to mitigate the effects of future disability, this same realisation may be leading to a state of mind (depression) that makes effective adherence and self-management difficult (Bane, Hughes & McElnay, 2006; Hertzog et al., 2000). Adherence also appears to be a dynamic process that is reliant on disease-specific experience. Patients with more active disease seem to be more adherent, possibly in response to the increased symptomology (Leventhal et al., 1980). An interaction between age and disease activity and age and quality of life was found in relation to adherence where younger patients with lower disease activity had much lower adherence whereas those with high disease activity had high adherence. Similarly, younger patients with low adherence had better quality of life than those with high adherence. If adherence is reactive to disease activity, then it would be expected that those who are receiving little benefit or have a high treatment burden

would have worse quality of life. If increased symptomology, a realistic illness representation, depression and adherence are all associated, this could explain how the "rational" decisions (that are assumptions of models of illness) made by patients result in different outcomes, which may be contributing to the lack of fit of the structural equation models. Although this interaction demonstrates a limitation of this research in including patients in all stages of disease who have experienced different levels of disease activity, it also highlights an important point that adherence is dependent on context and experience and should not be treated in a prescriptive, inflexible way.

12.5: The clinical importance of adequate adherence to DMARDs

The results presented in this programme of research indicate that non-adherence to DMARDs is a substantial problem with 37.5% of patients demonstrating sub-optimal adherence. There is a possibility that this is an underestimate as patients who did not attend their appointment during the recruitment period may be more likely to be non-adherent and those who reported forgetting at baseline were more likely not to respond to the follow-up questionnaire. There was evidence that newly diagnosed patients were more susceptible to forgetting their DMARD doses which could lengthen the time it takes to establish an effective regimen to promote remission and may lead to irreversible joint damage during the first three years of illness (Young, 2008).

It is well established that non-adherence to treatment leads to increased disease progression (Sharp, 1999) and wasted resources through treatment escalation and increased healthcare contact (Brunzel & Laederach-Hofmann, 2000; DiMatteo, 1994; Steiner & Prochazka, 1997). This was evident to some extent in this study as patients who reported forgetting their DMARDs were more likely to be prescribed Leflunamide which is equally as efficacious as Methotrexate but much more expensive (Chapter 10). There were no significant differences in other costs that were collected prospectively over the six month follow-up period; however this may be because of the advanced disease duration of most patients and the short follow-up period. However, as the cost of non-adherence has not been calculated in rheumatoid arthritis before, this study highlights the importance of tracking the prescribing practices and NHS contacts of patients with sub-optimal adherence over the long term to establish the effects in a concrete way. Although this has been done retrospectively in other chronic illnesses (Balkrishnan et al., 2003; Balkrishnan et al., 2006), little is currently known about the impact to rheumatology clinics.

Although these results refer mainly to consultant-run outpatient clinics, with more specialist nurses taking responsibility for long term care of patients, it is important for all healthcare practitioners to be aware of the impact of non-adherence and the possible reasons behind it, particularly the differences between intentional and unintentional non-adherence. Using peer support and small

nurse-led patient groups to advise and support patients, particularly after initial diagnosis could help to promote adaptive social cognition models that facilitate good adherence to DMARDs. In addition, the move towards more patients being responsible for self-administered anti-TNF α medication reiterates the need for more information about adherence to be known as these drugs are very expensive and have potentially harmful side effects if not administered properly. By being aware of the issues surrounding different types of adherence and the ways that patients in different stages of illness respond to medication and the information presented to them, healthcare practitioners can move towards an effective and suitable treatment plan for patients.

12.6: Strengths and limitations of this programme of research

The main strength of this programme of research was systematically measuring both intentional and unintentional non-adherence in patients at different stages of rheumatoid arthritis as well as establishing which of the most commonly used social cognition models of illness were predictive of medication adherence. In addition, the main study involved a large sample contributing to a prospective longitudinal study which is currently lacking in the literature. The inclusion of structural equation modelling also allows for more subtle analysis of the predictors of adherence which have identified a more coherent and informative model of medication non-adherence to DMARDs.

There were some methodological limitations to these studies which should be discussed. Firstly, although the shortened Compliance Questionnaire for Rheumatology was subjected to confirmatory factor analysis in a sample different to the sample used to reduce the number of items, due to time constraints the CQR5 was not tested against an objective measure of adherence such as eMEMs. Although the fact that the hypothesis proposing that the social cognitive models would only be related to intentional non-adherence (measured by the CQR5) was supported which provides some assurance that the CQR5 was a valid measure, more robust psychometric testing is desirable.

For the longitudinal study, patients were recruited mostly in the clinic with some additional patients being recruited by post. It may be that patients that were better at self-managing were recruited, however this potential bias would have underestimated non-adherence so the levels found in this study can be assumed to be at the lower end of what is apparent in the population. The recruitment rate shown in Chapter 7 was very high and the attrition rate shown in Chapter 8 was relatively low indicating that the sample is representative of the rheumatoid arthritis population so the results can be interpreted with some confidence. Although a very high percentage of available newly diagnosed patients were recruited, the sample size was too small to perform regression analyses for this group only. This would provide interesting and relevant results as they differed from the established patients both in their social cognitive models of illness and in adherence itself. The low number of

new diagnoses per year in the UK prohibited a larger sample. The difficulties in recruiting these patients means that the majority of previous research has not isolated them and so very little is known about changes in adherence and the effects that this may have on the disease course. However, based on the preliminary results for new patients presented here, it is clear that this should be a priority for research in the future in order to identify the best ways to develop interventions to aid self-management as the population ages and more patients are expected to suffer from auto-immune diseases.

Although the Theory of Planned Behaviour was found to be predictive of adherence in the structural equation modelling, the high rate of missing responses for the Attitudes questions meant that this component could not be included in the analysis. This is a major limitation of the evaluation of this model as it has been shown that attitudes are strongly related to intentions to perform a behaviour (Armitage & Conner, 2001) and adherence behaviours themselves (Orbell et al., 2006). Although the questionnaire included clear instructions, the pattern of answering indicated that patients did not realise they were required to provide a preference for each attitude with most patients identifying only one out of the possible eight.

Although this study provides some of the first longitudinal results for rheumatoid arthritis patients in respect to medication adherence, the follow-up of six months is relatively short and should be extended in order to provide more useful and relevant information in the relationship between social cognition models of illness, medication adherence and disease progression to inform clinical practice to improve prognosis and quality of life for rheumatoid arthritis patients in the future.

12.7: Future work on adherence to DMARDs in rheumatoid arthritis

Future research should focus specifically on the different types of non-adherence and the differing experience of newly diagnosed and established patients. By using a simple self-report screening measure such as the CQR5 and the RAM, adherence to medication should be routinely assessed in the clinic in order to identify patients for whom adhering to the regimen is difficult. This would allow for targeted interventions to address the likely problems around adherence and provide an opportunity for the clinician to address the topic in a non-threatening but open way. Disclosure of non-adherence by patients is often not apparent in a clinical setting (Belcher, Fried, Agostini & Tinetti, 2006; Maidment, Livingston & Katona, 2002; Treharne et al., 2006), but by being aware of intolerable side effects or other barriers to medication taking, a clinician could engage more in collaborative healthcare, as set out by NICE (2009).

As this longitudinal study has identified some of the predictors of non-adherence, future research should deliver a targeted intervention to address these issues. Two approaches should be considered. Firstly, it was shown that unintentional adherence primarily affects younger, newly diagnosed patients. An SMS message reminder tailored to the individual should be trialled as an attempt to prompt patients into taking their medications. Chapter 5 indicates that 90% of patients would be contactable via SMS message and other researchers have found that using this type of technology is suitable for delivering informative messages to patients (see systematic literature review in Chapter 4). This would provide a cheap and simple method of reminding patients about their medication doses and could also apply to other self-management behaviours such as attendance to outpatient appointments and regular blood tests. It is anticipated that these medication reminders would be required for 6-12 months to help patients to establish a habit of medication taking, after which these messages would no longer be required. Given the advanced technology available, this could be a simple automated service provided by the clinic which requires little maintenance after initial set-up.

The longitudinal study found that perceptions of the illness chronicity, consequences and seriousness of symptoms, along with perceptions about the necessity and concerns of DMARDs were significantly related to adherence. After screening for patients that exhibit low levels of intentional adherence, an intervention that includes both psychological and behavioural training as well as education about the medication should be implemented in an attempt to establish suitable perceptions to aid adherence. Improving patients' self-efficacy as well as including friends and family in a multifaceted design is likely to be the most successful (Kripalani et al., 2007; McDonald et al., 2002; Peterson et al., 2003). However, it is important for clinicians to be aware that adherence is not static and that experience with disease activity could lead to changes in adherence. Regular screening to address these changes is required and patient training may well need to be refreshed to address any illness perceptions that have changed within the individual. This would be particularly apparent after a significant change in treatment such as escalation to anti-TNF α therapy or orthopaedic surgery.

In order to further inform these interventions, and to establish the impact of newer therapies on treatment adherence, it is also very important that adherence and social cognition models of illness are measured within individuals regularly over a long period of time to better understand the effects of disease activity and treatment on adherence to medication. This would be particularly beneficial for newly diagnosed patients who were shown in this research to be more reactive to acquired knowledge and experience over a relatively short period of time but whose adherence is particularly important as a large amount of joint damage often occurs in the three years from diagnosis (Conoghan et al., 2010). A cohort study that recruits patients at diagnosis and follows them up over a

number of years that measures adherence to medication, social cognition models of illness as well as related aspects such as treatment changes and contacts with the health service would provide invaluable evidence regarding which patients are most vulnerable to non-adherence, the possible causes and what affects non-adherence has in the long term, both for the patient and the health service. This kind of large, prospective longitudinal study is not currently available in rheumatoid arthritis looking specifically at adherence and the psychology of adjustment to chronic illness but would provide additional, related information to the cohort studies that are currently available such as the Early Rheumatoid Arthritis Network (ERAN), the Early Rheumatoid Arthritis Study (ERAS) and the Norfolk Arthritis Register (NOAR).

12.8: Final conclusions

This programme of research has demonstrated that adherence to medication is a complex, multifaceted process that involves both social cognition models of illness in a cost-benefit decision as well as relatively simple omissions that are unintentional. By measuring both intentional and unintentional non-adherence and testing each of the commonly used social cognition models, this study has provided evidence for some of the factors that influence adherence in different stages of rheumatoid arthritis, identifying potential areas for targeted intervention in the future. Few previous studies have systematically collected this information in RA or other chronic illnesses. These results should be carried forward to the clinical setting to address potential non-adherence in patients in a multifaceted way, focussing on the needs of the patient in relation to their knowledge, experience, perceptions of their illness and treatment and the ways in which they struggle to take their medications in an optimum fashion.

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Appendices

Appendix 4.1: Full list of references retrieved for the ICT systematic literature review

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Appendix 5.1: Using Information and Communication Technology in the Rheumatology clinic survey

Where did you hear about this survey? (Please tick all that apply)

In clinic	☐	By post	☐	At the University of Hertfordshire	☐
By an email	☐	Via facebook	☐	Via another website	☐
Friend/family member	☐				

What is your gender (please circle) Male Female

What is your current age (please circle)

18 – 24 25 – 34 35 – 44 45 – 54 55 – 64 65+ 75+

Please write down your postcode (this is to check the broadband connection in your area)

.....

What is your highest level of education (please circle)

No formal qualification	Secondary school (GCSEs or equivalent)	College (A levels or equivalent)	University (Degree or equivalent)	Postgraduate (Degree or equivalent)

Please name your illness below and answer **SECTIONS A & B**

.....
.....

SECTION A

Internet and Email

Please answer the following question by ticking the boxes "yes", "no" or "don't know" boxes for both your home and place of work.

1. If you do not currently work, please tick this box ☐

	At home		Don't	**At work**		Don't
	Yes	No	know	Yes	No	know
Do you have access to a computer (including a laptop)						
Do you have internet access						
Do you have broadband internet access						
Do you have dial up internet access						
Do you use the internet						

2. When did you last use the internet?

Within the last 3 months ☐ More than 3 months ago ☐ Never ☐

3. How often, on average, do you access the internet

Every day or almost every day		A couple of times a week		Once a week	
Once a month		Less than once a month		Never	

4. Do you have an email address?

Yes ☐ *Go to Q4a* No ☐ *Go to Q6*

4a. Is this:

Private/personal use ☐ Work use ☐ I have at least one of each ☐

5. How often do you access your emails?

More than once a day		Once a day		Once a week	
Once a month or less		I don't have an email address			

6. How often have you used the internet for the following activities (please tick)

		Never	Occasionally	Frequently	Very often
Shopping					
Working					
Looking up general health information for yourself					
Looking up general health information for a friend or family member					
Looking up specific health information about your chronic illness					
MSN (instant messenger)					
Using these social networking sites:	Facebook				
	Bebo				
	MySpace				
	Friends Reunited				
	Other				

7. Do you experience any of the following problems on a regular basis when using a computer (tick all that apply)

Have difficulty seeing the screen	
Have difficulty seeing the keyboard	
Have difficulty in pressing the keys on the keyboard	
Have difficulty moving the mouse	
Have difficulty in setting up and maintaining an email account	
None of these	

SMS Text messaging

8. Do you own a mobile phone?

Yes ☐ *Go to Q9* No ☐ *Go to Section B.*

9. How often do you have your mobile phone switched on?

All the time	☐	During the day only	☐	If I forget to turn it off	☐
Only if I'm using it	☐	Don't know/Can't remember	☐		

10. How often do you take your mobile phone out with you when you leave the house?

Always	☐	Most of the time	☐	Sometimes	☐
Never	☐	Don't know/can't remember	☐		

11. What do you use your mobile phone for most of the time?

Text messaging	☐	Phone calls	☐	About the same for both	☐

12. How often, on average, do you <u>receive</u> text messages?

More than once a day	☐	Once a day	☐	Once a week	☐
Once a month or less	☐	Never	☐		

13. How often, on average, do you <u>send/reply</u> to text messages?

More than once a day	☐	Once a day	☐	Once a week	☐
Once a month or less	☐	Never	☐		

14. How confident would you say you are in <u>reading</u> text messages?

Very confident	☐	Quite confident	☐	Not confident at all	☐

15. How confident would you say you are in <u>sending</u> text messages?

Very confident	☐	Quite confident	☐	Not confident at all	☐

16. Do you experience any of the following problems on a regular basis when using your mobile phone (tick all that apply)

Have difficulty seeing the screen	
Have difficulty seeing the buttons	
Have difficulty holding the phone	
Have difficulty pressing the buttons	
Have difficulty in using the text message features (e.g. predictive text)	
None of these	

Section B continues on the next page

SECTION B

17. Does your arthritis hospital department or nurse have the facility for you to exchange emails with them?

Yes ☐ *Go to Q17a* No ☐ *Go to Q17b* Don't know ☐

17a. Have you ever used this service if it is available?

Yes ☐ No ☐ Don't know/can't remember ☐

17b. If it were available, do you think you would use this service?

Yes ☐ No ☐ Not sure ☐

18. Have you ever received an email or text message from a healthcare representative in the following situations

	I have previously received a text message	I would like to receive a text message	I have previously received an email	I would like to receive an email
Appointment reminder				
Medication reminder				
Response to your question				
Inviting you to participate in research				
Telling you the results of some research				
None of these				

19. Have you ever visited any websites that are specifically aimed at people with arthritis?

Yes ☐ No ☐ Don't know/can't remember ☐

20. Are there any health websites that you have visited and found particularly helpful? If yes, please state

.....
.....

21. Would you use a forum dedicated to discussions about arthritis?

Yes ☐ No ☐ Don't know/not sure ☐

22. Would you be happy to provide your mobile phone number and/or email address for research using text messaging or emails to remind you about hospital appointments or to take your medication (this will not be taken at this point)

	Text message	Email
Appointment reminder		
Medication reminder		
Neither		

Appendix 7.1: Using social cognition models of illness to predict adherence questionnaire

ID no: .....

Demographic Information

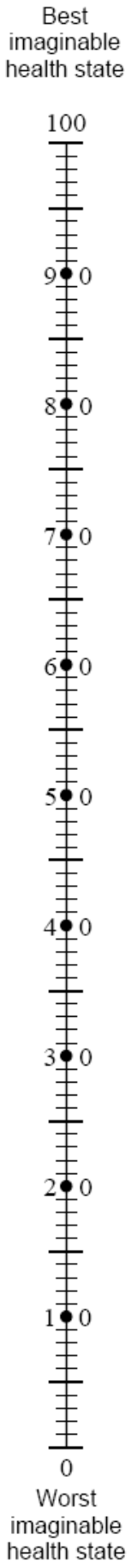
Please circle the answer to each question that applies to you

1.	Age:	18-29	30-39	40-49	50-59	60-69	70+
2.	Gender:	Male	Female				
3.	Highest level of education:	Secondary school	College	University	Post graduate		
4.	Are you currently working:	Yes	No				
4a.	If not currently working, is this due to your illness?	Yes	No				
5.	Occupation	.....					
6.	Previous occupation (if not currently working	.....					
7.	How long have you had your illness?	.....					
8.	Which medications are you currently taking? (please circle ALL that apply)	Disease Modifying anti-rheumatic drugs (e.g. Methotrexate, Leflunamide, Sulfasalazine, Hydroxychloroquine)		Biologic (e.g. Rituximab, Adalimumab, Etanercept, Infliximab)		Other	
9.	What is the current status of your illness?	Active	Remission				
12.	How many times in the past 4 weeks have you visited your GP for any reason?	.....					

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



By placing a tick in **one box in each group** below, please indicate which statements best describe your own health state today

Mobility	I have no problems in walking about	
	I have some problems in walking about	
	I am confined to bed	
Self Care	I have no problems with self care	
	I have problems washing or dressing myself	
	I am unable to wash or dress myself	
Usual Activities (e.g. work, study, housework, family or leisure activities)	I have no problems with performing my usual activities	
	I have some problems with performing my usual activities	
	I am unable to perform my usual activities	
Pain/Discomfort	I have no pain or discomfort	
	I have moderate pain or discomfort	
	I have extreme pain or discomfort	
Anxiety/Depression	I am not anxious or depressed	
	I am moderately anxious or depressed	
	I am extremely anxious or depressed	

These items deal with ways you've been coping with the stress in your life since you were diagnosed with arthritis. Obviously, different people deal with things in different ways but I'm interested in how you've tried to deal with it. Each question says something about a particular way of coping. I want to know to what extent you've been doing what the item says. Don't answer on the basis of whether it seems to be working or not – just if you're doing it. Please read the statements and tick the box which best describes the way you have been coping. Try to rate each item separately in your mind from the others. Make your answers as true to **you** as you can

	I haven't been doing this at all	I've been doing this a little bit	I've been doing this a medium amount	I've been doing this a lot
I've been concentrating my efforts on doing something about the situation I'm in				
I've been saying to myself "this isn't real"				
I've been taking action to try to make the situation better				
I've been refusing to believe it has happened				
I've been getting help and advice from other people				
I've been trying to come up with a strategy about what to do				
I've been accepting the reality of the fact that it has happened				
I've been trying to get advice or help from other people about what to do				
I've been learning to live with it				
I've been thinking hard about what steps to take				

The following questions are about how you take the medications for your arthritis. Please read the statements and tick the box which best describes the way you take your medications. Think about how you have taken your **Disease Modifying Anti-Rheumatic Drugs (DMARDs)** only (e.g. Methotrexate, Leflunamide, Sulfasazine, Hydroxychloroquine) in the **past month**.

	Don't agree at all	Don't agree	Agree	Agree very much
I take my anti-rheumatic medicines because I then have fewer problems				
I definitely don't dare to miss my anti-rheumatic medications				
My medicines are always stored in the same place and that's why I don't forget them				
I take my medications because I have complete confidence in my rheumatologist				
What the doctor tells me, I hang on to				
I sometimes forget to take my medicines				
I sometimes alter the dose of my medication to suit my own needs				

The following question is about the symptoms of your arthritis. Please read each symptom and tick the box to show whether:

a) You have experienced this symptom in the past 2 months
b) If you have experienced it, do you believe this symptom was caused by your arthritis

Symptom	a) Have you experienced this symptom is the past 2 months?	b) Do you believe this symptom was caused by your arthritis?
Pain		
Sore throat		
Stiff joints		
Headache		
Blocked or runny nose		
Tiredness		
Fever		
Weight loss		
Poor sleep		
Loss of appetite		
Swelling of the joints		
Sickness: vomiting or nausea		
Breathlessness		
Abdominal cramps		

The following questions are about what you think about your arthritis and how it affects you. Please read the statements carefully and tick the box which best describes how much you agree with the statement.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
My arthritis will last a short time					
My arthritis is likely to be permanent rather than temporary					
My arthritis will last for a long time					
My arthritis will pass quickly					
I expect to have arthritis for the rest of my life					
The symptoms of my arthritis change a great deal from day to day					
My symptoms come and go in cycles					
My arthritis is very unpredictable					
I go through cycles in which my arthritis gets better and worse					

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
My arthritis is a serious condition					
My arthritis has major consequences on my life					
My arthritis does not have much effect on my life					
My arthritis strongly effects the way others see me					
My arthritis has serious financial consequences					
My arthritis causes difficulties for those that are close to me					

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
There is a lot that I can do to control my symptoms					
What I do can determine whether my arthritis gets better or worse					
The course of my arthritis depends on me					
Nothing I do will effect my arthritis					
I have the power to influence my arthritis					
My actions will have no effect on the outcome of my arthritis					

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
My arthritis will improve in time					
There is little that can be done to improve my arthritis					
My medicines will be effective in curing my arthritis					
The negative effects of my arthritis can be prevented (avoided) by my medicines					
My medicines can control my arthritis					
There is nothing which can help my arthritis					

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
The symptoms of my arthritis are puzzling to me					
My arthritis is a mystery to me					
My arthritis doesn't make any sense to me					
I have a clear picture or understanding of my arthritis					
I don't understand my arthritis					

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
I get depressed when I think about my arthritis					
When I think about my arthritis, I get upset					
My arthritis makes me feel angry					
My arthritis does not worry me					
Having arthritis makes me feel anxious					
My arthritis makes me feel afraid					

The following questions are concerned with how you feel about taking your arthritis medications and your attitudes towards them. Read each statement carefully and circle the comment that you agree with most strongly. When reading these statements, please think about how you take **all** of your **Disease Modifying Anti-Rheumatic Drugs only** (e.g. Methotrexate, Leflunamide, Sulfasalazine, Hydroxychloroquine).

For the next question, please circle **one** comment that you agree with most strongly for **each numbered option**.

TPBA Taking all of the Disease modifying anti-rheumatic drugs for my arthritis would be:

1.	Wise	Foolish
2.	Important	Unimportant
3.	Satisfying	Unsatisfying
4.	Pleasant	Unpleasant
5.	Worthwhile	Not worthwhile
6.	Necessary	Unnecessary
7.	Good	Bad
8.	Useful	Of no use

For the following questions, please read the statement and circle the answer that you agree with most

Most people important to me think that I should take all of my tablets	Extremely unlikely	Unlikely	Neither likely nor unlikely	Likely	Extremely likely
Most people who have arthritis take all of their medications	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
People who are important to me think that I should/should not take all of my medicines	Definitely shouldn't	Shouldn't	Neither should nor shouldn't	Should	Definitely should
Do you think it would be easy or difficult to take all of your medication	Extremely difficult	Difficult	Neither easy nor difficult	Easy	Extremely easy
How much personal control do you have over taking all of your medications	Extremely low control	Low control	Neither high nor low control	High control	Extremely high control
How confident are you that you will be able to take all of your medicines for the next month	Very unconfident	Unconfident	Neither confident nor unconfident	Confident	Very confident
How confident are you that over the next month, you could overcome obstacles that	Very unconfident	Unconfident	Neither confident nor	Confident	Very confident

prevent you from taking all of your medicines?			unconfident		
I believe that I have the ability to take all of my medicines	Definitely don't	Don't	Neither do nor don't	Do	Definitely do
Whether or not I take all of my medicines is entirely up to me	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
How much do you feel that taking all of your medicines is beyond your control	Very much	Some	Neither beyond nor not beyond my control	A little	Not at all

Over the next month, my goal is to take my arthritis medicines: (please circle)

Not at all Some of the time Most of the time All of the time

a) According to the prescription from your doctor, how often should you take your disease modifying anti-rheumatic medication?

Once a *week* Once a *day* More than once a day As needed Don't know

b) How often do you take your disease modifying anti-rheumatic medication?

Once a *week* Once a *day* More than once a day As needed Can't remember

c) If your answer to question (b) was different to question (a) please state why:

.....
.....
.....
.....

How often have you visited your GP in the last 4 weeks? .....

The following questions are about how you feel about your medicines and your arthritis. Please read the statements carefully and then tick the box which most closely describes how much you agree or disagree with the statement.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
I do not want to take medications					
My arthritis medications have unpleasant side effects					
In general I am opposed to medications					
It is too much trouble for me to get my prescriptions					
My arthritis medicines weaken my immune system					
My medications are too expensive					
My arthritis medications are effective in improving my symptoms					
I suffer more symptoms than other people with arthritis					
I am concerned about the risk of falling seriously ill					
I get sick more easily than other people with arthritis					
My arthritis may lead to serious health problems					
If I had a severe flare up of my arthritis, I would not be able to manage my daily activities					
I am afraid a flare up of my arthritis would make me very sick					
I am worried about having a flare up of my arthritis					
Whenever I get sick it seems to be serious					

The following questions are about the way you feel about medications in general. Please read the statement and tick the box which best describes how much you agree or disagree with the statement

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Most medicines are addictive					
People who take medicines should stop their treatment for a while every now and again					
Medicines do more harm than good					
All medicines are poisons					
Natural remedies are safer than medicines					
Doctors place too much trust in medicines					
If doctors had more time with patients they would prescribe fewer medicines					
Doctors use too many medicines					

The following questions are about the **disease modifying anti-rheumatic drugs** (e.g. Methotrexate, Leflunaminde, Sulfasazine, Hydroxychloroquine) that you take for your arthritis. When reading the statements, **please think about these medicines only** and tick the box which best describes how much you agree or disagree with the statement.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
My medicines disrupt my life					
Having to take medicines worries me					
I sometimes worry about becoming too dependent on my medicines					
My medicines are a mystery to me					
I sometimes worry about the long term effects of my medicine					
My life would be impossible without my medicines					
My health in the future will depend on my medicines					
Without my medicines I would be very ill					
My medicines protect me from becoming worse					
My health, at present, depends on my medicines					

The following questions are about how you have been feeling in the last few weeks. Please read each statement and circle the number indicating how often you feel that way, where 1 is almost never and 5 is almost all the time.

	Almost never				Almost all the time
I feel like a failure	1	2	3	4	5
I get a frightened feeling, as if something awful is about to happen	1	2	3	4	5
I feel guilty	1	2	3	4	5
I can laugh and see the funny side of things	1	2	3	4	5
I am disappointed in myself	1	2	3	4	5
I get a frightened feeling, like butterflies in the stomach	1	2	3	4	5
I feel cheerful	1	2	3	4	5
I blame myself constantly	1	2	3	4	5
I get a sudden feeling of panic	1	2	3	4	5
I look forward with enjoyment to things	1	2	3	4	5
I think about harming myself	1	2	3	4	5

The following questions are about how you manage day to day activities with your arthritis. Please read the statements and tick the response which best describes your usual abilities **over the past week**

	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
DRESSING and GROOMING				
Are you able to:				
Dress yourself, including tying shoelaces and doing buttons?				
Shampoo your hair?				
ARISING				
Are you able to:				
Stand up from an armless straight chair?				
Get in and out of bed?				
EATING				
Are you able to:				
Cut your meat?				
Lift a full cup or glass to your mouth?				
Open a new carton of milk (or soap powder)?				
WALKING				
Are you able to:				
Walk outdoors on flat ground?				
Climb up five steps?				

Please tick any **aids or devices** that you usually use for any of the above activities:

Cane/walking stick		Walking frame	
Built-up or special utensils		Crutches	
Wheelchair		Special or built-up chair	
Devices used for dressing (button hooks, zip pull, long-handled shoe horn)			
Other (please specify)			

Please tick any category for which you usually need **help from another person**:

Dressing and grooming		Eating	
Arising		Walking	

	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
HYGIENE				
Are you able to:				
Wash and dry your body?				
Take a bath?				
Get on and off the toilet?				
REACH				
Are you able to:				
Reach and get down a 5lb object (e.g. a bag of potatoes) from just above your head?				
Bend down to pick up clothing off the floor?				
GRIP				
Are you able to:				
Open car doors?				
Open jars which have been previously opened?				
Turn taps on and off?				
ACTIVITIES				
Are you able to:				
Run errands and shop?				
Get in and out of a car?				
Do chores such as vacuuming, housework or light gardening?				

Please tick any **aids or devices** that you usually use for these activities:

Raised toilet seat		Bath seat	
Bath rail		Long-handled appliances for reach	
Long-handled appliances in the bathroom		Jar opener (for jars previously opened)	
Other (specify)			

Please tick any categories for which you usually need **help from another person**:

Hygiene		Gripping and opening things	
Reach		Errands and housework	

Appendix 7.2: Principle components analysis of the social cognition models questionnaires

Factor loadings of the Theory of Planned Behaviour questionnaire

		Factor		
		1	2	3
		37.6%	12.2%	10.7%
Item	Question	Perceived behavioural control	Important others	Other RA
TPBSN1	Important others		.901	
TPBSN2	Other RA patients			.844
TPBSN3	Important others		.849	
TPBPC1	Easy to take meds	.691		
TPBPBC2	Personal control taking meds	.592		
TPBPBC3	Confident taking meds	.829		
TPBPBC4	Overcome obstacles	.720		
TPBPBC5	Ability to take meds	.780		
TPBPBC6	Entirely up to me	.373		
PTBPBC7	Beyond my control	.588		

Subjective Norm Cronbach's $\alpha = 0.526$

Perceived Behavioural Control Cronbach's $\alpha = 0.782$

Factor loadings of the Health Belief Model questionnaire

		Factor		
		1	2	3
		34.2%	11.1%	8.7%
Item	Question	Severity	Logistic barriers	Generally opposed to medication
HBMBar1	Don't want to take			.799
HBMBar2	Side effects	.471		
HBMBar3	Generally opposed			.835
HBMBar4	Too much trouble		.724	
HBMBar5	Weakens immunity	.509		
HBMBar6	Too expensive		.614	
HBMBen1	Improve symptoms		-.630	
HBMBen2	More symptoms than others	.504		
HBMBen3	Concerned seriously ill	.738		
HBMBen4	Get sick more easily than others	.625		
HBMSev1	Serious health problems	.767		
HBMSev2	Daily activities if flare	.763		
HBMSev3	Flare would make me very sick	.833		
HBMSev4	Worried about flare	.798		
HBMSev5	When I get sick it's serious	.652		

Barriers Cronbach's $\alpha = 0.633$

Benefits Cronbach's $\alpha = 0.632$

Severity Cronbach's $\alpha = 0.853$

Factor loadings of the revised illness perceptions questionnaire

		Factor loadings								
		1 20%	2 12%	3 8.6%	4 6.7%	5 5.6%	6 4.3 %	7 3.9%	8 3.2%	9 2.7 %
Item	Question	Cohesion	Emotion	Chronic	Personal control	Conseque-nces for others	Cyclical	Personal conseque-nces	Treatment control	Nothing can help
SRMT1	Short			.618						
SRMT2	Permanent			.829						
SRMT3	Long			.869						
SRMT4	Quick			.809						
SRMT5	Rest of life			.738						
SRMC1	Symptoms change						.618			
SRMC2	Symptoms cycle						.775			
SRMC3	Unpredictable						.745			
SRMC4	Better & worse						.784			
SRMCon1	Serious							.717		
SRMCon2	Major consequences					**.537**		**.585**		
SRMCon3	Not much effect					.538				
SRMCon4	Others see me					.800				
SRMCon5	Financial consequences					.701				
SRMCon6	Difficulties for others					.780				
SRMPC1	I can control symptoms				.676					
SRMPC2	What I do				.776					
SRMPC3	Course depends on me				.631					
SRMPC4	Nothing will effect				.748					
SRMPC5	Power to influence				**.484**			**-.501**		
SRMPC6	Actions no outcome				.702					
SRMTC1	Improve in time			**-.367**				**-.319**		**.324**
SRMTC2	Little can improve									.563
SRMTC3	Meds cure								.512	
SRMTC4	Meds prevent negative effects								.795	
SRMTC5	Meds control								.687	
SRMTC6	Nothing can help									.494
SRMCo1	Symptoms puzzling	.869								
SRMCo2	RA mystery	.884								
SRMCo3	RA makes no sense	.871								
SRMCo4	Clear understanding of RA	.729								
SRMCo5	Don't understand RA	.848								
SRME1	Depressed		.839							
SRME2	Upset		.858							
SRME3	Angry		.663							
SRME4	Does not worry me		**.465**							**.478**
SRME5	Anxious		.794							
SRME6	Afraid		.712							

Bold = more than 1 loading, underlined = unexpected factor loading

Appendix 7.3: Baseline mean sumscores for the new and established groups when new = 6 months (A) and new = 2 years (B)

	New A (6 months)	New B (2 years)	Established A	Established B
Total N	33	49	110	94
Demographics				
Female (%)	23 (69.7)	32 (65.3)	77 (70)	68 (72.3)
Age	55 (55, 22-81)	57 (55, 22-81)	61 (59, 33-89)	61 (62, 33-89)
Disease duration	7.10 (1, 0.5-54)	6.48 (2, 0.5-54)	12.78 (10, 1.5-40)	13.99 (10, 0.5-40)
Theory of Planned Behaviour				
Subjective norm	12.06 (12, 7-15)	12.00 (12, 7-15)	12.29 (12, 7-15)	12.36 (12, 7-15)
Personal control	29.48 (33, 18-35)	29.96 (33, 18-35)	30.74 (31, 21-35)	30.72 (31, 19-35)
Health Belief Model				
Barriers	16.48 (17, 6-24)	16.16 (17, 6-25)	15.56 (15, 6-27)	15.57 (14, 6-27)
Benefits	11.83 (11, 4-16)	11.77 (12, 4-16)	11.96 (12, 6-17)	12.01 (17, 6-17)
Severity	16.79 (18, 5-24)	16.30 (16, 5-24)	15.85 (17, 5-25)	15.93 (9, 4-16)
Self Regulation Model				
Identity	3.58 (4, 0-5)	3.53 (4, 0-5)	3.43 (4, 0-5)	3.43 (4, 0-5)
Chronicity	20.52 (24, 12-25)	20.11 (22, 5-25)	21.89 (23, 5-25)	22.33 (23, 9-25)
Cyclical	13.42 (15, 6-20)	13.30 (14, 6-20)	13.48 (14, 4-20)	13.55 (14, 4-20)
Consequences	20.97 (20, 12-28)	20.17 (20, 10-30)	20.29 (20, 10-30)	20.58 (21, 10-30)
Personal control	19.39 (20, 11-30)	19.79 (20, 11-26)	18.86 (20, 6-28)	18.57 (20, 6-28)
Treatment control	21.16 (21, 14-30)	20.89 (21, 14-30)	19.86 (20, 7-28)	19.77 (20, 6-28)
Cohesion	13.96 (12, 5-20)	13.43 (12, 5-21)	12.75 (12, 5-25)	12.81 (11, 5-25)
Emotional effect	18.87 (16, 7-30)	18.19 (16, 7-30)	17.29 (18, 7-30)	17.37 (14, 7-30)
Beliefs about medications				
General Harm	9.13 (7, 4-16)	9.0 (8, 4-16)	9.10 (9, 4-16)	9.16 (11, 4-16)
General Overuse	10.94 (11, 4-16)	10.66 (11, 4-16)	10.45 (11, 4-17)	10.52 (13, 4-17)
Specific Concern	14.37 (16, 5-20)	13.98 (15, 5-20)	13.38 (13, 5-23)	13.41 (20, 5-23)
Specific Necessity	16.47 (15, 5-23)	16.89 (17, 5-23)	19.26 (20, 5-25)	19.51 (20, 5-25)
Depression, Anxiety & Positive Outlook				
Depression	9.19 (5, 5-23)	8.85 (6, 5-23)	8.19 (7, 5-21)	8.20 (6, 5-21)
Anxiety	5.90 (3, 3-15)	5.72 (3, 3-15)	5.19 (4, 3-13)	5.17 (4, 3-13)
Positive outlook	10.16 (10, 3-15)	10.17 (10, 3-15)	10.34 (11, 3-15)	10.36 (11, 3-15)
Disease outcomes				
HAQ	1.00 (0.25, 0-2.75)	0.98 (0.38, 0-2.75)	1.21 (1.13, 0-2.88)	1.26 (1.13, 0-2.88)
DAS28	3.98 (4.33, 0-5.4)	3.52 (3.59, 0-5.4)	3.06 (2.82, 0-6.87	3.07 (2.78, 0.5-6.87)
EQ5D VAS	61.27 (73, 20-95)	63.04 (74, 20-95)	64.15 (70, 10-100)	63.76 (70, 10-100)
EQ5D utility	0.52 (0.73, -0.18-1)	0.57 (0.69, -.018-1)	0.61 (0.69, -0.07-1)	0.60 (0.69, -0.07-1)
Adherence				
Low intentional	6 (18.2%)	9 (18.4%)	32 (29.1%)	29 (30.9%)
Forget	7 (21.2%)	10 (20.4%)	19 (17.3%)	16 (17.0%)
Overall low	11 (33.3%)	16 (32.7%)	43 (39.1%)	38 (40.4%)

Appendix 8.1: Internal consistency shown by Cronbach's α for each of the model factors at six month follow-up

Scale	Cronbach's α
Theory of Planned Behaviour	
Social Norm	0.62
Perceived Behavioural Control	0.77
Important others	*0.80*
Health Belief Model	
Barriers	0.64
Benefits	0.52
Severity	0.84
Self Regulatory Model	
Identity 1 – general unwell	SR identity – 0.75
Identity 2 – RA symptoms	
Identity 3 – weight	
Chronic timeline	0.83
Cyclical timeline	0.74
Consequences	0.85
Personal control	0.78
Treatment control	0.55
Cohesion	0.90
Emotion	0.89
Beliefs about Medications Questionnaire	
General harmful	0.71
General overuse	0.81
Specific concerns	0.75
Specific necessity	0.91

Appendix 8.2: Mean model factor sumscores at six month follow-up for the 3 treatment groups

	Whole sample	Newly diagnosed	Established	Biologic
Total N	171	42	68	61
Theory of Planned Behaviour				
Subjective norm	12.17 (1.78)	12.34 (1.70)	11.92 (1.78)	12.33 (1.82)
Important others	8.63 (1.43)	8.82 (1.31)	8.41 (1.59)	8.74 (1.32)
Personal control	30.86 (3.54)	30.79 (3.68)	30.86 (3.36)	30.90 (3.69)
Health Belief Model				
Barriers	16.46 (3.98)	16.59 (4.12)	16.08 (4.36)	16.77 (3.49)
Benefits	12.38 (2.22)	12.30 (2.74)	11.92 (2.10)	12.88 (1.89)
Severity	16.74 (3.82)	16.30 (4.34)	16.27 (3.81)	17.48 (3.41)
Self Regulation Model				
Identity	3.89 (2.36)	3.70 (2.58)	3.62 (1.84)	4.30 (2.66)
Chronic timeline	22.10 (3.52)	**20.86 (4.92)***	22.22 (2.72)	**22.69 (3.15)***
Cyclical timeline	13.01 (3.15)	13.11 (2.73)	13.72 (2.83)	12.22 (3.54)
Consequences	21.31 (4.81)	**21.90 (4.08)***	**19.52 (5.42)*+**	**22.69 (4.08)+**
Personal control	18.87 (4.19)	18.36 (4.43)	19.30 (3.30)	18.77 (3.91)
Treatment control	19.62 (3.01)	19.18 (2.83)	19.67 (3.30)	19.84 (2.84)
Cohesion	12.36 (4.22)	13.54 (4.56)	12.51 (4.09)	11.50 (3.99)
Emotional effect	17.22 (5.30)	17.93 (5.40)	16.31 (5.58)	17.64 (4.90)
Beliefs about medications				
General harm	9.05 (2.40)	9.33 (2.98)	9.32 (2.32)	8.61 (2.02)
General overuse	10.82 (2.68)	11.15 (3.12)	10.71 (2.54)	10.72 (2.55)
Specific concern	13.69 (3.43)	14.42 (4.04)	13.42 (3.43)	13.52 (3.00)
Specific necessity	19.45 (3.46)	18.79 (3.99)	**18.92 (3.17)***	**20.41 (3.24)***
Necessity-concerns differential	5.76 (4.59)	**4.37 (5.26)***	5.51 (4.22)	**6.89 (4.30)***
Depression, Anxiety and Positive Outlook				
Depression	8.45 (4.05)	9.35 (4.64)	7.65 (3.05)	8.70 (4.44)
Anxiety	5.48 (2.93)	5.90 (3.13)	5.17 (2.77)	5.54 (2.96)
Positive outlook	10.83 (3.09)	10.65 (3.17)	10.21 (3.44)	11.57 (2.51)
Disease outcomes				
HAQ	1.26 (0.83)	**1.05 (0.82)***	1.16 (0.84)	**1.48 (0.79)***
DAS	3.35 (1.03)	3.28 (0.98)	3.13 (1.16)	3.47 (1.01)
EQ5D VAS	62.88 (19.64)	64.22 (20.35)	61.11 (20.48)	63.86 (18.40)
EQ5D utility	0.59 (0.28)	0.56 (0.31)	0.63 (0.26)	0.56 (0.29)
Adherence				
Low intentional	40 (23.4%)	7 (17.1%)	18 (27.3%)	15 (23.4%)
Forget	37 (21.6%)	12 (29.3%)	11 (16.7%)	14 (21.9%)
Overall low	62 (36.3%)	16 (39%)	23 (34.8%)	23 (35.9%)

Appendix 9.1: Mean model factor sumscores at six month follow-up for the different adherence groups

	Intentional low	Intentional high	Forget	Don't forget	Overall low	Overall high
Total N	40	125	37	126	62	103
Theory of Planned Behaviour						
Subjective norm	8.18 (1.60)	8.78 (1.36)	8.53 (1.38)	8.66 (1.47)	8.34 (1.49	8.80 (1.38)
Personal control	30.50 (3.66)	30.96 (3.51)	**29.92 (3.94)**	**31.17 (3.38)***	30.49 (3.52)	31.06 (3.55)
Health Belief Model						
Barriers	17.38 (4.19)	16.15 (3.95)	17.11 (4.33)	16.26 (3.96)	16.89 (4.20)	16.18 (3.92)
Benefits	11.98 (1.9)	12.61 (2.23)	12.41 (2.60)	12.48 (2.07)	12.13 (2.36)	12.65 (2.05)
Severity	**15.73 (3.71)**	**17.19 (3.82)***	16.30 (4.19)	16.96 (3.76)	**15.95 (3.86)**	**17.37 (2.05)***
Self Regulation Model						
Identity	3.78 (2.35)	3.97 (2.40)	3.72 (2.13)	4.02 (2.46)	3.61 (2.82)	4.11 (2.43)
Chronic timeline	22.10 (3.02)	22.18 (3.41)	21.85 (3.87)	22.26 (3.19)	21.81 (3.39)	22.36 (3.26)
Cyclical timeline	13.40 (2.74)	12.93 (3.28)	13.51 (3.36)	12.93 (3.10)	13.30 (3.21)	12.90 (3.12)
Consequences	20.60 (5.03)	21.54 (4.82)	21.72 (4.17)	21.20 (5.10)	20.90 (4.52)	21.55 (5.08)
Personal control	18.73 (3.90)	18.96 (4.26)	19.08 (4.63)	18.90 (3.98)	19.10 (4.01)	18.78 (4.27)
Treatment control	18.85 (3.56)	19.90 (2.80)	19.53 (3.57)	19.70 (2.86)	19.30 (3.28)	19.85 (2.86)
Cohesion	12.20 (4.50)	12.53 (4.16)	12.75 (4.23)	12.35 (4.27)	12.23 (4.27)	12.58 (4.24)
Emotional effect	16.30 (4.98)	17.72 (5.35)	17.65 (5.64)	17.22 (5.20)	16.53 (5.01)	17.89 (5.40)
Beliefs about Medications Questionnaire						
General harm	8.90 (2.28)	9.14 (2.48)	9.32 (2.70)	9.02 (2.37)	9.11 (2.55)	9.06 (2.37)
General overuse	10.78 (2.12)	10.81 (2.87)	11.84 (2.81)	10.47 (2.60)	11.34 (2.62)	10.47 (2.71)
Specific concern	13.15 (2.70)	13.88 (3.65)	14.16 (3.51)	13.54 (3.44)	13.63 (3.19)	13.74 (3.61)
Specific necessity	18.60 (3.36)	19.72 (3.48)	18.54 (4.17)	19.71 (3.44)	**18.40 (3.56)**	**20.09 (3.27)***
Necessity-concerns differential	5.45 (4.42)	5.85 (4.67)	**4.38 (5.17)**	**6.17 (4.37)***	**4.77 (4.48)**	**6.35 (4.59)***
Depression, Anxiety and Positive Outlook						
Depression	8.05 (3.41)	8.70 (4.27)	9.43 (4.39)	8.19 (3.91)	8.66 (4.10)	8.47 (4.07)
Anxiety	4.75 (2.51)	5.80 (3.04)	6.24 (3.24)	5.27 (2.79)	5.29 (2.93)	5.70 (2.95)
Positive outlook	11.23 (3.41)	10.63 (2.99)	10.64 (3.19)	10.85 (3.09)	11.05 (3.27)	10.61 (2.99)
Disease outcomes						
HAQ	1.10 (0.81)	1.31 (0.84)	**0.97 (0.77)**	**1.34 (0.84)***	**1.02 (0.79)**	**1.40 (0.83)***
DAS	3.27 (1.05)	3.38 (1.02)	3.59 (0.66)	3.25 (1.13)	3.42 (0.87)	3.28 (1.15)
EQ5D VAS	**70.95 (17.07)**	**60.07 (19.80)***	64.30 (19.21)	62.81 (19.70)	**67.66 (18.67)**	**59.73 19.77)***
EQ5D utility	**0.67 (0.19)**	**0.56 (0.30)***	0.59 (0.29)	0.58 (0.28)	0.64 (0.25)	0.55 (0.30)

Appendix 9.2: Using baseline model factor sumscores to predict change in intentional adherence when baseline is high

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications		Clinical factors	
Variable	Wald	OR	Wald	OR	Wald	OR	Wald	OR	Wald	OR
TPB important others	2.14	1.29								
TPB perceived control	0.73	0.92								
HBM barriers			1.61	0.90						
HBM benefits			3.73	1.44*						
HBM severity			1.10	0.89						
SRM Identity					0.03	1.06				
SRM chronicity					3.81	0.76*				
SRM cyclical					2.07	0.85				
SRM consequences					0.65	1.07				
SRM personal control					2.57	0.88				
SRM treatment control					3.08	1.22				
SRM coherence					0.001	0.997				
SRM emotion					0.19	1.03				
BMQ harmful							2.06	1.26		
BMQ overuse							0.13	1.04		
BMQ necessity							1.74	1.10		
BMQ concern							3.07	0.85		
HAQ									0.05	0.89
DAS28									0.14	0.88
EQ5D VAS									0.59	1.02
EQ5D utility									2.59	0.03
Model	χ^2 (2) = 2.33, p=0.313 Nagelkerke R^2 = 0.037 85% correct (0% of changers)		χ^2 (3) = 4.93, p=0.177 Nagelkerke R^2 = 0.077 85.6% correct (0% of changers)		χ^2 (8) = 12.79, p=0.119 Nagelkerke R^2 = 0.188 85.5% correct (0% of changers)		χ^2 (4) = 5.34, p=0.254 Nagelkerke R^2 = 0.082 86.8% correct (6.3% of changers)		χ^2 (4) = 3.88, p=0.423 Nagelkerke R^2 = 0.082 87.4% correct (0% of changers)	

Appendix 9.3: Using baseline model factor sumscores to predict change in intentional adherence when baseline is low

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications		Positive Outlook	
Variable	Wald	OR	Wald	OR	Wald	OR	Wald	OR	Wald	OR
TPB important others	0.73	0.83								
TPB perceived control	<0.001	1.00								
HBM barriers			0.08	0.97						
HBM benefits			1.21	1.27						
HBM severity			2.05	0.84						
SRM Identity					0.64	0.78				
SRM chronicity					0.67	0.88				
SRM cyclical					0.18	0.95				
SRM consequences					0.31	1.07				
SRM personal control					0.14	1.03				
SRM treatment control					0.58	1.14				
SRM coherence					0.02	0.98				
SRM emotion					1.78	0.89				
BMQ harmful							1.33	0.83		
BMQ overuse							0.001	1.00		
BMQ necessity							0.73	0.90		
BMQ concern							0.49	1.07		
Positive outlook									5.01	1.38*
Model	χ^2 (2) = 0.84, p=0.66 Nagelkerke R^2 = 0.026 50% correct (54.5% of changers)		χ^2 (3) = 2.91, p=0.41 Nagelkerke R^2 = 0.089 57.1% correct (72.7% of changers)		χ^2 (8) = 5.27, p=0.73 Nagelkerke R^2 = 0.157 59.5% correct (63.6% of changers)		χ^2 (4) = 2.27, p=0.69 Nagelkerke R^2 = 0.072 70.7% correct (86.4% of changers)		χ^2 (1) = 5.77, p=0.016 Nagelkerke R^2 = 0.171 66.7% correct (63.6% of changers)	

Appendix 9.4: Change in model factor sumscores to predict change in forgetting for patients who do not forget at baseline

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications		Combined model	
Variable	Wald	OR	Wald	OR	Wald	OR	Wald	OR	Wald	OR
TPB important others	1.65	0.83							1.78	0.77
TPB perceived control	1.42	1.09							0.91	1.10
HBM barriers			2.01	1.12					1.19	1.12
HBM benefits			0.06	1.04					0.01	1.02
HBM severity			0.61	1.09					0.47	1.10
SRM Identity					1.10	1.17			0.61	1.15
SRM chronicity					0.36	0.96			0.02	0.99
SRM cyclical					0.50	0.93			0.15	0.96
SRM consequences					0.07	0.97			<0.001	1.00
SRM personal control					0.93	1.08			0.44	1.06
SRM treatment control					1.45	0.88			0.99	0.89
SRM coherence					0.20	0.96			0.11	0.96
SRM emotion					0.03	0.99			0.10	0.97
BMQ harmful							0.47	1.10	0.06	0.96
BMQ overuse							0.09	0.97	0.002	1.01
BMQ necessity							0.03	0.99	0.10	1.04
BMQ concern							0.40	0.94	0.79	0.91
Model	χ^2 (2) = 2.72, p=0.26		χ^2 (3) = 3.08, p=0.38		χ^2 (8) = 4.77, p=0.78		χ^2 (4) = 0.96, p=0.92		χ^2 (17) = 10.20, p=0.90	
	Nagelkerke R^2 = 0.037		Nagelkerke R^2 = 0.043		Nagelkerke R^2 = 0.071		Nagelkerke R^2 = 0.013		Nagelkerke R^2 = 0.158	
	85.2% correct		85.8% correct		87% correct		86.4% correct		86.8% correct	
	(0% of changers)		(0% of changers)		(0% of changers)		(0% of changers)		(6.7% of changers)	

Appendix 9.5: Change in model factor sumscores to predict change in forgetting for patients who forget at baseline

	Theory of Planned Behaviour		Health Belief Model		Self Regulatory Model		Beliefs about Medications	
Variable	Wald	OR	Wald	OR	Wald	OR	Wald	OR
TPB important others	0.004	0.98						
TPB perceived control	0.52	0.91						
HBM barriers			0.37	1.11				
HBM benefits			0.78	0.81				
HBM severity			0.08	1.05				
SRM Identity					1.00	0.68		
SRM chronicity					1.57	1.48		
SRM cyclical					0.48	0.71		
SRM consequences					3.32	0.66		
SRM personal control					2.36	1.55		
SRM treatment control					0.65	0.86		
SRM coherence					0.92	0.77		
SRM emotion								
BMQ harmful							0.18	0.90
BMQ overuse							0.24	1.12
BMQ necessity							0.06	1.06
BMQ concern							<0.001	1.002
Model	χ^2 (2) = 0.55, p=0.76		χ^2 (3) = 1.17, p=0.76		χ^2 (8) = 4.77, p=0.78		χ^2 (4) = 0.55, p=0.97	
	Nagelkerke R^2 = 0.032		Nagelkerke R^2=0.068		Nagelkerke R^2 = 0.071		Nagelkerke R^2 = 0.033	
	70.8% correct (0% of changers)		75% correct (14.3% changers)		87% correct (0% of changers)		69.6% correct (0% of changers)	

Appendix 10.1: Change in medication doses from baseline to six month follow-up for those prescribed these medications at baseline

	MTX (mg)	N (%)	SSZ (mg)	N (%)	HCQ (mg)	N (%)	LFM (mg)	N (%)	>1 DMARD
Intentional adherence									
Low	0 (0.48)	31 (73.8%)	-576.92 (374.88)	14 (33.3%)	-16.67 (16.67)	8 (19%)	-11.67 (8.33)	2 (4.8%)	13 (31%)
High	-0.86 (0.50)	103 (85.1%)	-421.05 (260.07)	25 (20.7%)	-46.15 (40.22)	23 (19%)	none	3 (2.5%)	38 (31.4%)
Unintentional adherence									
Forgetful	-0.78 (1.33)	17 (70.8%)	-285.71 (473.80)	7 (29.2%)	None	3 (12.5%)	2.50 (2.50)	2 (8.3%)	6 (25%)
Not forgetful	-0.64 (0.41)	118 (84.3%)	-540.00 (243.10)	32 (22.9%)	-41.18 (30.99)	28 (20%)	-13.33 (6.67)	3 (2.1%)	45 (32.1%)
Overall adherence									
Not adherent	-0.32 (0.63)	42 (73.7%)	-558.82 (290.42)	18 (31.6%)	-14.29 (14.29)	9 (15.8%)	-8.75 (6.57)	3 (5.3%)	16 (28.1%)
Adherent	-0.82 (0.51)	93 (86.9%)	-400.00 (324.40)	21 (19.6%)	-50.00 (43.52)	22 (20.6%)	None	2 (1.9%)	35 (32.7%)

Appendix 10.2: Percentage of patients whose DMARD prescription changed from baseline to six month follow-up

	MTX change	Baseline N (%)	SASP	T1 N (%)	HCQ	T1 N (%)	LFM	T1 N (%)
Intentional adherence								
Low	Stop = none Same = 39 (92.9%) Start = 3 (7.1%)	37 (64.4)	Stop = 4 (9.5%) Same = 33 (78.6%) Start = 5 (11.9%)	18 (30.5)	Stop = none Same = 40 (95.2%) Start = 2 (4.8%)	7 (11.9)	Stop = 2 (4.8%) Same = 39 (92.9%) Start = 1 (2.4%)	4 (6.8)*
High	Stop = 3 (2.5%) Same = 102 (84.3%) Start = 16 (13.2%)	114 (72.3)	Stop = 5 (4.1%) Same = 105 (86.8%) Start = 11 (9.1%)	38 (23.9)	Stop = 2 (1.7%) Same = 107 (88.4%) Start = 12 (9.9%)	19 (11.9)	Stop = none Same = 120 (99.2%) Start = 1 (0.8%)	3 (1.9)
Unintentional adherence								
Forgetful	Stop = 1 (4.2%) Same = 21 (87.5%) Start = 2 (8.3%)	28 (65.9)	Stop = 1 (4.2%) Same = 22 (91.7%) Start = 1 (4.2%)	19 (43.2)*	Stop = none Same = 23 (95.8%) Start = 1 (4.2%)	3 (6.8)	Stop = none Same = 24 (100%) Start = none	4 (9.1)*
Not forgetful	Stop = 2 (1.4%) Same = 121 (86.4%) Start = 17 (12.1%)	123 (71.6)	Stop = 8 (5.7%) Same = 117 (83.6%) Start = 15 (10.7%)	37 (21)	Stop = 2 (1.4%) Same = 125 (89.3%) Start = 13 (9.3%)	23 (13.1)	Stop = 2 (1.4%) Same = 136 (97.1%) Start = 2 (1.4%)	3 (1.7)
Overall adherence								
Not adherent	Stop = 1 (1.8%) Same = 52 (91.2%) Start = 4 (7.0%)	56 (66.7)	Stop = 4 (7.0%) Same = 48 (84.2% Start = 5 (8.8%)	31 (35.6)*	Stop = none Same = 55 (96.5%) Start = 2 (3.5%)	9 (10.3)	Stop = 2 (3.5%) Same = 54 (94.7%) Start = 1 (1.8%)	6 (6.9)*
Adherent	Stop = 2 (1.9%) Same = 90 (84.1%) Start = 15 (14.0%)	95 (72.7)	Stop = 5 (4.7%) Same = 90 (84.1%) Start = 11 (10.3%)	25(18.9)	Stop = 2 (1.9%) Same = 93 (86.9%) Start = 12 (11.2%)	17 (12.9)	Stop = none Same = 106 (99.1%) Start = 1 (0.9%)	1 (0.8)