BODY COMPOSITION OF RHEUMATOID ARTHRITIS PATIENTS AND THEIR PERCEPTIONS AND PRACTICES REGARDING DIET, NUTRITIONAL SUPPLEMENTS AND OTHER TREATMENTS

by
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DECLARATION

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December 2011
ABSTRACT

Introduction

Rheumatoid Arthritis (RA) is a chronic, inflammatory, autoimmune disorder characterized by inflammation of the joints and surrounding tissue causing pain, swelling and stiffness. Studies suggest that aspects of the diet may alleviate symptoms and decrease the risk of complications. The scientific basis for a role of dietary therapy in RA has grown although there is still no consensus on the optimum diet. It has been shown that persons with RA tend to have a poor nutritional status; and rheumatoid cachexia, the loss of body cell mass, occurs in nearly two-thirds of all patients with RA. The study aimed to establish what RA patients are practicing and their perceptions regarding the effect of diet, nutritional supplements, medication and complementary and alternative medicines (CAM) and therapies on their symptoms as well as determining their body composition and the possible presence of rheumatoid cachexia.

Methodology

The study design was a cross-sectional study with an analytical component. The study population consisted of adult (18 years or older) RA patients in the Cape Metropole from the private and public sector. An interviewer-administered questionnaire was used followed by the measurement of weight, height, waist circumference and skinfold thickness. Information was also gathered from the medical records.

Results

The sample size comprised of 251 RA patients (n=201 public sector; n=50 private sector). The mean body mass index (BMI) was 30.3 kg/m$^2$ for females and 26.6 kg/m$^2$ for males. BMI was used to classify obesity (n=133; 45.9%), overweight (n=66; 26.8%), normal weight (n=63; 25.6%) and underweight (n=4; 1.6%). Waist circumference measurement classifications showed a substantially increased risk for metabolic complications in 51.8% of participants (n=127) and an increased risk in 21.2% of participants (n=52). Just over half of the participants (n=65; 55.6%) had an unhealthy high body fat percentage classification. Rheumatoid cachexia was seen in 10.3% participants (n=12). Low fat-free mass (Fat-free mass index <10$^{th}$ percentile) was seen in 21% participants (n=24) and obesity (Fat mass index >90$^{th}$ percentile) was seen in 27% of participants (n=31). Twenty nine percent of participants (n=73) believed that certain types of food could improve their symptoms of RA and 60% of participants (n=151) believed that certain foods worsened their symptoms. Sixty four percent of participants (n=161) thought that nutritional supplements or complementary and alternative medicines and therapies could improve their symptoms of RA and 98% (n=246) of participants used nutritional supplements. The most frequently used supplements included folic acid (n=218; 91.6%), calcium (n=182; 76.5%), vitamin D (n=185; 77.7%), omega-3 fatty acids (n=48; 64.9%) and multivitamin and mineral preparations (n=22; 29.7%).

Conclusion

The obesity and waist circumference figures were unacceptably elevated in this population and the body composition of these RA patients should be highlighted as a concern. The high prevalence of risk factors for cardiovascular disease (CVD) need to be urgently addressed since CVD is the leading cause of mortality in RA patients. This study highlights the important role of the intra-professional team, including the dietitian, in the management of RA patients.
OPSOMMING

Inleiding
Rumatoïede artritis (RA) is ’n chroniese, inflammatoriese, outo-immuun siekte wat gekenmerk word deur inflammasie van die gewrigte en omliggende weefsel en veroorsaak pyn, swelling en styfheid. Studies dui daarop dat aspekte van die dieet simptome kan verlig en die risiko van komplikasies kan verminder. Die wetenskaplike basis vir die rol van dieetterapie in RA het gegroei, hoewel daar nog geen konsensus aangaande die optimale dieet is nie. Dit is al bewys dat persone met RA geneig is om ’n swak voedingstatus te hê; en rumatoïede cachexia, die verlies van liggaam selmassa in byna twee-derdes van alle pasiënte met RA voorkom. Die doel van die studie was om te bepaal wat RA-pasiënte se praktyke en persepsies ten opsigte van die uitwerking van dieet, voedselaanvullings, medikasie en aanvullende of alternatiewe medisyne (CAM) en terapieë op hul simptome het, sowel as om hul liggaamsamesthesing en die moontlike teenwoordigheid van rumatoïede cachexia te bepaal.

Metodiek
Die studie ontwerp was ’n dwarssnitstudie met ’n analitiese komponent. Die studiepopulasie bestaan uit volwassene (18 jaar of ouer) RA pasiënte uit die privaat en openbare sektore in die Kaapse Metropool. Onderhoude was gevoer met behulp van vraeliste. Gewig, lengte, middelomtrek en velvoudikte was ook gemete. Inligting was ook versamel uit mediese rekords.

Resultate
Die steekproefgrootte het uit 251 RA pasiënte (n=201 openbare sektor, n=50 privaat sektor) bestaan. Die gemiddelde liggaamsmassa-indeks (LMI) was 30.3 kg/m\(^2\) vir vroue en 26.6 kg/m\(^2\) vir mans. LMI was gebruik om vetsug te klassifiseer (n=133; 45.9%), asook oorgewig (n=66; 26.8%), normale gewig (n=63; 25.6%) en ondergewig (n=4; 1.6%). Klassifikasie van middelomtrek metings het ’n aansienlike verhoogde risiko vir metabolishe komplikasies in 51.8% van die deelnemers (n=127) en ’n verhoogde risiko in 21.2% van die deelnemers (n=52) getoon. Net meer as die helfte van die deelnemers (n=65; 55.6%) het ’n ongesonde hoë liggaamsvet persentasie klassifikasie getoon. Rumatoïede cachexia was by 10.3% van die deelnemers (n=12) gevind. Lae vetvrye massa (vetvrye massa indeks <10de persentiel) was by 21% deelnemers (n=24) en vetsug (vet massa indeks >90ste persentiel) in 27% van die deelnemers (n=31) teenwoordig. Nege-en-twintig persent van die deelnemers (n=73) het gedink dat sekere voedselsoorte hul simptome van RA kon verbeter en 60% van die deelnemers (n=151) was van mening dat sekere kosse die simptome kon vererger. Vier-en-sestig persent van die deelnemers (n=161) het gedink dat voedingsaanvullings of aanvullende en alternatiewe medisyne en terapieë hulle simptome van RA kon verbeter en 98% (n=246) van die deelnemers het voedingsaanvullings gebruik. Die mees algemene gebruikte aanvullings was foliensuur (n=218; 91.6%), kalsium (n=182; 76.5%), vitamien D (n=185; 77.7%), omega-3 vetsure (n=48, 64.9%) en multi-vitamien en minerale preparate (n=22; 29.7%).

Gevolgtrekking
Die vetsug en middelomtrek syfers was onaanvaarbaar verhoog in die studiepopulasie en die liggaamsamesthesing van hierdie RA pasiënte is ’n bekommernis. Die hoë voorkoms van risikofaktore vir kardiovaskulêre siekte (KVS) moet dringend aangespreek word, aangesien die KVS die grootste oorsaak van sterfte in RA pasiënte is. Hierdie studie beklemtion die belangrike rol van die intra-professionele span, met inbegrip van die dieetkundige, in die bestuur van RA pasiënte.
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CONTRIBUTIONS BY PRINCIPAL RESEARCHER AND FELLOW RESEARCHERS

The principal researcher (Louise Ann Lombard) developed the idea and the protocol. The principal researcher planned the study, undertook data collection, captured the data for analyses (with a research assistant), analysed the data with the assistance of a statistician (Prof DG Nel), interpreted the data and drafted the thesis. Mrs Lisanne du Plessis and Mrs Janicke Visser (Supervisors) provided input at all stages and revised the protocol and thesis.
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LIST OF ABBREVIATIONS

ACR  American College of Rheumatology
AIDS Acquired Immune Deficiency Syndrome
BF   Body Fat
BMD  Bone Mineral Density
BMI  Body Mass Index
BSF  Biceps Skinfold
CAM  Complementary and Alternative Medicines
CCP  Cyclic Citrullinated Peptide
COX  Cyclo-Oxygenase
CRP  C-Reactive Protein
CVD  Cardiovascular Disease
DAS  Disease Activity Score
DEP  Dynamic Exercise Programmes
DEXA Dual X-Ray Absorptiometry
DMARD Disease Modifying Anti-Rheumatic Drug
FA   Fatty Acids
FFM  Fat-Free Mass
FFMI Fat-Free Mass Index
FM   Fat Mass
FMI  Fat Mass Index
GI   Gastrointestinal
HAQ  Health Assessment Questionnaire
HDL  High-Density Lipoprotein
IBW  Ideal Body Weight
IL-1 Interleukin-1β
LDL  Low-Density Lipoprotein
LMAL Lean Mass of Arms and Legs
MTX  Methotrexate
NICE National Institute for Health and Clinical Excellence
NSAID Non-Steroidal Anti-Inflammatory Drugs
PRT  Progressive Resistance Training
RA   Rheumatoid Arthritis
RACGP Royal Australian College of General Practitioners
RCT  Randomised Controlled Trial
RF   Rheumatoid Factor
SADHS South African Demographic Health Survey
SISF  Supra-Ileac Skinfold
SSSF Sub-Scapular Skinfold
TFD  Truncal Fat Distribution
TG   Triglyceride
TNF-α Tumour Necrosis Factor-A
TSF  Triceps Skinfold
UAMC Upper Arm Muscle Circumference
US   United States
VLDL Very Low-Density Lipoprotein
WHR  Waist-Hip Ratio
CHAPTER 1: LITERATURE REVIEW AND MOTIVATION FOR STUDY
1.1 INTRODUCTION

Rheumatoid Arthritis (RA) is known to be a chronic, inflammatory, autoimmune disorder characterized by inflammation of the joints and surrounding tissue causing pain, swelling and stiffness.\(^1,2\) As the disease progresses, if left untreated, it may eventually result in damage to the joints and permanent disability.\(^2\) The synovium of the joint is the site of onset of joint deterioration and is characterized by a large number of proliferating T-lymphocytes, marked immunoglobulin production, and increased inflammatory cytokine production. The inflammatory cytokines, tumor necrosis factor-\(\alpha\) (TNF-\(\alpha\)) and interleukin-1\(\beta\) (IL-1), are believed to play central roles in the pathogenesis of RA.\(^2\)

1.1.1 Prevalence

In South Africa, the latest prevalence rates of persons with RA were found to be 408,533 in 2003,\(^3\) it affects \(~0.5\) - \(1\%\) of the population worldwide and is three times more common in women than in men.\(^1,2,4,5,6\) The peak incidence of onset occurs between the fourth and sixth decades of life.\(^7\)

1.1.2 Diagnosis and Symptoms

The diagnosis of RA is primarily clinical, but also relies on laboratory tests such as serum rheumatoid factor (RF) or anti-cyclic citrullinated peptide antibody (anti-CCP) and typical radiographical changes as seen on an x-ray.\(^8\) Anti-CCP antibodies tend to be more specific but equally as sensitive as RF and are of value in the diagnosis of early RA and in predicting joint damage and is currently used in combination with RF for an improved accurate diagnosis. The 1987 American College of Rheumatology (ACR) criteria for classification of RA (Table 1.1) is usually used as entry criteria for clinical trials, but can also guide a clinician with an assessment. The patient must have at least four of the seven criteria and criteria 1 to 4 must be present for at least 6 weeks.\(^1,8\)

Table 1.1 Summary of 1987 ACR classification criteria for RA\(^5,8\)

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<td>3. Arthritis of hand joints</td>
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ACR= American College of Rheumatology; RF= rheumatoid factor; RA= Rheumatoid Arthritis
Symptoms of RA include symmetrical pain, tenderness and swelling of the affected joints with morning stiffness, afternoon fatigue and malaise, anorexia, weakness, and occasionally low-grade fever. The joints involved include the following: wrists and the index and middle metacarpophalangeal joints (most commonly involved), proximal interphalangeal joints, metatarsophalangeal joints, shoulders, elbows, hips, knees and ankles. (Figure 1.1)

Figure 1.1. Illustration of the joints commonly affected in Rheumatoid Arthritis.

1.3 Aetiology and Risk Factors
RA is a multi-factorial disease of unknown aetiology resulting from the interaction of genetic and environmental factors. Due to the difference seen in prevalence between men and women, an influence of reproductive and hormonal factors is suggested but it is unclear how gender influences the occurrence of RA. Infectious agents may also be involved in the occurrence of RA, however, this role also remains unclear. Smoking may influence the risk of developing RA as well as the course of the disease and an increased risk for seropositive disease is related to smoking habits. Socioeconomic factors such as occupation, educational level, marital status, and social group appear to influence the course and the outcome of RA rather than the risk of developing RA and available data suggests an association of poor socioeconomic status with a worse prognosis. It has also been shown that obesity is associated with the development of RA. Diet may have a role to play in that several studies have suggested a potential protective effect of oily fish, olive oil, and vegetables. The protective role of fish consumption has been attributed to the effect of omega-3 fatty acids (FA). The Mediterranean diet has also been reported as a lifestyle...
factor which may reduce the risk of developing RA and protects against the severity of the course of disease.⁴,⁵,¹³,¹⁴

1.1.4 Co-morbidities

1.1.4.1 Cardiovascular disease and osteoporosis in rheumatoid arthritis

An increased risk of cardiovascular disease (CVD) exists among patients with RA, especially those with seropositive RA.¹⁵ The exact reasons for this increased risk of heart disease is unclear but is likely to relate to certain traditional and novel risk factors. The traditional risk factors include a consistent finding among RA patients of low levels of high-density lipoprotein (HDL) cholesterol and higher levels of small, dense low-density lipoprotein (LDL) cholesterol which is known to be more atherogenic than regular LDL cholesterol.¹⁵ A study conducted by Brady et al¹⁶ showed that compared to controls, RA subjects were more likely to smoke (p<0.001), be physically inactive (p=0.006), and have higher mean measurements of body mass index (p=0.040) and waist circumference (p=0.049). They found that the mean absolute risk of CVD was higher in the RA group, even after excluding smokers (p = 0.036).¹⁶

The novel risk factors include systemic inflammation and while traditional cardiovascular risk factors appear to play an important role, they do not fully explain the increased risk of CVD in RA. Inflammation is common to both CVD and RA and there are similarities between the inflammatory responses seen in atherosclerosis and RA. Furthermore, the association between RA and CVD might also be attributable to the atherogenic side effects of corticosteroids and selective cyclooxygenase-2 inhibitors, which are commonly used in RA.¹⁵,¹⁶ Significantly lower levels of serum antioxidants carotenoids (β-cryptoxanthin, α-carotene, lycopene and lutein/zeaxanthin) and significantly higher C-reactive protein (CRP) levels have also been shown in RA cases compared to controls, and this too has been proposed as a novel risk factor for CVD in RA, although it is uncertain whether low serum carotenoid levels explain the increased incidence of CVD in RA.¹⁷,¹⁸

In another study, compared to healthy controls, older women with RA had poor vitamin B₆ status and elevated plasma homocysteine concentrations and this could also contribute to an increased risk of cardiovascular disease.¹⁹

Osteoporosis is a complication of RA that results in increased risk of fractures and is associated with resultant morbidity, mortality, and increased healthcare costs.¹⁸,²⁰ Bone metabolism in RA is altered by the chronic inflammatory process via the activation/inhibition of bone cell function, modification of body composition, corticosteroid use, diet and low levels of physical activity. Furthermore, elevated levels of inflammatory cytokines during the active phase of the disease lead to reductions in fat-free mass with a loss of body cell mass and consequent reduction in muscle strength.²¹ This loss may negatively affect bone mineral density due to the fact that lean mass is a predictor of bone mass through its mechanical pull on the skeleton.²² Corticosteroid treatment in RA also induces osteoporosis by decreased calcium absorption, increased renal calcium excretion
and inhibition of oestrogen production in women, with direct and indirect effects on osteoblast and osteoclast function.\textsuperscript{22,23} Corticosteroids result in low bone mass by directly affecting osteoblastic activity and hence, reducing bone formation that predominantly affects the trabecular bone. It is well known that long-term use of glucocorticoids increases the risk of all osteoporotic fractures and it is therefore recommended that the use of more than 5 mg prednisolone for three months or longer requires careful vigilance with regular investigation and subsequent treatment in order to prevent osteoporosis.\textsuperscript{24}

### 1.1.5 Prognosis

The disease progresses rapidly during the first 6 years, particularly during the first year and 80% of patients develop some permanent joint abnormalities within 10 years. The course of the disease is unpredictable in individual patients.\textsuperscript{1} RA patients have a higher mortality rate than the general population and according to the disease severity and the age of disease onset, their survival is expected to decrease by three to ten years.\textsuperscript{1,4} The leading cause of mortality is cardiovascular disease, and other causes include infection, gastro-intestinal bleeding, respiratory disease, and several malignancies.\textsuperscript{4,25} Reasons for the increased mortality are likely to be multifactorial and may include the effects of chronic inflammation, disability, and co-morbidity as well as the effects of concurrent immunosuppressive therapy. The results of previous studies have however suggested that mortality may be improved by the control of inflammation with methotrexate, a disease modifying anti-rheumatic drug (DMARD).\textsuperscript{25} Approximately 10% of RA patients are eventually severely disabled despite full treatment. Caucasians and the female sex seem to have a poorer prognosis, as well as those with subcutaneous nodules, advanced age at the onset of disease, inflammation in more than 20 joints, early erosions, cigarette smoking, high erythrocyte sedimentation rate, and high levels of RF or anti-CCP.\textsuperscript{1}

### 1.1.6 Effect of Rheumatoid Arthritis on Quality of Life

Quality of life can be defined as “the extent to which an individual is able to meet his/her needs”.\textsuperscript{26} The goals of treatment of RA are to reduce symptoms and improve functional status by limiting disease activity and improving quality of life. Consequences of the disease include loss of employment, reduced social functioning and significant healthcare costs.\textsuperscript{27} Although arthritis is not considered as a major health problem; it is the highest cause of physical disability in the United Kingdom (UK), affecting 8.2% of the UK population. Challenges that RA patients are faced with include the unpredictability of the disease coarse, uncertain prognosis and the physical, psychological and social functioning impact of the disease.\textsuperscript{27,28} A study conducted in China showed that depression and anxiety were common in patients with RA and patients who lacked social support or relied on economic assistance were more prone to the development of psychiatric disorders.\textsuperscript{29} Another study conducted in the United States (US) also showed a strong association
of depression with functional severity in RA patients. The pain and disability caused by RA certainly has a significant negative effect on the quality of life of people living with RA.

1.1.7 Economic Burden of Rheumatoid Arthritis
The economic burden of RA is thought to be substantial for people with RA as well as the relevant health services. A systematic review reported that the mean annual direct costs associated with RA were US$5720 and the mean annual indirect costs were US$5822. The mean costs for outpatient visits were US$1855 and US$4944 for in-patient stays. The percentage of RA patients that were hospitalized ranged from 12% to 26% and for all studies, except two, in-patient costs were found to be the largest constituent of the total annual medical costs associated with RA. Indirect costs relating to the number of days absent from work per annum due to RA ranged from 2.7 days/year to 30 days/year per patient.

A study conducted in the US showed that the use of biologic therapy (a relatively expensive new-line cytokine inhibitor or receptor site antagonist treatment) for RA was sensitive to the benefit generosity of the patient’s health insurance plan as well as their household financial burden. They found that RA patients on plans with less generous coverage of biologic therapies were less likely to commence a biologic therapy and were more likely to discontinue its use. They also found that individuals in households with high financial burden of health care expenses are also less likely to initiate a biologic therapy.

1.2 MANAGEMENT

1.2.1 Medical Management
A rheumatologist is the primary physician in treatment but other health care practitioners, such as nurses, physical therapists, dietitians, occupational therapists, social workers, psychologists and orthopaedic surgeons also play an important role in the management of RA and provision of supportive care.

1.2.1.1 Non-pharmacological treatment
Non-pharmacological treatment involves educating the patient and their family about the disease and about becoming involved in the decision making process with regard to the course of treatment. Rest and exercise may help to maintain joint mobility and reduced stress and a healthy diet may also be beneficial in treating RA.
1.2.1.2 Pharmacological treatment
Pharmacologic treatment of RA involves the use of various medications such as analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), disease modifying anti-rheumatic drugs (DMARDs), corticosteroids and biologic DMARDs.1

1.2.1.3 Management strategies
Studies have shown that early aggressive management of RA provides better outcomes in terms of quality of life and disability.8,34 The goal of an aggressive treatment strategy in RA is to modify the natural course of the disease which will lead to alleviating pain, reducing inflammation and the risk of structural damage, improving functional status and quality of life and preventing joint deformity and disability.8,34 In achieving the treatment goals it is important to determine the most effective combination of pharmacologic therapy, which may include NSAID, DMARD(s), low-dose prednisone, local injection of glucocorticoid, rehabilitation support, and analgesics.33 Current treatment guidelines highlight the use of DMARDs early in the disease within 3 months of diagnosis.34 The arrival of newer treatments and strategies such as biologic agents, the use of combination DMARD therapy and the resurgence of low-dose corticosteroid therapy have been shown to improve outcomes in clinical trials.34 The use of DMARD combination therapy or DMARD(s) plus a biologic agent with or without low-dose corticosteroids is now used relatively commonly in current clinical practice.34

1.2.1.4 Non-steroidal anti-inflammatory drugs
NSAIDs such as aspirin and ibuprofen relieves pain, improves joint function and reduces inflammation.3,33 It however does not reduce joint destruction and has serious gastrointestinal (GI) side effects such as nausea, vomiting, diarrhea, GI bleeding and peptic ulcers.33 Peptic ulcers may cause malabsorption of certain nutrients.35 NSAIDs may also cause renal damage and controversies exist regarding the possible increase in cardiovascular morbidities, more significant with cyclo-oxygenase-2 (COX-2) selective blockers.8 Choosing a NSAID which is appropriate for the individual involves considering effectiveness of the drug, safety, convenience and costs.33 The mechanism of action of NSAIDs involves the inhibition of cyclo-oxygenase (COX) of which there are two types, namely COX-1 and COX-2, and thus decrease production of prostaglandins. Some prostaglandins under COX-1 control have important effects such as the protection of gastric mucosa. Selective COX-2 inhibitors seem to have efficacy comparable to non-selective NSAIDs and are less likely to cause GI damage; however, they do not seem less likely to cause renal toxicity. Although COX-2 inhibitors have a significantly lower risk of gastrointestinal damage than other NSAIDS, they are not more effective and are much more expensive than non-selective NSAIDS.1,33
1.2.1.5 Disease modifying anti-rheumatic drugs

DMARDs are used as the main treatment of RA and Methotrexate (MTX) is widely considered the cornerstone of RA treatment and may be used as monotherapy or in combination with other agents. MTX is a folate antagonist with immunosuppressive effects at high dose and has anti-inflammatory effects at the doses used in RA. MTX is frequently the first DMARD prescribed subsequent to the diagnosis of RA, and a significant proportion of patients respond favourably to MTX monotherapy. It is one of the most effective DMARDs in reducing signs and symptoms, disability and structural damage along with less toxicity and improved tolerability. MTX alone however may not fully control disease activity in some patients and is increasingly being used in combination with other DMARDs. A recent systematic review showed that there is no statistically significant advantage of MTX combination therapy versus monotherapy. However, significant pain reduction and improvement in physical function were found in the MTX combination group in patients with inadequate MTX response. Another recent systematic review suggests the early use of conventional DMARDs with escalation to biologic agents only for patients who have responded inadequately to conventional DMARDs. Although the development of biologic agents has revolutionized the treatment of RA, they have not necessarily replaced the role of conventional DMARDs. MTX remains the cornerstone of nearly all anti-rheumatic regimens, whether they include synthetic or biologic DMARDs or not. Combination therapy with conventional DMARDs may well be as effective as therapy with biologics and is associated with a significantly lower cost. Other conventional DMARDs used in the treatment of RA include Hydroxychloroquine, Leflunomide and Sulfasalazine and immunosuppressive immunomodulatory or cytotoxic DMARDS include Azathioprine Cyclophosphamide Cyclosporine.

1.2.1.6 Glucocorticoids

Glucocorticoids at low doses (<10 mg/day prednisone) and local injections of glucocorticoids are very effective for relieving symptoms in patients with active RA. They appear to have disease modifying effects by slowing down the rate of joint damage. Evidence exists that low-dose glucocorticoids can significantly reduce the rate of erosions in early RA and their addition to standard therapy can be beneficial in the short term. Long-term continuous use beyond 4 years is however not indicated because of their serious side effects such as osteoporosis, hypertension, weight gain, fluid retention, hyperglycaemia, cataracts and skin fragility. These side effects should be taken into consideration when deciding to administer glucocorticoids.

1.2.1.7 Biologic disease modifying anti-rheumatic drugs

Biologic DMARDs are a new type of therapy which has developed during the past decade due to an increasing knowledge of the pathogenesis of RA and have revolutionized the management of RA. Their considerable economic impact and long-term safety concerns have however excluded their routine use at the onset of disease before traditional DMARDs are attempted.
most commonly used biologic agents are TNF-α inhibitors such as Etanercept, Adalimumab, Infliximab, Golimumab and Certolizumab. Tocilizumab is an IL-6 receptor antagonist and Rituximab is an anti-B-cell biologic agent. Anakinra (an IL-1 receptor antagonist) and Abatacept (a selective co-stimulation modulator that blocks the interaction between T lymphocytes and antigen-presenting cells) are not recommended by the National Institute for Health and Clinical Excellence (NICE) for the treatment of RA. When compared with TNF-α inhibitors, Anakinra has shown less benefit in clinical outcomes and frequent injection site reactions. It is seldom used now, because of the availability of better therapies. Several studies have shown that TNF-α inhibitors are highly effective in decreasing the risk of joint damage with a rapid onset of action, especially when combined with MTX in patients who have not responded well to traditional DMARDs. They also improve physical function and quality of life. There is however a lack of head-to-head comparison studies among the different types of biologics but indirect comparison in systematic reviews does not show substantial differences in efficacy among them, although there are some differences in their toxicity profiles. Choosing between different biologic agents is usually based on their safety profile, routes of administration, costs, health insurance coverage and patient preferences. Biologics are much more costly than traditional DMARDs due to the higher cost of production and the development of the complex proteins and antibodies.

1.2.1.8 Drug-nutrient interactions

Drug-nutrient interactions are commonly overlooked when physicians prescribe drugs and as more pharmaceutical agents become available, attention should be focused on the interactions of drugs with certain food and nutrients. Drugs can have an effect on nutritional status by altering nutrient absorption, metabolism, utilization or excretion and, on the other hand, food, beverages and vitamin or mineral supplements can have an effect on the absorption and effectiveness of drugs. Patients at risk of developing drug induced deficiencies are those whose diets are inadequate, those who have increased nutritional needs such as pregnant or lactating women and children, the elderly, persons with chronic illnesses, those who are on long term medication and those who abuse substances such as alcohol and recreational drugs. It is important that a well balanced diet is eaten to ensure that these drug-induced deficiencies do not occur.

1.2.1.8.1 Aspirin and Ibuprofen

Studies have shown that aspirin may block vitamin C from being transported to cells but the importance of this interaction is not known. With large doses of aspirin, folic acid levels decrease and iron levels may also drop due to small amounts of blood which are lost due to GI bleeding when aspirin is taken. These small losses over time may lead to an iron deficiency. It is recommended that the intake of foods rich in vitamin C, folic acid and iron should be increased or supplementation of these nutrients can be prescribed. Common nutritional side effects of
these drugs include nausea, vomiting, GI bleeding and constipation. It is advised to avoid GI irritants such as pepper, caffeine and alcohol with long term use.

1.2.1.8.2 Methotrexate
This drug affects the lining of the GI wall and may cause malabsorption of vitamin B₁₂ and β-carotene and is said to be a folate antagonist. MTX binds to dihydrofolate reductase and prevents the conversion of folic acid and dihydrofolate to its active form, tetrahydrofolate, which is required for purine synthesis. MTX also causes nausea and vomiting, diarrhoea, anorexia and GI distress. It is recommended that an intake of foods rich in these nutrients should be included in the diet. A supplement should be considered if signs of deficiency of these nutrients should appear.

1.2.1.8.3 Azathioprine
Azathioprine may cause symptoms of nausea, vomiting and anaemia. Depletion in folic acid and vitamin B₁₂ levels may occur. Supplementation may therefore be required. An increased fluid intake may also be needed.

1.2.1.8.4 Cyclosporine
This drug may cause nausea, vomiting, GI distress, diarrhoea and hyperkaleamia. It is suggested that a low fat, low potassium diet be followed.

1.2.1.8.5 Penicillamine
Penicillamine may not be optimally absorbed if taken simultaneously with iron or magnesium. It is therefore recommended to only eat foods rich in magnesium and iron, as well as supplements which contain magnesium and iron, several hours after this medication has been taken. This medicine may also cause a depletion of zinc and copper levels. A high dietary intake or supplementation of these minerals can be considered. This drug can also cause altered taste, nausea, vomiting, diarrhoea and loss of appetite.

1.2.1.8.6 Corticosteroids
Corticosteroids can deplete the body’s vitamin D stores, impair calcium absorption from the GI and impair calcium metabolism and long-term use may eventually result in bone loss and osteoporosis.

1.2.1.9 Biologic disease modifying anti-rheumatic drugs and effect on body composition
It is not yet known what the effect of the new biologic agents is on body composition. A study by Serelis et al showed no significant changes on body composition and lumbar spine bone mineral density in women with RA after 1 year of anti-TNF treatment. Metsios et al also did not show any significant changes in fat free mass after 12 weeks of anti-TNF-therapy. A study conducted
by Engvall et al\textsuperscript{49} however showed that patients who received anti-TNF treatment had a significant increase in fat mass at 2 years of 3.8 kg (1.6 to 5.9), in contrast to patients treated with sulphasalazine and hydroxychloroquine [0.4 (-1.5 to 2.2) kg ($P = 0.040$)], despite similar disease activity reduction. Both treatment strategies prevented loss of muscle mass and bone. Infliximab therapy increased body fat mass, which was an effect that was not achieved with the combination of traditional DMARDs, despite a similar reduction in disease activity, and thus seems to be drug specific.\textsuperscript{49} There is a need for longer-term studies in this field in order to determine whether or not biologics indeed cause an increase in body fat and if so, close attention needs to be paid to this as being overweight not only increases the risk of cardiovascular disease further but also puts extra strain on the joints.

\subsection*{1.2.1.10 Surgery}
Surgical treatment of RA can be considered when levels of pain are unbearable or loss of joint function has occurred. Carpal tunnel release, synovectomy, metatarsal head resection, total joint arthroplasty and joint fusion are surgical procedures which can be done.\textsuperscript{33}

\subsection*{1.2.1.11 Current management practices in South Africa}
In Cape Town, the public sector tertiary facilities use analgesics such as Paracetamol, alone or in combination with codeine and in severe cases with Tramadol. NSAIDS such as Diclofenac and Ibuprofen are widely used. Disease modifying agents such as Methotrexate (with folate supplementation), Azathioprine, Chloroquine, Cyclphosphamide and Cyclosporin are also used. Steroids are used short term and in combination with calcium and vitamin D supplements. Biological agents are not used often as the budgets do not permit it. In the primary health care clinics, Paracetemol and Ibuprofen are mainly used also due to budget constraints. In the private sector, the use of biologics is employed if all other treatment options have failed in providing relief from symptoms. [Personal communication: Dr H Reuter (2010) and Dr D Whitelaw (2010)]

\subsection*{1.2.2 Exercise and Physical Therapy}
Regular aerobic and resistance activity does not necessarily decrease inflammation in RA, but has been shown to improve range of joint movement and strength and endurance. It also helps to preserve bone mass and lean body mass and prevents fatigue and depression. It is also said to improve the distribution of forces of muscle contraction more evenly over the joint surfaces.\textsuperscript{9} Regular exercises, physical therapy and occupational therapy can help in symptomatic and functional improvement.\textsuperscript{8} Exercise is a non-pharmacological intervention effective in managing fatigue for some people with RA and a systematic review found that low-impact aerobics, walking, cycling, and jogging were effective interventions.\textsuperscript{50} Exercise has become an essential part of the rehabilitation of patients with RA during recent years, and the benefits of both aerobics and hand-strengthening exercises have been reported. Studies have shown that daily hand exercise is
effect in increasing hand grip strength. A recent study showed a significant improvement in hand force and hand function in patients with RA after 6 weeks of hand training and the improvement was even more marked after 12 weeks. Hand exercise is thus an effective intervention for rheumatoid arthritis patients, leading to better strength and function.51

Dynamic exercise programmes (DEPs) studies have provided evidence for quality of life improvement and have shown an improvement in Health Assessment Questionnaire (HAQ) measurement in the DEP group.52 Joint rehabilitation constitutes the cornerstone of physical therapy and DEPs are now being used for the rehabilitation of RA patients. There is no standardized design of DEP for patients suffering from RA, but most of the programmes follow the American College of Sports Medicine for healthy individuals’ recommendations. These recommendations state that exercise must lead to a 60% increase of predicted maximal heart rate for 20 minutes, at least twice a week to show improvement of muscular strength and aerobic capacity.52 Previous studies also support the evidence for improvement of aerobic fitness and muscle strength after exercise interventions in RA. It has been shown that this type of intervention has positive consequences on aerobic fitness with excellent compliance.52 Randomised controlled trials (RCT) have shown that joint specific dynamic exercises may improve strength and physical function in RA, but without a clear effect on pain or disease activity. The optimal exercise programmes however still need to be determined.53

Progressive Resistance Training (PRT) significantly increases muscle mass and muscle growth and restores physical function in patients with RA.54,55 A study recently confirmed that PRT is a safe and effective means of restoring muscle mass and functional capacity in patients with stable RA and concluded that PRT programs should be included in disease management.54,55 Pending confirmation of these results in a larger randomized controlled trial that includes a wider range of RA patients with more active and severe disease, PRT programs should be included in the management of RA as well as an adjunct treatment for rheumatoid cachexia.56

Yoga is another type of exercise which has been studied and a small study found that it may decrease the HAQ disability index, decrease the perception of pain and depression and improve balance.56 Yoga involves rotating joints through their full range of motion which increases flexibility. Standing poses promote balance by strengthening and stabilizing muscles to reduce falls. Yoga therefore incorporates several elements of exercise that may be beneficial for RA.57

1.2.3 Occupational Therapy
The main goals of occupational therapy in RA are to decrease pain, prevent deformity, improve function and promote participation.58 One recent RCT and a Cochrane review reported a positive effect of occupational therapy on functional ability and self management, but without an effect on
disease activity. Work disability is a serious adverse outcome of RA. Occupational therapists have a key role to play in assisting people to remain working by enhancing functional ability. Timely comprehensive occupational therapy can significantly improve functional and work-related outcomes in employed patients with RA who are at risk of work loss. A significant improvement in physical function, work productivity and coping indicates that even if the disease severity remains unchanged, a positive effect on work participation is accomplished by influencing environmental factors.

1.2.4 Complementary and Alternative Medicines (CAM)

The use of complementary and alternative supplements and practices has become a growing and ever more popular field, especially within population groups suffering from a chronic disease. Research has shown that 60%–90% of persons with arthritis use CAM and the main reason given for its use was to overcome pain. A survey in America found that about two thirds of RA patients used some form of complementary or alternative therapy such as chiropractic, acupuncture, supplements and special diets. Supplements and herbal treatments for the treatment of RA are vast and include to name a few Glucosamine, Chondroitan, Gamma Linolenic Acid, Thunder God Vine and Plant-Mineral Preparations. Therapies include Acupuncture, Hydrotherapy and Homeopathy.

There is a large variety of complementary and alternative treatments available on the market and the majority of these products do not distinguish between osteoarthritis and rheumatoid arthritis in their marketing and on the labels. Patients often use these treatments as it is generally believed that they are “safer” and more “natural” than conventional medications. These treatments can however in some cases even be dangerous. For example, while Tripterygium wilfordii (Chinese herb known as Thunder God Vine) may have beneficial effects on the symptoms of RA, it is associated with serious adverse effects such as impaired renal function, haematotoxic and immunosuppressive effect, hair loss, diarrhoea and nausea. The Royal Australian College of General Practitioners (RACGP) guidelines for management of early rheumatoid arthritis state that this Chinese herb must not be recommended to RA patients. Extensive research with regard to safety, effectiveness and dose required must still be conducted before many of the above mentioned products should be allowed to target and be advertised to a population with a chronic disease such as RA.

1.2.4.1 Alternative supplements

1.2.4.1.1 Glucosamine and chondroitan

Glucosamine sulphate (recommended at a dosage of 1,500mg/day), extracted from chitin from crab, lobster or shrimp shells, is a precursor to the glycosaminoglycan molecule used by the body to form and repair cartilage. Chondroitin sulphate (recommended at a dosage of 1,200mg/day), an
extract from cattle tracheas and shark cartilage, is the most abundant glycosaminoglycan in cartilage and is responsible for its elasticity. These substances may be taken in a supplement together or apart. Glucosamine has undergone many clinical trials in the field of osteoarthritis and was previously shown to be effective with regard to alleviating pain and narrowing joint space after a period of six to eight weeks. However a meta analysis conducted in 2010 showed that, compared with placebo, glucosamine, chondroitin, and the combination of the two does not reduce joint pain or have an impact on the narrowing of joint space in osteoarthritis. A small recent study on glucosamine-chondroitin-quercetin glucoside supplement on the synovial fluid properties of patients with osteoarthritis and rheumatoid arthritis showed no benefit in the RA patients. More research must be done with regard to the effects of these supplements on rheumatoid arthritis and at this stage cannot be recommended to patients with RA.

1.2.4.1.2 Gamma linolenic acid

Gamma Linolenic Acid (GLA) is advertised to have anti-inflammatory effects. It is found in evening primrose oil (2% GLA), blackcurrant seed oil (6% GLA) and borage seed oil (9% GLA), and has been found to improve joint tenderness, morning stiffness, swelling and pain in a number of studies. The RACGP guidelines for management of early rheumatoid arthritis provides a grade C recommendation for its use at a dosage of 1400 mg/day of GLA or 3000 mg/day of evening primrose oil. (Table 1.2)

Table 1.2. Royal Australian College of General Practitioners (RACGP) recommendation grading

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<th>Excellent evidence – body of evidence can be trusted to guide practice</th>
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<tr>
<td>A</td>
<td>Good evidence – body of evidence can be trusted to guide practice in most situations</td>
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<tr>
<td>B</td>
<td>Some evidence – body of evidence provides some support for recommendation(s) but care should be taken in its application</td>
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<tr>
<td>C</td>
<td>Weak evidence – body of evidence is weak and recommendation must be applied with caution</td>
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1.2.4.1.3 Plant-mineral preparations

Ayurvedic plant-mineral preparations, RA-1 and RA-11, often containing ingredients such as ginger, curcumin (an extract of turmeric), boswellia (Indian frankincense) and feverfew (a botanical folk medicine), are used to apparently “provide significant pain relief and improvement of objective signs of pain and inflammation.” A small clinical trial was conducted on feverfew and reported no beneficial difference in results between the placebo and feverfew. Ginger was found to increase the side effects of NSAID’s and creates blood-thinning effects. All components were reported to cause side effects such as nausea, diarrhoea and stomach upset.
1.2.4.2 Alternative therapies

1.2.4.2.1 Acupuncture
Acupuncture, originally a Chinese practice, is “the stimulation of anatomical points on the body by a variety of methods, including the insertion and manipulation of thin needles or the use of pressure from the practitioner's hands.” Very few appropriate studies have been done on the effectiveness for the relief of symptoms of RA. This treatment is generally safe, however it is advised that patients should only be treated by licensed practitioners.

1.2.4.2.2 Hydrotherapy
Hydrotherapy is the use of water for therapeutic purposes. A few examples of hydrotherapy include bathing in heated water, for example hot springs or the sea; mineral baths; and water-jet massages. A recent systematic review has shown that there is improvement of symptoms with this therapy however the safety of hydrotherapy has not been well studied. Hygiene and irritants to substances in the water should be monitored. Overall, it appears to be a low-risk practice for most people. However, hydrotherapy is riskier and could even be dangerous for people whose condition could be worsened by exposure to extremes of heat or cold or by strong motions from water jets. Hydrotherapy in RA has been evaluated in two recent meta-analyses [reported in the European League Against Rheumatism (EULAR) report] with positive findings but there is insufficient evidence to support a strong recommendation. More research on this therapy is needed.

1.2.4.2.3 Homeopathy
Homeopathy, developed in Germany, is the practice based on the theory of “giving very small doses of substances called remedies that would produce the same or similar symptoms of illness in healthy people when given in larger doses.” Little rigorous research has been done on homeopathy for RA and has shown positive and negative results with regard to effectivity. Most remedies are considered safe.

1.2.5 Dietary Management
1.2.5.1 Dietary manipulation
Studies suggest that aspects of the diet may alleviate symptoms, combat the side-effects of therapy and decrease the risk of complications. The possible benefits may be due to altered gut flora, a reduced permeability to bacteria and other antigens, altered antioxidant levels, weight loss and the elimination of offending foods. The improved symptoms seen in clinical studies may also be due to the change from an unhealthy diet to a healthier diet involving an increased fruit and vegetable consumption and a reduction in saturated fats. The effects of dietary manipulation require further randomized, long-term studies to confirm the benefits of specific diets in order to make specific recommendations. It has been reported that 33% to 75%
of RA patients believe that food plays an important role in the severity of their symptoms and 20% to 50% have tried to manipulate their diet in order to relieve their symptoms.\textsuperscript{14}

The scientific basis for a role of dietary therapy in RA has grown in the last few years although there is still no consensus on the optimum diet. The abnormal regulation of the cytokines TNF-\(\alpha\) and IL-1 have been identified as primary factors in the pathogenesis of RA and this has provided the rational for the use of dietary treatment in the form of the so-called “anti-inflammatory diet”.\textsuperscript{14} Current literature states that no specific food group has been proven to reduce or increase symptoms of RA because the evidence is inconclusive. A diet high in red meat, dairy, cereals, citrus, chocolate, alcohol and spices has been said to have adverse effects for some RA sufferers, but as of yet, there is no solid evidence proving this statement correct.\textsuperscript{14,45} Food members of the nightshade family including tomatoes, white potatoes, eggplant and peppers have also been believed to have adverse effects for RA sufferers. Also, some suggested foods that have supposedly positive effects on RA include Brewer’s yeast, apple cider vinegar, honey, wheat germ, molasses, ginger and garlic. There is however no solid evidence proving that any of these foods has a definite effect on RA symptoms.\textsuperscript{45,75} This subject is however controversial as patients’ reactions to specific foods are highly individualized especially if a food allergy or intolerance is present and this point must be emphasized.\textsuperscript{14}

\textbf{1.2.5.2 Food allergies or intolerances}

Food allergies or intolerances to various food items such as dairy products and cereals have been reported in several RA case studies and in all reports the removal of the specific food type resulted in a favourable response and on reintroduction of the food into the diet, developed symptoms again.\textsuperscript{14} It has been recommended that if a patient feels he/she has a reaction to a specific food, or that food seems to worsen or alleviate symptoms of RA, then the patient should avoid or increase (in moderation) consumption, respectively, of that particular food group.\textsuperscript{45,75}

A study by Karatay et al\textsuperscript{79} linked food allergy testing and cytokines and found that 13 out of 20 RA patients with a positive skin prick test experienced disease exacerbations in clinical symptoms and experienced increased levels of TNF-\(\alpha\), IL-1, and C-reactive protein with food allergen challenges. The authors therefore put forward that food allergy triggers, rather than acts, as a causative agent.\textsuperscript{79} The link between food allergy or food intolerance and joint complaints is particularly referred to when patients with a known food allergy and intolerance are concerned. Food is the greatest source of exposure to foreign antigens. The literature suggests that food allergy or intolerance appears to play a role in only a small proportion of rheumatic patients.\textsuperscript{42} This implies that it is unnecessary to put all people with chronic joint symptoms on a strict diet. When the medical history suggests possible food intolerance, further investigations need to be carried out.
and an elimination diet and an open or double-blind challenge test are the only way to identify both the affected patients and the offending foods.\textsuperscript{42}

\subsection*{1.2.5.3 Types of diets}

A systematic review by Smedslund et al\textsuperscript{80} describes the common diets used by people with RA which include vegetarian or vegan, Mediterranean, elemental and elimination diets.\textsuperscript{80} Vegetarian diets exclude all meat and vegan diets (which exclude all animal products) are higher in antioxidants and this may be a factor in reducing pain and stiffness. The Mediterranean diet is high in fruit, vegetables, cereals and legumes; low in red meat; and high in fish and olive oil. This diet's possible protective effect could be due to the high levels of unsaturated fats and antioxidants.\textsuperscript{80} An elimination diet involves the removal of one or more potentially offending foods one at a time and then gradually reintroducing them to determine whether any of them aggravates symptoms. The elimination diet is based on the principle that food antigens potentially play a role in the pathogenesis of a disease and that its elimination from the diet should result in the improvement of symptoms.\textsuperscript{80} The elemental diet is believed to be hypoallergenic and consists of amino acids, glucose, medium-chain triglycerides, vitamins, and minerals. It is industrially premade, packaged in sachets and is used as a meal replacement for one or more meals per day.\textsuperscript{80}

Results from trials with moderate risk of bias indicate that fasting followed by a vegetarian diet as well as fasting followed by a Mediterranean diet may improve symptoms of pain in RA patients when compared to an ordinary diet.\textsuperscript{80} No effects were seen however in physical function, stiffness, or other important outcomes. Although some studies have reported improvements in some symptoms of RA, the definite mechanisms of action are still not unequivocally known. When looking at the common denominators for most of the diets, there is an increase in fruits, vegetables and fibre, a reduction in saturated fat, and energy restriction. And as discussed earlier, this results in altered antioxidant levels, resultant weight loss, and the removal of allergies/intolerances and changing from an unhealthy to a healthier diet could explain some of the positive changes seen in the RA symptoms.\textsuperscript{77,80}

Dietary manipulation may improve symptoms in some RA patients, but these diets are often associated with a high dropout rate.\textsuperscript{77} A very important issue when looking at the dietary management of RA patients is that many of the patients may already be nutritionally compromised due to a number of reasons discussed in sections 1.2.1.8 and 1.5. Smedslund et al\textsuperscript{80} describe that it is therefore very important to weigh up the benefits and harm of very restrictive diets such as the vegan, elimination and elemental diets as these patients are especially vulnerable to the adverse effects of diet restrictions.\textsuperscript{80} Dietary manipulation is not appropriate for everyone, especially those who are at nutritional risk. The palatability and strict regimens of some of these eating plans leads to a reduced dietary intake and a very serious consequence of diet manipulation.
is that one or more food groups are eliminated from the diet which may lead to the risk of nutritional deficiencies of key nutrients. For example, without specialized diet and meal planning, a strict vegan diet could cause a deficiency in protein and several vitamins and minerals. Another important aspect to take into consideration is that a strict dietary program not only affects nutrition, but is also difficult to maintain in terms of social life where a special diet must be catered for. The most important aspect in dietary manipulation is that the safety is uncertain and must not be recommended or practiced without consulting a registered dietitian. On the other hand, a diet such as the Mediterranean diet is nutritionally adequate and well balanced and includes moderate amounts of lean meat, unsaturated fats replacing saturated fats, plenty of fruits, vegetables and fish. It is also recommended for people with heart disease and osteoporosis, and RA patients are at risk of developing both conditions.

1.2.5.4 Supplementation

1.2.5.4.1 Omega-3 fatty acid supplementation

It has been shown in many studies that supplementation with fish oil, rich in omega-3 fatty acids (FA), reduces inflammatory markers and decreases the need for NSAIDS and DMARDS. Anti-inflammatory doses range between 2.6g/day and 7.1g/day with an average of 3.5g/day of omega-3 FA supplements in the form of eicosapentanoic acid and docosahexanoic acid. The RACGP guidelines for management of early RA provides a grade A recommendation (Table 1.2) for omega-3 supplementation as an adjunct for management of pain and stiffness in patients with RA. A recent meta-analysis of 17 studies involving 823 patients showed significant effects for four out of six pain outcomes including patient assessed pain (Standardized Mean Differences (SMD): -0.26; 95% CI: -0.49 to -0.03; p=0.03), morning stiffness (SMD: -0.43; 95% CI: -0.72 to -0.15; p=0.003); number of painful and/or tender joints (SMD: -0.29; 95% CI: -0.48 to -0.10; p=0.003); and NSAID consumption (SMD: -0.40; 95% CI: -0.72 to -0.08; p=0.01). Significant effects were however not detected for physician assessed pain and the Ritchie articular index which is used to calculate a disease activity score (DAS). Eleven of the 16 studies used high doses (above 2.7 g omega-3 FA per day) and significant improvements were noted in patient assessed pain and morning stiffness in the studies providing high dose, but not low dose, omega-3 FA. These results suggest a role for high dose omega-3 supplements as adjunctive treatment for the pain and stiffness associated with RA.

While omega-3 FA stimulates the production of anti-inflammatory compounds, omega-6 FA stimulates the production of pro-inflammatory compounds. Mono-unsaturated FA reduces the competition for absorption between omega-3 FA and omega-6 FA and therefore increases the uptake of omega-3 FA into the cell membranes. Omega-9 FA (oleic acid), in olive oil, also competes with omega-6 FA for absorption. The decrease in absorption of omega-6 FA will
therefore decrease the undesired pro-inflammatory effects in RA.\textsuperscript{46} Data on the optimal omega-6 FA to omega-3 FA ratio in RA is scarce.

1.2.5.4.2 Micronutrient supplementation

Based on the low antioxidant status of persons with RA shown in studies, claims have been made that micronutrient supplementation may be beneficial in the dietary treatment of RA.\textsuperscript{45,84} Selenium, Zinc, Magnesium, Niacin and beta-carotene have been identified to potentially have beneficial effects.\textsuperscript{85} However, results of clinical trials have been disappointing with no significant anti-inflammatory effects being shown with antioxidant supplementation compared to a placebo in studies done with high doses of vitamin E and selenium.\textsuperscript{86,87} It has been suggested that a supplement with a combination of several antioxidants may be more effective than a single antioxidant supplement as they are known to work synergistically.\textsuperscript{85} The first double blind, placebo controlled study to investigate whether or not a combination of polyunsaturated fatty acids (PUFA) and micronutrients indeed does have a positive effect on tender joint count, was done but no significant differences were found.\textsuperscript{85}

Folate supplementation has been shown to decrease the toxicity and mucosal and GI side effects of MTX which is known to be a folate antagonist.\textsuperscript{46,88} It has also been shown to improve the continuation of MTX therapy by reducing the incidence of liver function test abnormalities and GI intolerance. Furthermore, supplementation with folic acid compensates for the elevation in plasma homocysteine associated with the use of MTX and this may in turn decrease the risk of cardiovascular disease which is known to be present in persons with RA and for which hyperhomocysteinaemia is now recognized as an independent risk factor for cardiovascular disease. Routine folic acid supplementation should be prescribed to all patients receiving MTX and a dose of 5 mg oral folic acid given on the morning following the day of MTX administration is recommended. Folate supplements do not appear to significantly reduce the effectiveness of MTX in the treatment of RA.\textsuperscript{89}

RA patients with documented osteoporosis or those at high risk for the development of osteoporosis should receive calcium and vitamin D supplementation as well as an anti-resorptive agent.\textsuperscript{90} In selected patients with RA who are at high risk of vitamin D deficiency, correction of deficiency may be important in both the management of osteoporosis and decreasing the risk of falls and fractures. Vitamin D supplementation in this patient group may also reduce RA disease activity although there is currently a lack of studies to prove this.\textsuperscript{91} Vitamin D supplementation in RA reduces bone loss, and the combination of vitamin D and calcium supplementation significantly reduces fracture rates.\textsuperscript{92} The recommendations for vitamin D supplementation to correct deficiency and manage osteoporosis includes bolus oral dosing of 100 000U vitamin D, together with daily oral vitamin D tablets (with or without calcium supplementation), with monitoring and repeat dosing
at regular intervals. The ACR recommends that patients receiving glucocorticoids should receive calcium and vitamin D supplementation for any dose or duration of glucocorticoids. Calcium intake with oral intake plus supplementation should reach 1200 to 1500mg/day. Vitamin D supplementation should aim to achieve therapeutic levels of 25-hydroxyvitamin D, or dosages of 800 to 1000 IU/day are two dosing regimens which could be utilized. It should also be taken into account though that glucocorticoids can interfere with vitamin D absorption and may require a higher supplementation dose to achieve therapeutic levels.

1.3 NUTRITIONAL REQUIREMENTS
1.3.1 Energy Requirements
The impact of the inflammatory process differs from person to person and activity levels may also vary greatly. This, therefore, makes it difficult to establish specific energy requirements for persons with RA. Energy intake should be sufficient to achieve or maintain an ideal body weight. The Harris Benedict equation, a formula used to calculate energy requirements, with a stress factor of 1.14-1.35 (to compensate for the effects of hypermetabolism) and an activity factor of between 1.2 and 1.3 (depending on the mobility of the patient and the intensity of physical therapy) can be used to determine energy requirements. Another guideline of 114-135% of the dietary reference intake (DRI) for healthy persons can be used during periods of active RA. If the patient is immobile, the Harris Benedict equation can be used without an activity factor and energy intake should be adjusted for weight changes that may occur over time. If the dietary intake is inadequate, a supplement should be taken to ensure that the energy requirements are met.

1.3.2 Protein Requirements
Well nourished individuals with RA do not have increased protein requirements and the DRI for age and sex will provide sufficient protein in these patients. Patients with a poor nutritional status or those who are in the inflammatory phase have protein requirements of between 1.5 and 2 g protein/kg/day. In a study conducted by Marcora et al, the effect of amino acid mixtures administered to RA patients (as part of the protein requirements) significantly increased fat-free mass, total body protein, arm and leg lean mass, and some measures of physical function.

1.3.3 Fat Requirements
A low intake of fats aggravates RA because the resulting low levels of vitamin A and vitamin E stimulates lipid peroxidation and eicosanoid production. An intake of 30% of total energy requirements is therefore recommended. It is also recommended that the types of fats consumed are changed (e.g. replacing omega 6 FA with omega 3 FA) rather than eliminating fat from the diet.
1.3.4 Micronutrient Requirements
It has been said that patients with RA may have increased requirements for folic acid, vitamin B<sub>6</sub>, vitamin E, vitamin D, zinc and antioxidants but no specific recommendations on exact quantities exist. Patients with RA may also have increased requirements of calcium and vitamin D.<sup>45,94,96</sup> Little is known about the micronutrient doses needed to induce immunomodulation in RA and in the absence of clear guidelines, it is therefore advisable to reach at least the micronutrient intake of the DRI guidelines.<sup>85,94</sup>

1.4 DIETARY RECOMMENDATIONS FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS
Patients with RA should follow an individualized, healthy, balanced diet. It is important to avoid being overweight as this puts extra stress on the joints.<sup>45</sup> Patients with RA should eat oily fish (e.g. mackerel, tuna, pilchards and salmon) three times a week or take omega 3 FA supplements.<sup>45</sup> Foods that tend to worsen the disease for that individual (e.g. dairy products, eggs, red meat, cereals, alcohol and chocolate) should be excluded.<sup>45</sup> Sunflower oil used in cooking or salad dressings should be replaced with olive oil for the benefits of oleic acid. Foods containing high vitamin E content such as cereals, avocados, nuts, fruit and vegetables are recommended. Supplementation of vitamin B<sub>6</sub>, vitamin B<sub>12</sub> and folate may be beneficial in patients with high homocysteine levels.<sup>46</sup> Low doses of folate supplementation may have a supportive effect in patients using MTX however; vitamin B<sub>12</sub> levels must be adequate to prevent deficiency of vitamin B<sub>12</sub> due to nutrient-nutrient interactions.<sup>46</sup> It is also recommended that adequate iron, calcium and vitamin D status is achieved from dietary intake or supplementation if necessary, especially in patients using prednisone.<sup>46</sup> Foods rich in β-carotene such as carrots and sweet potatoes and foods rich in vitamin C such as broccoli, oranges and guavas are also recommended. Foods rich in selenium such as whole grains, cereals and eggs should also be eaten.<sup>45</sup> Other recommendations which may be useful is to eat in a relaxed environment and to modify the kitchen layout of the patients home and use adapted cutlery to help with improving the ability of patients with RA to maintain adequate nutritional status.<sup>45,46</sup>

In general, the diet recommended for arthritis is similar to that of good health with special emphasis on cardiovascular risk prevention (Table 1.3). These recommendations are according to the RACGP and include:<sup>45,70</sup>
Table 1.3. Dietary recommendations for RA

<table>
<thead>
<tr>
<th>Dietary recommendations for RA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Eat plenty of fruit, vegetables and wholegrain cereal foods</td>
</tr>
<tr>
<td>2. Eat foods rich in fish oil (omega-3)</td>
</tr>
<tr>
<td>3. Eat a diet low in saturated fat</td>
</tr>
<tr>
<td>4. Maintain a healthy body weight</td>
</tr>
<tr>
<td>5. Limit alcohol intake</td>
</tr>
<tr>
<td>6. Eat only a moderate amount of sugar and foods containing sugars</td>
</tr>
<tr>
<td>7. Choose low salt foods and use salt sparingly</td>
</tr>
</tbody>
</table>

1.4.1 Dietary Recommendations for the Management of Cardiovascular Disease and Osteoporosis

Due to the increased risk for CVD and osteoporosis, preventative lifestyle and dietary measures should be encouraged. Modifiable CVD risk factors such as dyslipidaemia and weight control should be addressed with dietary and lifestyle measures and serum carotenoid levels have been shown to increase with inclusion of fruit and vegetables in the diet. RA patients who present with osteoporosis as discussed earlier should meet the dietary recommendations for calcium intake from dietary sources where possible and calcium and vitamin D supplementation in older patients, particularly if housebound and/or in those with a poor dietary intake can be considered.

1.4.2 Omega 3 Fatty Acids and Exercise in Cardiovascular Disease and Osteoporosis

The benefit of omega 3 FA and exercise is that it decreases the risk for CVD and osteoporosis and counteracts the complications associated with the natural course of RA and the effects associated with corticosteroids as discussed earlier.

Omega 3 fatty acids act to prevent heart disease in a number of ways including: prevent arrhythmias (ventricular tachycardia and fibrillation); are prostaglandin and leukotriene precursors; have anti-inflammatory properties; inhibit synthesis of cytokines and mitogens; stimulate endothelial-derived nitric oxide; are anti-thrombotic; have hypolipidaemic properties with effects on triacylglycerols and very low-density lipoprotein (VLDL); and inhibit atherosclerosis. Research has shown that omega 3 supplementation (0.045 to 5.9 g/day) lowers triglyceride levels while improving the HDL cholesterol and the ratio of total cholesterol to high-density-lipoprotein cholesterol with no changes in LDL cholesterol. Omega 3 PUFA supplementation has therefore shown the advanced beneficial effects of treatment of the disease and its potential complications.
The anti-inflammatory properties of omega 3 FA have also shown to have potential positive effects on osteoporosis and general bone health. The basis of this involves the inverse relationship of omega 3 PUFA and pro-inflammatory eicosanoids such as cytokines that stimulate bone resorption by activating osteoclasts, cells that demineralise and degrade bone during bone remodeling. Furthermore, Omega 3 FA supplementation (2.7 to 4.0 g/day) has been shown to decrease the need for high doses of corticosteroids in the treatment of RA. It would therefore be beneficial to note that supplementation with omega 3 FA may decrease required dosage of corticosteroids and therefore decrease risks of developing osteoporosis as a complication of RA.

Exercise has been shown to decrease the risk of cardiovascular disease by reducing the risk of atherosclerosis due to decreased triglyceride (TG) and circulating atherogenic lipoproteins in the blood while also increasing the levels of beneficial HDL cholesterol. A study by Ho et al of 30 minutes of different types of exercise showed that in overweight and obese men and women, aerobic exercise lowered postprandial serum triacylglycerol concentrations (the first blood sample was taken in the fasting condition and then at 1, 2, 3, 4, 5, 6 and 8 h after the meal) compared with the control, resistance exercise or combined trial groups and resistance exercise improved indicators of insulin sensitivity compared with aerobic exercise group. A reduction in postprandial serum triacylglycerol concentrations, postprandial insulin concentrations and insulin resistance was also shown in obese men with fasting hypertriglyceridaemia and insulin resistance after low to moderate intensity aerobic exercise performed for one hour.

1.5 IMPACT OF RHEUMATOID ARTHRITIS ON NUTRITIONAL STATUS

It has been shown that persons with RA tend to have a poor nutritional status, reduced energy intake from carbohydrates, a high intake of saturated FA and a poor micronutrient intake. The prevalence of malnutrition (rheumatoid cachexia and wasting) in RA varies widely due to different methods of determining malnutrition and various populations and has been reported to be between 26 and 71%. The chronic inflammation seen in RA increases metabolic rate and nutritional requirements and can therefore lead to impaired nutritional status. A few other factors which could also contribute to a poor nutritional status are an inadequate dietary intake and drug-nutrient interactions. Decreased dietary intake attributes to the poor nutritional status of many patients with RA. Nausea and reduced appetite, due to medication, as well as fatigue and pain with difficulty in chewing and swallowing caused by temporo-mandibular involvement, are contributory factors. Dry mouth, dental caries and infection of gums causes a change in taste sensation. Another important aspect is that patients with RA who are experiencing pain may have a limited ability to go shopping for food, or prepare healthy, well balanced meals. These patients often resort to eating low energy, nutritionally poor snacks which are quick and convenient. Another factor is that drug-nutrient interactions may result in increased nutrient requirements, decreased absorption of nutrients and gastro-intestinal discomfort.
1.5.1 Body Composition

Changes in body composition occur in patients with RA where progressive erosion of fat-free mass (FFM) occurs. Assessment of body composition can demonstrate this in obese as well as normal and undernourished RA patients. Loss of FFM is very important because in starvation, critical illness, and normal aging, a loss of greater than 40% of baseline FFM has been shown to be associated with death. As little as a 5% loss of FFM has caused changes in morbidity, including loss of muscle strength, altered energy metabolism, and increased susceptibility to infections. The average loss of FFM among patients with RA is between 13% and 15%, which is roughly one third of the maximum survivable loss of FFM.\(^\text{104}\)

Book et al\(^\text{105}\) found that lean mass of arms and legs (LMAL) was low in RA patients for both women and men (p=0.007 and <0.001, respectively). Body mass index (BMI) (p=0.012), body fat mass (BFM) (p=0.014) and truncal fat distribution (TFD) (p<0.001) was higher than expected in RA women. With adjustment for age and current smoking, disease duration was independently associated with low LMAL in women (p=0.021). High TFD was associated with a history of diabetes or CVD in men with RA (p=0.005). The authors concluded that low LMAL, high BFM and high TFD are present in early RA patients.\(^\text{105}\) Resmeni et al\(^\text{106}\) found that RA patients had a greater waist-hip ratio (WHR) (p<0.01), less lean body mass (LBM) (p<0.01), and lumbar bone mineral density (BMD) (p<0.01) than controls.\(^\text{106}\) Giles et al\(^\text{107}\) found that the HAQ score was strongly correlated with levels of physical and sedentary activity and body composition, with increasing fat and decreasing lean mass associated with higher HAQ scores. The mean HAQ score was 0.52 units higher for subjects in the highest versus the lowest quartile of appendicular fat mass (p<0.001), and 0.81 units higher for subjects in the lowest versus the highest quartile of appendicular lean mass (p<0.001). Body composition, particularly the amount of fat and lean mass located in the arms and legs, is therefore strongly associated with disability in RA patients.\(^\text{107}\)

1.5.2 Rheumatoid Cachexia and Cachetic Obesity

The term rheumatoid cachexia is used to describe the loss of body cell mass, mainly in skeletal muscle, that occurs in nearly two-thirds of all patients with RA.\(^\text{108}\) It differs from acquired immune deficiency syndrome (AIDS), cancer and cardiac cachexia in that it does not necessarily manifest in weight loss.\(^\text{102,108}\) Rheumatoid cachexia generally occurs without a loss of fat mass and body weight. In actual fact, body cell mass is often lost in the presence of increased fat mass and stable body weight. This predisposes to a condition that has been termed ‘rheumatoid cachetic obesity’.\(^\text{108}\) Rheumatoid cachexia leads to muscle weakness and a loss of functional capacity, and is said to accelerate morbidity and mortality in RA.\(^\text{108}\) The exact mechanism for rheumatoid cachexia is not known, but it is accompanied by increased resting energy expenditure, increased whole-body protein catabolism, and excess production of the inflammatory cytokines, TNF-\(\alpha\) and IL-1.\(^\text{24}\) TNF-\(\alpha\) is believed to be the central mediator of muscle wasting in RA, and is known to act

\footnote{Stellenbosch University http://scholar.sun.ac.za}
together with IL-1 and influence muscle protein turnover. The exact mechanism by which this happens has yet to be revealed, but may involve other cytokines, sarco-active (muscle active) transcription factors and hormones. In addition to excess inflammatory cytokine production, decreased peripheral insulin action and low physical activity are believed to play important roles in the general development of rheumatoid cachexia and contributes towards muscle wasting. Low physical activity also leads to fat gain and is believed to precipitate a negative reinforcing cycle of muscle loss, reduced physical function, and fat gain in RA. No consensus exists for the exact cut-off values for rheumatoid cachexia but has been defined as fat-free mass index (FFMI) below the 10th percentile and FMI above the 25th percentile or FFMI below the 25th percentile and FMI above the 50th percentile of a reference population of age and sex-matched Europeans. (2,982 men and 2,647 women from Switzerland).

There is currently no standard treatment for rheumatoid cachexia. However, physical exercise is believed to be the most important and clinically relevant countermeasure against this condition. In general, a combination of skeletal muscle strength training and aerobic exercise is recommended, but must be prescribed with the patient’s disease status, overall health, and safety in mind.

In a study by Elkan et al on RA patients, the simultaneous decrease in fat free mass and increase in fat mass was shown in 18% of the women and 21% of the men and it was shown that 57% of the women and 89% of the men presented with central obesity. In another study done by Elkan et al, the mean BMI for women and men was 25.0 and 27.0 kg/m², respectively. Central obesity was found in 57% of the women (waist circumference >80 cm) and in 89% of the men (waist circumference >94 cm). In this study, 18% of the women and 26% of the men had rheumatoid cachexia. This condition was also associated with high levels of LDL cholesterol, low levels of atheroprotective anti-PC and a high frequency of hypertension, which is of interest in the context of CVD in RA. The increase in FM seen in RA patients, especially central obesity may also add to the CVD morbidity. Data on waist circumference in RA patients in other studies are sparse.

In another study by Elkan et al, BMI for women and men were 24.4 and 26.9 kg/m² respectively and according to a BMI of < 18.5 kg/m², only 12% of the women and none of the men were malnourished. FFMI however indicated that 52% of the women and 30% of the men were in fact malnourished according to their body composition. Because rheumatoid cachexia is common in patients with RA, and BMI alone cannot detect it, it is important to evaluate body composition and ensure that the fat free mass as well as the fat mass is determined in order to detect rheumatoid cachexia.

In the South African context, a study done by Kalla et al in 1992 showed that young RA patients did not differ in nutritional status compared with healthy matched controls. Mody et al in 1989 found that 20.5% of RA patients had a reduction of one or more anthropometric measurements.
[triceps skinfold (TSF), upper arm muscle circumference (UAMC) and/or percentage ideal body weight (IBW)] and obesity was seen in 10.5% of the RA patients.\textsuperscript{111} Both these studies were done many years ago and changes in healthcare and medication in RA patients as well as dietary intake and patterns (i.e. the nutrition transition) and nutritional status in the general population may have occurred and data on nutritional status, specifically regarding waist circumference, fat free mass and fat mass, is warranted.

1.5.3 Body Composition Measurement Techniques

Anthropometry is the measurement of body size, weight, proportions and skinfolds and can be used to evaluate nutritional status and is considered as a method of choice for estimating body composition and is comparable to hydrostatic weighing. The advantages of this method are that the equipment is relatively inexpensive and requires little space. Dual X-Ray Absorptiometry (DEXA) scans are primarily used to evaluate bone mineral density and can also be used to measure total body composition and fat content with a high degree of accuracy comparable to hydrostatic weighing. Advantages of this method are that it is easy to perform with no discomfort for the participant. It is however considerably more expensive than anthropometric measurements.\textsuperscript{112} Another method which can be used to calculate body composition is bioelectrical impedance. The problem with this method however is that it assumes that the subject is normally hydrated. Dehydration can result in the overestimation of fat mass and subjects therefore need to be instructed prior to their appointment to prevent dehydration by drinking plenty of water, refraining from the consumption of any alcohol or caffeine the day before testing and avoiding heavy exercise for 12 hours before the test.\textsuperscript{112}

1.5.4 Nutritional Status of South Africans

The nutritional status of South Africans is outlined in Table 1.4. In South Africa, the 1998 South African Demographic Health Survey (SADHS)\textsuperscript{113} showed that the mean BMI for women was 27 kg/m\textsuperscript{2} which is classified as being overweight (BMI of 25-29.9 kg/m\textsuperscript{2}) and 23.4 kg/m\textsuperscript{2} for men which is classified as normal (BMI of 18.5-25 kg/m\textsuperscript{2}). These statistics proved to be very similar in 2003 SADHS\textsuperscript{114} with a BMI of 27 kg/m\textsuperscript{2} for women and 23.3 kg/m\textsuperscript{2} for men. In 1998, the obesity (BMI > 30 kg/m\textsuperscript{2}) statistics stood at 30.1% for women and 9.3% for men whereas in 2003 it showed 27.4% in women and 8.8% in men.\textsuperscript{113,114} The waist circumference measurement is an indicator of central obesity and according to the World Health Organization, a waist circumference of higher than 80cm in women and 94cm in men indicated an increased risk of metabolic complications and 88cm in women and 102cm in men indicates a substantially increased risk of metabolic complications.\textsuperscript{115} In 1998 the SADHS showed that women had a mean waist circumference of 85.8cm (indicating an increased risk) and 82.1cm for men (indicating no increased risk). In 2003, the figures had decreased slightly to 82.7cm in women (still indicating an increased risk) and decreased to 78.2cm in men.\textsuperscript{113,114}
Obesity is found to be common among South African women (refer to Table 1.5). The obesity prevalence is highest in the African population, specifically the urban African population. The highest prevalence of obesity of 59% has been observed among Black women aged 45-54 years in the BRISK study. The Black women aged 15-64 years in the BRISK study also had the highest mean obesity prevalence of 34.4%. The prevalences are much lower for men.

It is therefore apparent that South Africa has a very high obesity prevalence, especially among women. It is therefore plausible to assume that a high prevalence of obesity could be found in the South African RA population.

### Table 1.4. Anthropometrical status of South African individuals

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Women</th>
<th>Men</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BMI (kg/m²)</td>
<td>27</td>
<td>23.4</td>
<td>1998 SADHS¹¹³</td>
</tr>
<tr>
<td>Percentage of overweight (BMI of 25-29.9 kg/m²)</td>
<td>26.1%</td>
<td>19.8%</td>
<td>1998 SADHS¹¹³</td>
</tr>
<tr>
<td>Percentage of obesity (BMI &gt; 30 kg/m²)</td>
<td>30.1%</td>
<td>9.3%</td>
<td>1998 SADHS¹¹³</td>
</tr>
<tr>
<td>Waist circumference (Mean values in cm)</td>
<td>85.8cm</td>
<td>82.1cm</td>
<td>1998 SADHS¹¹³</td>
</tr>
</tbody>
</table>

BMI= Body mass index / SADHS= South African Demographic and Health Survey.

### Table 1.5. Obesity statistics of South African individuals

<table>
<thead>
<tr>
<th>Obesity statistic</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>African women aged 15 years and above</td>
<td>28.5%  2003 SADHS¹¹⁴</td>
</tr>
<tr>
<td>African urban women aged 15 years and above</td>
<td>33.8%  2003 SADHS¹¹⁴</td>
</tr>
<tr>
<td>Coloured women aged 15 years and above</td>
<td>26.5%  2003 SADHS¹¹⁴</td>
</tr>
<tr>
<td>White women aged 15 years and above</td>
<td>13.7%  2003 SADHS¹¹⁴</td>
</tr>
<tr>
<td>Indian women aged 15 years and above</td>
<td>24.8%  2003 SADHS¹¹⁴</td>
</tr>
<tr>
<td>Black women aged 15-64 years</td>
<td>34.4%  BRISK study¹¹⁶</td>
</tr>
<tr>
<td>Black women aged 45-54 years</td>
<td>59%  BRISK study¹¹⁶</td>
</tr>
<tr>
<td>Coloured women aged 45-54 years</td>
<td>42.6%  CRISIC study¹¹⁷</td>
</tr>
<tr>
<td>Indian women aged 45-54 years</td>
<td>40%  Indian Study¹¹⁸</td>
</tr>
<tr>
<td>White women aged 45-54 years</td>
<td>23.8%  CORIS study¹¹⁹</td>
</tr>
<tr>
<td>Obeseity statistic</td>
<td>Study</td>
</tr>
<tr>
<td>--------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Black men aged 15 to 64 years</td>
<td>7.9%</td>
</tr>
<tr>
<td>Black men aged 55 to 64 years</td>
<td>28.6%</td>
</tr>
<tr>
<td>White men aged 15-64 years</td>
<td>14.7%</td>
</tr>
</tbody>
</table>

SADHS = South African Demographic and Health Survey

1.6 MOTIVATION FOR STUDY

RA is a potentially debilitating disease with high healthcare costs to both the private and public health sectors. There are no recent studies in SA investigating the nutritional status and/or body composition of patients suffering from RA. It is evident from studying the literature that there are a number of areas of concern in terms of health and nutrition in RA patients and in South Africa too, such as the high obesity statistics. The study aimed to establish what RA patients are practicing and their perceptions regarding the effect of diet, nutritional supplements, medication and CAM on their symptoms as well as determining their body composition and the possible presence of rheumatoid cachexia. It is worthwhile investigating this area if their symptoms could be improved by diet or nutritional supplementation and by paying attention to the anthropometrical status especially if obesity and rheumatoid cachexia are found in the SA RA population. This will certainly be valuable information for healthcare workers, particularly rheumatologists and dietitians, in South Africa in benefiting and optimising the healthcare and support of RA patients.
CHAPTER 2: METHODOLOGY
2.1 AIM
The aim of the study was to determine the body composition of RA patients in the private and public health sector in the Cape Metropole as well as their perceptions and practices regarding the use of diet, nutritional supplements, medication, complementary and alternative medicines/therapies and exercise in the treatment of the disease.

2.2 OBJECTIVES
1. To determine the body composition of RA patients by using weight, height, bicep-, tricep-, supra-ileac and subscapular-skinfolds, waist circumference and the appropriate prediction equations.
2. To determine the perceptions and practices of RA patients regarding the use and adaptation of diets and nutritional supplements in the treatment of RA.
3. To determine the perceptions and practices of RA patients regarding the use of medication and other forms of complementary and alternative medicines/therapies in the treatment of RA.
4. To determine the perceptions and practices of RA patients regarding the use of exercise in the treatment of RA.
5. To compare the nutritional status, diet and medication facets of private and public health sector patient groups.

2.3 NULL HYPOTHESIS (H₀)
There are no differences in terms of body composition, diet and medication use between the private and public sector participants.

2.4 STUDY METHODOLOGY
2.4.1 Study Type
The study design was a descriptive, cross-sectional study with an analytical component in the quantitative domain. The study techniques included an interviewer-administered questionnaire and anthropometrical measurements.

2.4.2 Study Population
The study population consisted of adult (18 years or older) RA patients in the Cape Metropole from the private as well as the public sector.
2.4.3 Sample Selection and Size
The sampling frame consisted of all RA patients attending the public sector RA clinics at Tygerberg Hospital (TBH) and Groote Schuur Hospital (GSH) in order to reach the lower socio-economic groups. RA patients utilising private medical care were also recruited in order to reach the higher socio-economic groups. Purposive sampling was used since the study population is small.

Approval to conduct the research study in the above mentioned tertiary hospitals was sought from the Western Cape Provincial Health Research Committee. The Rheumatology clinics at TBH and GSH were contacted thereafter for logistical arrangements. Permission to conduct the study in the clinics was obtained from the Medical Superintendents and the respective heads of the clinics also granted their permission. All private practicing rheumatologists in the Cape Metropole were contacted to request permission for their patients to be approached to be included in the study population.

The total required population sample size was calculated in consultation with a statistician. With a confidence interval of 95% and a precision error of 0.6, a total of 267 RA patients were required. In order to compare the private and public sector groups, 67 RA patients were required in the private sector group according to a 1-way ANOVA power analysis with an effect size of 0.4.

2.4.4 Inclusion Criteria
All English, Afrikaans and Xhosa speaking RA patients living in the Cape Metropole area who were 18 years and older were eligible for inclusion.

2.4.5 Exclusion Criteria
RA patients younger than 18 years, those who did not give consent to partake in the study or those who participated in the pilot study were excluded.

2.5 METHODS OF DATA COLLECTION
Data collection was conducted by the investigator and took place from 11 January until the 25 February 2011 from GSH in Cape Town, TBH in Bellville, and three private practices that agreed to partake in the study across the Cape Metropolitan area including Stellenbosch, Pinelands and Panorama. An interviewer-administered questionnaire (Addendum A and B) followed by the measurement of weight, height and waist circumference in all patients and skinfold thickness measurements in patients with a BMI of <30 was conducted. Information was also gathered from the medical records.

The TBH clinic was attended on Monday and Tuesday mornings between 09h00 and 13h00. The RA clinic at GSH was attended on Friday mornings between 08h00 and 13h00. The
patients were seen according to a schedule on the remaining open time slots. The private patients were approached at the rooms of the private practicing rheumatologists and invited to participate in the study and those who agreed were then seen after their doctor’s appointment. In order to ensure privacy, a vacant room with sufficient space to conduct the measurements was utilized.

The questionnaires were administered and filled out by the investigator in a face-to-face manner for both private and public participants in a private room to ensure that the participant was comfortable and confidentiality was kept. The questionnaire was structured as to limit potential detection/observer bias and the investigator was well trained and followed standardized interviewer and measurement procedures. The questionnaire was compiled by the investigators and questions included were based on the latest literature and according to the objectives so that the answers would provide the relevant data to be able to determine the objectives. The questionnaire included questions on personal information (7 questions), the practices regarding the use of special diets, nutritional supplements and other forms of CAM (6 questions), perceptions regarding foods which improve or worsen their symptoms (5 questions), known/history of food allergies (1 question) and questions on the use of medication - both prescribed and self-medication (8 questions) and exercise (6 questions). A consent form (Addendum C and D) stated the details about what the study was about, how the results would be used, how long it would take to complete as well as the details regarding obtaining consent to partake in the study. The consent form was signed for each participant before data collection commenced in order for them to partake in the study. The questionnaire and consent forms were translated into Afrikaans and Xhosa with the help of a translator. Consent on the part of the participant included consent for the questionnaire, measurements taken as well as access to their medical records in order to obtain any relevant information regarding existing co-morbidities which could affect their nutritional status and what medication had been prescribed (See Table 2.1). No follow up was required.

<table>
<thead>
<tr>
<th>Information</th>
<th>Reason/ Relevance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidities/ Medical history of note</td>
<td>Possible influence on nutritional status or the type of medication used.</td>
</tr>
<tr>
<td>Prescribed Medication</td>
<td>Quantitative data and for statistical analysis and comparison between the public and private sector.</td>
</tr>
</tbody>
</table>

Table 2.1. Information gathered from medical records of each patient

Anthropometrical measurements including weight, height, and waist circumference were measured according to the Nutritional assessment method and the bicep-, tricep-, supra-ileac and subscapular-skinfolds were measured according to International Standards for Anthropometric
Assessment by the International Society for the Advancement of Kinanthropometry (ISAK). The anthropometrical measurements were measured as outlined in Table 2.2 below.

Table 2.2. Anthropometrical measurements taken

<table>
<thead>
<tr>
<th>Measurement &amp; equipment</th>
<th>Details of how it was taken</th>
<th>Standardization and reliability techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Electronic scale (AEG Electrolux) | • Scale placed on a flat, hard surface  
• Measure without shoes and with minimum clothing  
• Participant stands in the middle of the platform without support and weight distributed evenly on both feet  
• Measurement taken correctly to the nearest 0.1 kg | • Zero calibration before each weight measure |
| Height                  |                             |                                            |
| Stadiometer             | • Nothing covering the head  
• Feet together and flat on the floor  
• Legs straight and knees together  
• Arms relaxed at the sides  
• Heels, buttocks, and upper part of the back touching the stadiometer  
• Frankfurt plane forms a 90 degree angle with the baseboard  
• Measurement taken at maximum inspiration  
• Measuring stick is brought down until it touches the head  
• Measurement taken correctly to the nearest 0.1cm | • Standardised equipment used |
| Skinfolds (General)     | • Measurements taken on the right hand side  
• Locate the skinfold site by marking the correct anatomical landmark once it is identified  
• Skin and subcutaneous fat layer are grasped and picked up on the skinfold site by the thumb and index finger of the left hand  
• Care must be taken not to pick up the underlying muscle tissue in the grasp  
• Calliper held in right hand, perpendicular to the long axis of the skinfold and with the dial facing up  
• Blades of the calliper are applied 1cm away from the edge of the thumb and index finger  
• Calliper blades to be placed in the middle of the base and top of the skinfold  
• Skinfold is held while the measurement is taken  
• Take measurement 2 seconds after releasing the calliper blades fully  
• Measurement taken correctly to the nearest 1 millimetre  
• All skinfolds should be measured in succession and repeated three times (in other words, a complete data set of the whole proforma is taken and then repeated a second and then third time) | • Zero calibration before each measurement  
• Average of three measurements taken  
• Measurements should not differ by more than 1mm |
| Mid-acromiale-radiale   | • Midpoint of the straight line joining the Acromiale (superior aspect of the most lateral part of the acromion border) and the Radiale (point at the proximal and lateral border of the head of the radius) |                                            |
| Tricep Skinfold Site    | • Point on the posterior surface of the arm in the mid-line at the level of the marked Mid-acromiale-radiale  
• Subject stands relaxed with arms hanging by the side in the mid-prone position  
• Located by projecting the Mid-acromiale-radiale site perpendicularly to the long axis of the arm around to the back of the arm and intersecting the projected line with a vertical line in the middle of the arm when viewed from behind |                                            |
| Tricep Skinfold Measurement | • Measurement is taken parallel to the long axis of the arm at the Triceps skinfold site  
• Measurement taken correctly to the nearest 1 mm |                                            |
| Bicep Skinfold Site     | • Point on the anterior surface of the arm in the midline at the level of the Mid-acromiale-radiale  
• Subject stands relaxed with arms hanging by the side  
• Located by projecting the Mid-acromiale-radiale site perpendicularly to the long axis of the arm around to the front of the arm and intersecting the projected line with a vertical line in the middle of the arm when viewed from the front |                                            |
| Bicep Skinfold          | • Measurement is taken parallel to the long axis of the arm at the Biceps skinfold site  
• Measurement taken correctly to the nearest 1 mm |                                            |
<p>| Subscapular Skinfold    | • 2cm along a line running laterally and obliquely downward |                                            |</p>
<table>
<thead>
<tr>
<th>Measurement &amp; equipment</th>
<th>Details of how it was taken</th>
<th>Standardization and reliability techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td>from the Subscapulare (undermost tip of the inferior angle of the scapula) at a 45 degree angle • Subject stands relaxed with arms hanging by the side</td>
<td></td>
</tr>
<tr>
<td>Subscapular Skinfold</td>
<td>• Subject stands relaxed with arms hanging by the side • Taken with the fold running obliquely downwards at the Subscapular skinfold site as determined by the natural fold lines of the skin • Measurement taken correctly to the nearest 1 mm</td>
<td></td>
</tr>
<tr>
<td>Iliac Crest Skinfold Site (Supra-iliac)</td>
<td>• Site at the centre of the skinfold raised immediately above the illocristale (the point on the iliac crest where a line drawn from the mid-axilla on the longitudinal axis of the body meet the ilium) • Subject stands relaxed with the left arm hanging by the side and the right arm folded across the chest • Skinfold is raised superior to the illocristale by placing the left thumb tip on the illocristale and raise the skinfold and mark its centre with a cross • Skinfold runs slightly downwards anteriorly as determined by the natural fold of the skin • Measurement taken correctly to the nearest 1 mm</td>
<td></td>
</tr>
<tr>
<td>Supra-iliac Skinfold</td>
<td>• Subject stands relaxed with the left arm hanging by the side and the right arm folded across the chest • Taken near horizontally at the Iliac Crest skinfold site • Skinfold runs slightly downwards anteriorly as determined by the natural fold of the skin • Measurement taken correctly to the nearest 1 mm</td>
<td></td>
</tr>
<tr>
<td>Waist circumference</td>
<td>• Measurement is taken over minimal clothes • Measurement is taken at the narrowest point of the abdomen between the lower costal (10\textsuperscript{th} rib) border and the top of the iliac crest perpendicular to the long axis of the trunk • Subject stands relaxed with arms folded across the thorax • Measurer stands in front of the person • Measuring tape does not cut into the skin • Measurement is taken after exhalation</td>
<td>• Standardised equipment used.</td>
</tr>
</tbody>
</table>

The investigator received ISAK level 1 accreditation\(^*\) and was well trained and standardized in taking the measurements correctly by a trained and experienced ISAK accredited course instructor from Stellenbosch University during a three day workshop using training material and focusing on the practical aspects of taking the various measurements. This ensured that the investigator performed the measurements in a standardised manner and contributed to the reliability of the measurements. Reliability of the measurements was ensured by repeating the measurements three times and taking the average value where appropriate. This method (from Lee and Nieman\(^{112}\)) is a slight deviation from the ISAK method as the researcher was not able to carry a laptop around to compute the measurements due to safety reasons. The allowed error rate in ISAK (10\%) is however very similar to the method used in this study (<1mm difference). Skinfold measurements were not taken for individuals with a BMI of >30kg/m\(^2\) due to the reduced accuracy of the measurements taken in these individuals and the resulting measurement errors which may influence the prediction accuracy of body density. Also, the equations used to calculate body density show a lack of accuracy in predicting body composition in overweight populations.\(^{98,121,132}\)

\(^*\) ISAK level 1 accreditation: The International Society for the Advancement of Kinanthropometry (ISAK) has developed international standards for anthropometric assessment and an international anthropometry accreditation scheme (IAAS). Level 1 is designed for the majority of ISAK-accredited anthropometrists who require the measurement of height, weight, circumferences and skinfolds.
The pre-coded questionnaire and data collection sheet was sent to the statistician before pilot testing was conducted in order to ensure that the data obtained from the questionnaire would be useful and meaningful.

The questionnaire was tested for content validity by experts in the field, namely, Prof. Reuter (private practicing rheumatologist) and Dr Whitelaw (Head of Rheumatology: TBH). Face validity was tested by a sub-group of the population in a pilot test. Consensual validity was also reached whereby all the involved investigators, who are experts in their field, agreed on the validity of the questionnaire and the methodology aspects of the research study. Two participants each from TBH, GSH and the largest private practice was used for the pilot study. The pilot study took place during December 2010. Convenience sampling was used to select individuals for the pilot study. Small changes emanating from the pilot study were made to the questionnaire, these included removing ambiguous/repetitive questions and better phrasing some of the questions.

2.6 ANALYSIS OF DATA
The data was analyzed with the assistance of a statistician, Prof. Daan Nel, appointed by Stellenbosch University. MS Excel was used to capture the data and STATISTICA version 10 [StatSoft Inc. (2010) STATISTICA (data analysis software system) www.statsoft.com] was used to analyze the data. The data was captured by the researcher and a research assistant.

Summary statistics were used to describe the variables measured. Distribution of variables was presented with histograms and frequency tables. Means were used as the measures of central location for ordinal and continuous responses and standard deviations as indicators of spread. The relation between two nominal variables was investigated with contingency tables and maximum likelihood ratio chi-square tests. A p-value of p< 0.05 represented statistical significance in hypothesis testing.

The data was captured in a pre-coded data collection sheet and processed in order to obtain results. The anthropometrical data was used to calculate, interpret and classify/ categorise BMI, percentage body fat, waist circumference, fat mass index and fat-free mass index (Table 2.3). All skinfold measurements were interpreted using relevant reference standards, percentile distributions and indices (graphs and tables) referenced from appropriate sources. Education was classified into primary school level (Grade R to Grade 7), Secondary school level (Grade 8 to Grade 12), Secondary school graduate (Grade 12 graduate) and Tertiary education level (Degree/ Diploma). Exercise was classified according to the World Health Organization Global Strategy on Diet, Physical Activity and Health. Since absolute FFM and FM are dependent of height, the fat free mass index (FFMI; kg/m2) and fat mass index (FMI; kg/m2) were calculated. Fat mass index (FMI) and fat-free mass index (FFMI) was classified according to age-
matched and sex-matched data from a Swiss population of healthy adults (2986 men and 2649 women). No consensus exists about the cut-off levels for rheumatoid cachexia, we used the definition of FFMI below the 10th percentile together with FMI above the 25th percentile. A cut-off value for low FFM was defined as FFMI below the 10th percentile and obesity according to FMI was defined as FMI above the 90th percentile, as defined by the reference population.

Table 2.3. Calculation and classification of anthropometrical data

<table>
<thead>
<tr>
<th>Anthropometrical measurement</th>
<th>Calculation thereof/ equation</th>
<th>Interpretation and classification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body Mass Index (BMI)</strong> (kg/m²)</td>
<td>Weight(kg) / Height²(m)</td>
<td><strong>Undernutrition:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe thinness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate thinness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mild thinness</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Normal:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Overweight:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obese</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obese Class 1:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obese Class 2:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obese Class 3:</td>
</tr>
</tbody>
</table>

| Waist Circumference (cm) | N/A | * Increased risk: >94cm – Males >80cm – Females *Substantially increased risk: >102cm – Males >88cm – Females |

| Sum of skinfolds (mm) | Summation of all four skinfold values |

<table>
<thead>
<tr>
<th><strong>Body Density (D)</strong> (Durin and Womersley equation for calculating body density)</th>
<th>112</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>Equation:</td>
</tr>
<tr>
<td>17-19</td>
<td>1.1620 - 0.0630 x (log Σ)</td>
</tr>
<tr>
<td>20-29</td>
<td>1.1631 - 0.0632 x (log Σ)</td>
</tr>
<tr>
<td>30-39</td>
<td>1.1422 - 0.0544 x (log Σ)</td>
</tr>
<tr>
<td>40-49</td>
<td>1.1620 - 0.0700 x (log Σ)</td>
</tr>
<tr>
<td>50+</td>
<td>1.1715 - 0.0779 x (log Σ)</td>
</tr>
<tr>
<td>Females</td>
<td>Equation:</td>
</tr>
<tr>
<td>17-19</td>
<td>1.1549 - 0.0678 x (log Σ)</td>
</tr>
<tr>
<td>20-29</td>
<td>1.1599 - 0.0717 x (log Σ)</td>
</tr>
<tr>
<td>30-39</td>
<td>1.1423 - 0.0632 x (log Σ)</td>
</tr>
<tr>
<td>40-49</td>
<td>1.1333 - 0.0612 x (log Σ)</td>
</tr>
<tr>
<td>50+</td>
<td>1.1339 - 0.0645 x (log Σ)</td>
</tr>
</tbody>
</table>

| **Percentage Body Fat (%BF) Categories** (Siri equation for calculating percentage body fat) | 112 |
|----------------------------------------------------------|
| (495 / D) - 450                                          |
| Unhealthy range (too low)                                |
| Acceptable range (lower end)                             |
| Acceptable range (upper end)                             |
| Unhealthy range (too high)                               |
| Males ≤ 5%                                               |
| Females ≤ 8%                                             |
| 6-15%                                                    |
| 16-24%                                                   |
| ≥25%                                                     |

<table>
<thead>
<tr>
<th><strong>Fat Mass (kg)</strong></th>
<th>Body Weight x %BF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fat-free Mass (kg)</strong></td>
<td>Body Weight – Fat Mass</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Fat Mass Index (FMI) (kg/m²) plus Categories</strong></th>
<th>124</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat Mass / Height²(m)</td>
<td>See Reference 124</td>
</tr>
<tr>
<td>Low FFMI: &lt;10th percentile</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Fat-free Mass Index (FFMI) (kg/m²) plus Categories</strong></th>
<th>124</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat-free Mass / Height²(m)</td>
<td>See Reference 124</td>
</tr>
<tr>
<td>Obesity: FMI &gt;90th percentile</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Exercise Categories</strong></th>
<th>125</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Low intensity: Yoga, Pilates, Stretching, etc.</td>
<td></td>
</tr>
<tr>
<td>Moderate intensity: Walking, Running, Swimming, Cycling, etc.</td>
<td></td>
</tr>
<tr>
<td>High intensity: Weights, etc.</td>
<td></td>
</tr>
<tr>
<td>Low amount: &lt;150 mins/week</td>
<td></td>
</tr>
<tr>
<td>Moderate amount:150-300 mins/week</td>
<td></td>
</tr>
<tr>
<td>High amount: &gt;300 mins/week</td>
<td></td>
</tr>
</tbody>
</table>

* Disease risk for metabolic complications

BMI= Body Mass Index; D= Body Density; Σ=Sum of skinfolds; BF= Body fat; FFMI= Fat-free Mass Index; FMI= Fat Mass Index
2.7 ETHICS AND LEGAL ASPECTS
The protocol and all the relevant addenda were submitted to the Health Research Ethics Committee of Stellenbosch University for ethics approval (Approval number: N10/09/292; Addendum E). Autonomy was upheld by means of a consent form (in English and Afrikaans; translator used for Xhosa participants) that the participants had to sign in order to partake in the study. The consent form explained that participation was voluntary and explained all aspects of exactly what the study entailed regarding the questionnaire, the information that was sourced from the medical records (see Table 2.1), the measurements that were taken and how the information will be used. The participants were assured that the information would remain private and confidential at all times. The consent form obtained consent to partake in the study, to answer the questionnaire, to be measured, to obtain medical records and to use the information in the results of the study. The questionnaire was administered in the participant’s preferred language. The investigator is fluent in writing, reading and speaking English and Afrikaans. In the case of a Xhosa speaking participant, a translator was used. The individuals’ confidentiality and privacy was ensured by using a private room for the measurements to ensure the participant was comfortable as well as through a coding system whereby each participant received a coded number known only to the investigator.
CHAPTER 3: RESULTS
3.1 DEMOGRAPHICS

A total of 251 participants agreed to partake in the study of which 201 participants were from the public sector and 50 participants were from the private sector. Questionnaire data was obtained from all participants. Anthropometrical measurements were obtained for 246 participants of which weight and height only was obtained for 1 participant and weight, height and waist circumference was obtained for 245 of the participants while a full set of anthropometrical measurements with skinfold measurements could only be taken for 117 of participants due to the limitation of skinfolds in obese participants amongst other reasons. See Figure 3.1 for the reasons for missing data in some of the participants.

The mean age of the participants was 54.7 years (±SD:13.6) and the mean onset of disease was at 43.9 years of age (±SD:13.4). The study population consisted of 209 females (83%) [public sector: n=165 (66%); private sector: n=44 (18%)] and 42 males (17%) [public sector: n=36 (14%); private sector: n=6 (2%)]. The majority of the population were Coloured South Africans (n=172;
68%) and the rest were Caucasians (n=50; 20%) and Blacks (n=29; 12%). The mean duration of disease was 11 years (±SD:10.4) (Table 3.1).

Table 3.1. Participant demographics

<table>
<thead>
<tr>
<th>Participants</th>
<th>Demographic</th>
<th>Valid N</th>
<th>Mean</th>
<th>Minimum</th>
<th>Maximum</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants</td>
<td>Age (years)</td>
<td>251</td>
<td>54.7</td>
<td>18.0</td>
<td>83.0</td>
<td>13.6</td>
</tr>
<tr>
<td></td>
<td>Pre-disease age</td>
<td>251</td>
<td>43.9</td>
<td>11.0</td>
<td>80.0</td>
<td>13.4</td>
</tr>
<tr>
<td></td>
<td>Duration of disease</td>
<td>251</td>
<td>11.0</td>
<td>1.0</td>
<td>63.0</td>
<td>10.4</td>
</tr>
<tr>
<td>Females</td>
<td>Age (years)</td>
<td>209</td>
<td>55.1</td>
<td>18.0</td>
<td>83.0</td>
<td>13.7</td>
</tr>
<tr>
<td></td>
<td>Pre-disease age</td>
<td>209</td>
<td>44.2</td>
<td>11.0</td>
<td>80.0</td>
<td>13.6</td>
</tr>
<tr>
<td></td>
<td>Duration of disease</td>
<td>209</td>
<td>11.2</td>
<td>1.0</td>
<td>63.0</td>
<td>10.4</td>
</tr>
<tr>
<td>Males</td>
<td>Age (years)</td>
<td>42</td>
<td>52.3</td>
<td>19.0</td>
<td>78.0</td>
<td>13.3</td>
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<tr>
<td></td>
<td>Pre-disease age</td>
<td>42</td>
<td>42.4</td>
<td>16.0</td>
<td>75.0</td>
<td>12.2</td>
</tr>
<tr>
<td></td>
<td>Duration of disease</td>
<td>42</td>
<td>10.6</td>
<td>1.0</td>
<td>52.0</td>
<td>10.5</td>
</tr>
<tr>
<td>Public Sector</td>
<td>Age (years)</td>
<td>201</td>
<td>54.2</td>
<td>18.0</td>
<td>83.0</td>
<td>13.3</td>
</tr>
<tr>
<td></td>
<td>Pre-disease age</td>
<td>201</td>
<td>43.1</td>
<td>11.0</td>
<td>80.0</td>
<td>13.2</td>
</tr>
<tr>
<td></td>
<td>Duration of disease</td>
<td>201</td>
<td>11.4</td>
<td>1.0</td>
<td>63.0</td>
<td>10.6</td>
</tr>
<tr>
<td>Private Sector</td>
<td>Age (years)</td>
<td>50</td>
<td>56.4</td>
<td>21.0</td>
<td>82.0</td>
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</tr>
<tr>
<td></td>
<td>Pre-disease age</td>
<td>50</td>
<td>47.1</td>
<td>19.0</td>
<td>78.0</td>
<td>13.4</td>
</tr>
<tr>
<td></td>
<td>Duration of disease</td>
<td>50</td>
<td>9.8</td>
<td>1.0</td>
<td>47.0</td>
<td>9.4</td>
</tr>
</tbody>
</table>

N= Number of participants; SD= Standard Deviation.
3.2 PATIENT CHARACTERISTICS
Eighty percent (n=202) of the study population also suffered from diagnosed or self-reported co-morbidities and risk factors for heart disease (Figure 3.2), where 65.8% (n=133) of participants had hypertension and 49.0% (n=99) had speculated gastric side effects due to the RA medication. The prevalence of a combination of co-morbidities and risk factors for heart disease in this study population is shown in Table 3.2. A combination of hypertension with a high waist circumference, obesity and smoking was seen in 35% (n=87), 31% (n=78) and 29% (n=74) of participants respectively.

Figure 3.2. Co-morbidities and risk factors present in study population (n=202)
Table 3.2. Combinations of the presence of co-morbidities and risk factors in the study population

<table>
<thead>
<tr>
<th>Combinations of co-morbidities in study population</th>
<th>Number of participants</th>
<th>% of study population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension + Hypercholesterolaemia</td>
<td>34</td>
<td>14%</td>
</tr>
<tr>
<td>Hypertension + Diabetes Mellitus</td>
<td>24</td>
<td>10%</td>
</tr>
<tr>
<td>Hypertension + Smoker</td>
<td>74</td>
<td>29%</td>
</tr>
<tr>
<td>Hypertension + Obesity</td>
<td>78</td>
<td>31%</td>
</tr>
<tr>
<td>Hypertension + Substantially increased risk WC</td>
<td>87</td>
<td>35%</td>
</tr>
<tr>
<td>Hypercholesterolaemia + Smoker</td>
<td>24</td>
<td>10%</td>
</tr>
<tr>
<td>Hypercholesterolaemia + Obesity</td>
<td>25</td>
<td>10%</td>
</tr>
<tr>
<td>Hypercholesterolaemia + Substantially increased risk WC</td>
<td>30</td>
<td>12%</td>
</tr>
<tr>
<td>Smoker + Obesity</td>
<td>49</td>
<td>20%</td>
</tr>
<tr>
<td>Smoker + Substantially increased risk WC</td>
<td>59</td>
<td>24%</td>
</tr>
<tr>
<td>Hypertension + Hypercholesterolaemia + Obesity</td>
<td>24</td>
<td>10%</td>
</tr>
<tr>
<td>Hypertension + Hypercholesterolaemia + Substantially increased risk WC</td>
<td>27</td>
<td>11%</td>
</tr>
<tr>
<td>Smoker + Obesity + Substantially increased risk WC</td>
<td>46</td>
<td>18%</td>
</tr>
</tbody>
</table>

WC= Waist circumference.

Six percent (n=16) of the study population reported having a diagnosed food allergy with seafood (n=8; 50.0%) and fish (n=6; 37.5%) stated as the most common offenders (Figure 3.3). Fifty four percent (n=135) of the population were smokers/previous smokers with a mean of 26.1 years of smoking (±SD:14.3). Twenty four percent (n=61) did not attend secondary/high school and seventy five percent (n=114) of the study population that started to attend secondary/high school did not graduate. The distribution of the level of education in this study population is shown in Figure 3.4.

Figure 3.3. Description of types of food allergies present (n=16)
3.3 BODY COMPOSITION

The values for the anthropometrical measurements are outlined in Table 3.3. The average weight for females was 76.3kg (±SD:17.7) and 77.2kg for males (±SD:19.9). Seventy one percent (n=176) indicated self-reported weight gain (n=129) or weight loss (n=47) since their diagnosis of RA. The mean body mass index (BMI) was 30.3 kg/m² for females and 26.6 kg/m² for males. Body mass index, waist circumference, percentage body fat, fat mass index and fat free mass index for each individual was classified as described in the methodology section according to the classifications for men and women.

Table 3.3. Anthropometrical measurements of female and male participants

<table>
<thead>
<tr>
<th>Participants</th>
<th>Anthropometrical Measurement</th>
<th>Valid N</th>
<th>Mean</th>
<th>Min</th>
<th>Max</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants</td>
<td>BMI (kg/m²)</td>
<td>246</td>
<td>29.7</td>
<td>16.4</td>
<td>61.8</td>
<td>6.7</td>
</tr>
<tr>
<td></td>
<td>Gained weight (kg)</td>
<td>129</td>
<td>11.6</td>
<td>2.0</td>
<td>40.0</td>
<td>7.4</td>
</tr>
<tr>
<td></td>
<td>Lost weight (kg)</td>
<td>47</td>
<td>10.5</td>
<td>2.0</td>
<td>70.0</td>
<td>11.6</td>
</tr>
<tr>
<td>Females</td>
<td>Weight (kg)</td>
<td>204</td>
<td>76.3</td>
<td>36.8</td>
<td>141.1</td>
<td>17.7</td>
</tr>
<tr>
<td></td>
<td>Height (m)</td>
<td>204</td>
<td>1.6</td>
<td>1.4</td>
<td>1.8</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>BMI (kg/m²)</td>
<td>204</td>
<td>30.3</td>
<td>17.8</td>
<td>61.8</td>
<td>6.7</td>
</tr>
<tr>
<td></td>
<td>WC (cm)</td>
<td>203</td>
<td>91.3</td>
<td>60.0</td>
<td>125.0</td>
<td>14.4</td>
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<td>TSF Average (mm)</td>
<td>86</td>
<td>19.7</td>
<td>6.0</td>
<td>37.9</td>
<td>6.1</td>
</tr>
<tr>
<td></td>
<td>BSF Average (mm)</td>
<td>86</td>
<td>9.2</td>
<td>2.8</td>
<td>21.3</td>
<td>3.8</td>
</tr>
<tr>
<td></td>
<td>SISF Average (mm)</td>
<td>86</td>
<td>16.4</td>
<td>3.8</td>
<td>35.3</td>
<td>7.3</td>
</tr>
<tr>
<td>Participants</td>
<td>Anthropometrical Measurement</td>
<td>Valid N</td>
<td>Mean</td>
<td>Min</td>
<td>Max</td>
<td>SD</td>
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<td>--------------</td>
<td>-------------------------------</td>
<td>---------</td>
<td>------</td>
<td>-----</td>
<td>-----</td>
<td>----</td>
</tr>
<tr>
<td>SSSF Average (mm)</td>
<td>86</td>
<td>19.1</td>
<td>5.4</td>
<td>44.5</td>
<td>9.7</td>
<td></td>
</tr>
<tr>
<td>Sum of SF (mm)</td>
<td>86</td>
<td>64.3</td>
<td>25.3</td>
<td>130.2</td>
<td>23.1</td>
<td></td>
</tr>
<tr>
<td>% Body fat</td>
<td>86</td>
<td>33.8</td>
<td>13.7</td>
<td>46.2</td>
<td>5.9</td>
<td></td>
</tr>
<tr>
<td>Gained weight (kg)</td>
<td>115</td>
<td>11.6</td>
<td>2</td>
<td>40</td>
<td>7.2</td>
<td></td>
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<tr>
<td>Lost weight (kg)</td>
<td>40</td>
<td>11.4</td>
<td>2</td>
<td>70</td>
<td>12.4</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>Weight (kg)</td>
<td>42</td>
<td>77.2</td>
<td>45.2</td>
<td>138.3</td>
<td>19.9</td>
</tr>
<tr>
<td>Height (m)</td>
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<td>1.7</td>
<td>1.5</td>
<td>1.9</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>42</td>
<td>26.6</td>
<td>16.4</td>
<td>47.9</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td>WC (cm)</td>
<td>42</td>
<td>92.7</td>
<td>64.0</td>
<td>134.0</td>
<td>16.4</td>
<td></td>
</tr>
<tr>
<td>TSF Average (mm)</td>
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<td>9.3</td>
<td>4.0</td>
<td>17.4</td>
<td>3.6</td>
<td></td>
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<tr>
<td>BSF Average (mm)</td>
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<td>5.1</td>
<td>2.1</td>
<td>9.5</td>
<td>2.1</td>
<td></td>
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<tr>
<td>SISF Average (mm)</td>
<td>31</td>
<td>13.4</td>
<td>3.4</td>
<td>32.3</td>
<td>6.8</td>
<td></td>
</tr>
<tr>
<td>SSSF Average (mm)</td>
<td>31</td>
<td>14.0</td>
<td>6.2</td>
<td>32.8</td>
<td>7.6</td>
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</tr>
<tr>
<td>Sum of SF (mm)</td>
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<td>41.8</td>
<td>16.0</td>
<td>90.6</td>
<td>18.1</td>
<td></td>
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<tr>
<td>% Body fat</td>
<td>31</td>
<td>21.5</td>
<td>7.0</td>
<td>35.8</td>
<td>6.9</td>
<td></td>
</tr>
<tr>
<td>Gained weight (kg)</td>
<td>14</td>
<td>10.8</td>
<td>2</td>
<td>30</td>
<td>8.9</td>
<td></td>
</tr>
<tr>
<td>Lost weight (kg)</td>
<td>7</td>
<td>5.4</td>
<td>2</td>
<td>10</td>
<td>3.1</td>
<td></td>
</tr>
</tbody>
</table>

BMI = Body Mass Index; WC = Waist Circumference; TSF = Triceps Skinfold; BSF = Biceps Skinfold; SISF = Supra-Ileac Skinfold; SSSF = Subscapular Skinfold; SF = Skinfold

BMI was used to classify obesity (n=133; 45.9%), overweight (n=66; 26.8%), normal weight (n=63; 25.6%) and underweight (n=4; 1.6%) (Figure 3.5). Half of the females were classified as obese (n=103; 50.5%) and only 22.1% (n=45) as normal (Figure 3.5) while the males were classified as 23.8% (n=10) obese and 42.9% (n=18) as normal (Figure 3.5).
Waist circumference measurement classifications in all participants showed a substantially increased risk for metabolic complications in 127 participants (51.8%) and an increased risk for metabolic complications in 52 participants (21.2%) (Figure 3.6). In the women, 115 participants (55%) showed a substantially increased risk for metabolic complications and 43 participants (20.6%) had an increased risk for metabolic complications (Figure 3.6). The majority of men on the other hand had normal waist circumference values [50% (n=21)] (Figure 3.6).
All participants (n=245) Females (n=203) Males (n=42)

Substantially increased risk (n) 127 115 12
Increased risk (n) 52 43 9
Normal (n) 66 45 21

Figure 3.6. Waist circumference measurement classifications of participants (n=245)

Body fat percentage classification was distributed as shown in Figure 3.7. Just over half of all the participants (n=65; 55.6%) had an unhealthy high body fat percentage. In the female group (Figure 3.7), 64% (n=55) had an unhealthy high body fat percentage compared to the men with 32.3% (n=10) presenting with an unhealthy high body fat percentage (Figure 3.7).
All participants (n=117) Females (n=86) Males (n=31)

Unhealthy high (n) 65 55 10
Average (Upper range) (n) 44 29 15
Average (Lower range) (n) 8 2 6

n= number of participants

Figure 3.7. Body fat percentage classifications of participants (n=117)

A statistically significant positive linear relationship existed between waist circumference and percentage body fat, further indicating the presence of central obesity in this study population (Figure 3.8). This relationship was significant for both males and females, with p<0.0001 for both analyses.

Figure 3.8. Scatter plot of waist circumference versus body fat percentage for females and males

WC= Waist circumference.
Fat mass index and fat-free mass index classification was distributed as shown in Figures 3.9 to 3.11 and Figures 3.12 to 3.14 respectively. Sixty five percent of all participants (n=76) had a FMI of higher than the 50th percentile with 68.6% (n=59) FMI of higher than the 50th percentile for the women and 54.8% (n=17) for the men. A FFMI of lower than the 25th percentile was shown in 29.1% (n=34) of all participants, 24.4% (n=21) of women and in 41.9% (n=13) of men.

Figure 3.9. Percentile distribution of fat mass index for all participants (n=117)

Figure 3.10. Percentile distribution of fat mass index for women only (n=86)

Figure 3.11. Percentile distribution of fat mass index for men only (n=31)
Figure 3.12. Percentile distribution of fat-free mass index for all participants (n=117)

Figure 3.13. Percentile distribution of fat-free mass index for women only (n=86)

Figure 3.14. Percentile distribution of fat-free mass index for men only (n=31)

Of the 117 participants whose skinfold measurements could be taken, rheumatoid cachexia (determined as described in methodology) was seen in twelve participants (10.3%) and these
participants were classified as underweight (n=1; 1%), normal weight (n=8; 7%) or overweight (n=3; 3%) and not obese using the BMI classification. Low fat-free mass classification according to FFMI (FFMI <10th percentile) was seen in 24 participants (21%) and obesity according to FMI (FMI >90th percentile) was seen in 31 participants (27%).

3.4 DIET, NUTRITIONAL SUPPLEMENTS, COMPLEMENTARY AND ALTERNATIVE MEDICINES AND THERAPIES

Twenty nine percent of participants (n=73) believed that certain types of food could improve their symptoms of RA (Figure 3.15). Vegetables (n=56; 76.7%) and fruit (n=24; 32.9%) were mentioned most frequently (Figure 3.17). Sixty percent of participants (n=151) believed that certain foods worsened their symptoms of RA (Figure 3.16). Tomatoes (70%), spicy food (56%) and red meat (39%) were the most frequently mentioned offenders (Figure 3.18).

Figure 3.15. Foods improve the symptoms of RA

Figure 3.16. Foods worsen the symptoms of RA

Figure 3.17. Types of foods thought to improve their symptoms of RA (n=73)
Figure 3.18. Types of foods thought to worsen their symptoms of RA (n=151)

Half of the participants (n=126) stated that they avoid certain foods which they believe worsen their symptoms and 19% (n=48) increase their intake of certain foods to improve their symptoms of RA. Of those participants that avoid certain foods, 41% percent (n=52) replace that type of food with a different source of the nutrients which are consequently excluded from their diet. Of those participants who believed foods can improve their symptoms of RA (n=73), Figure 3.19 illustrates the distribution of those who actively increase their intake of the type of food they believe improves their symptoms and those who do not. In other words, of the people who indicated that they believe fruit improves their symptoms of RA (n=13), 12 of them (92%) actually increase their intake of fruit in order to improve their symptoms. Similarly, Figure 3.20 illustrates the distribution of those who actively avoid the type of food they believe worsens their symptoms and those who do not. In both cases, an apparent trend seems to occur with the majority of people following their own beliefs or advice regarding what they personally believe in terms of the impact food has on their symptoms except for in the case of gassy cooldrinks where only half (n=6; 54.5%) of participants avoid it.
Figure 3.19. Distribution of those who increased, vs. those who did not increase, their intake of the foods they believed improve their symptoms of RA

Figure 3.20. Distribution of those who avoided, vs. those who did not avoid, the foods they believed worsen their symptoms of RA

In terms of nutritional supplements, sixty four percent of participants (n=161) thought that nutritional supplements or complementary and alternative medicines (CAM) and therapies could improve their symptoms of RA (Figure 3.21). Calcium (n=90; 55.9%), vitamin D (n=83; 51.6%), folic acid (51.6%) and omega-3 FA (n=67; 41.6%) were believed to be the most beneficial (Figure 3.22) and other forms of CAM and therapies believed to be beneficial included glucosamine (n=12; 7.5%), chondroitan (n=10; 6.2%), proanthocyanidin (n=6; 3.7%) acupuncture (n=10; 6.2%), homeopathy (n=10; 6.2%) and chiropractor (n=7; 4.3%) (Figure 3.23). Those who did not
recognise the names of these supplements answered “don’t know” when asked if they believed them to be beneficial in RA. A comparison between age and the belief of whether or not nutritional supplements or CAM and therapies improved their symptoms of RA showed that those who responded that it could not improve their symptoms were slightly older (56.9 years vs. 55.0 years) but this did not reach statistical significance (p=0.6997).

Figure 3.21. Distribution of responses regarding nutritional supplements or complementary and alternative medicines and therapies can improve symptoms of RA

Figure 3.22. Nutritional supplements thought to improve symptoms of RA (n=161)
Ninety eight percent (n=246) of participants used nutritional supplements (prescribed or not prescribed) in order to treat and improve their symptoms of RA. Two hundred and thirty eight participants (95% of those who used nutritional supplements) used nutritional supplements which were prescribed by their rheumatologist to treat their RA. The most frequently prescribed supplements (Figure 3.24) included folic acid (n=218; 91.6%), calcium (n=182; 76.5%) and vitamin D (n=185; 77.7%). Seventy four participants (29%) used nutritional supplements which were not prescribed by their rheumatologist to treat their RA (Figure 3.25) with omega-3 FA (n=48; 64.9%), multivitamin and minerals (n=22; 29.7%), calcium (n=22; 29.7%), vitamin B complex (n=15; 20.3%) and vitamin D (n=15; 18.9%) being used most frequently. Thirty seven participants (15%) reported using other forms of CAM such as glucosamine (n=9; 24.3%), chondroitan (n=8; 21.6%), silicon (n=4; 10.8%) and proanthocyanadin (n=2; 5.4%). Only eight persons reported using alternative therapies, including massage (n=3), chiropractor (n=1), acupuncture (n=1), magnets (n=1), hydrotherapy (n=1), homeopathy (n=1), reflexology (n=1) and reiki (n=1). Thirty one percent of participants (n=78) spent money on purchasing nutritional supplements and other forms of CAM and therapies. The amount of money spent is depicted in Figure 3.26 with 55.1% (n=43) of these participants spending between R0 and R100 per month, 14.1% (n=11) between R101 and R200 per month and 9.0% (n=7) spending as much as between R501 and R1000 per month.
Figure 3.24. Prescribed supplement use of RA patients (n=238)

Figure 3.25. Non-prescribed supplement use of RA patients (n=74)
Figure 3.26. Amount of money spent by RA patients on nutritional supplements and other forms of complementary and alternative medicines and therapies

No relationship was seen with education level and the use of nutritional supplements ($p=0.3210$). A trend was seen in that those who used CAM had a higher education level (tertiary education); although it did not reach statistical significance ($p=0.0514$). A significant difference was however seen in the use of alternative therapies and education level where those with tertiary education were the highest users ($p=0.0068$).

3.5 MEDICATION

Ninety percent (n=226) of the participants believed that medication could improve their symptoms of RA while eight percent (n=20) responded that they did not believe medication improved their symptoms and two percent (n=5) did not know. Ninety nine percent (n=247) of the participants used medication and the medication used in all but one participant was prescribed by their rheumatologist. Ninety four percent (n=237) claimed to always take their medication as prescribed and four percent (n=11) of participants used medication for their RA which was not prescribed by their rheumatologist such as Arthrexin (Indomethacin) (n=6) which is an over the counter anti-rheumatic, anti-inflammatory agent. Eighty two percent (n=205) used various types of prescribed pain medication (Figure 3.27 and 3.28), 60% (n=150) used prescribed NSAIDS (Figure 3.29 and 3.30), 97% (n=243) used prescribed DMARDS (Figure 3.31 and 3.32), and 9% (n=23) used prescribed biologic agents (Figure 3.33 and 3.34). The differences in use of certain medications between the public and private sectors are discussed in more detail in section 3.7.4.
Figure 3.27. Types of pain medication used for all participants (n=205)

Figure 3.28. Types of pain medication used for public and private sectors (n=205)
Figure 3.29. Types of non-steroidal anti-inflammatory drugs used (n=150)

Figure 3.30. Types of non-steroidal anti-inflammatory drugs used for public and private sectors (n=150)
Figure 3.31. Types of disease modifying anti-rheumatic drugs used (n=243)

Figure 3.32. Types of disease modifying anti-rheumatic drugs used for public and private sectors (n=243)
Seventy eight percent (n=195) used corticosteroids such as prednisone and cortisone. Of those 195 participants who were prescribed corticosteroids, 154 (79%) participants had another co-morbid disease (Table 3.4). Fifty one percent (n=99) of those using corticosteroids presented with hypertension and only four percent (n=7) presented with osteoporosis. The use of corticosteroids did not seem to show a relationship with a simultaneous presence of hypertension or osteoporosis as these statistics are not significant (p=0.39932; p=0.33479 respectively). The use of corticosteroids also had no statistically significant effect on the self-reported weight gain experienced (p=0.49051), waist circumference categories (p=0.33881), percentage body fat categories (p=0.95904) or fat mass index categories (p=0.05464).
Of those 195 participants who were prescribed corticosteroids, 165 participants (85%) were also prescribed calcium supplements, 167 participants (86%) were prescribed vitamin D supplements and 163 participants (84%) were prescribed a combination of both calcium and vitamin D supplements. The composition and doses of the specific supplements were not recorded.

Table 3.4. Frequency of additional co-morbidities in those RA patients receiving corticosteroids

<table>
<thead>
<tr>
<th>Condition</th>
<th>No. of participants</th>
<th>% of those receiving corticosteroids</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Disease</td>
<td>13</td>
<td>7%</td>
<td>0.11995</td>
</tr>
<tr>
<td>Hypertension</td>
<td>99</td>
<td>51%</td>
<td>0.39932</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>50</td>
<td>26%</td>
<td>0.52188</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>22</td>
<td>11%</td>
<td>0.95911</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>7</td>
<td>4%</td>
<td>0.33479</td>
</tr>
</tbody>
</table>

Eighteen percent (n=46) of participants had medical aid of which most (n=40; 15.9%) were from the private sector and 6 participants (2.4%) from the public sector. Of those who had medical aid, 29 participants (63%) reported that the medical aid covered all their medication costs. For those who did not have medical aid or those who had to pay in an amount every month to cover their medication costs, the amount of money spent on medication is depicted in Figure 3.35.

Figure 3.35. Distribution of amount of money spent on medication by patients per month (n=222)

3.6 EXERCISE

Seventy one percent (n=178) of the participants reported that they exercised, with most (n=139; 78.1%) performing cardiovascular exercise (walking, swimming, cycling, etc.) (Figure 3.36)
The mean total minutes per week spent on doing exercise was 241.6 minutes/week (±SD:173.6). The exercise categories were distributed as shown in Figure 3.37. Myself/internal motivation (67%; n=120), rheumatologists/doctor (19%; n=34), physiotherapist/biokineticist (12%; n=21), and family or friends (7%; n=12) were the highest given responses to who suggested that they do exercise. Seventy six percent (n=136) of those who did exercise stated that they exercised specifically to improve their symptoms of RA.

Figure 3.36. Different types of exercise performed (n=178)

Figure 3.37. Distribution of exercise intensity and amount categories (n=178) of participants
3.7 PUBLIC VERSUS PRIVATE SECTORS

3.7.1 Demographics and Patient Characteristics

When comparing the public and private sectors, statistical differences were seen in the distribution of race, where the public sector consisted mostly of coloured South Africans and the private sector consisted mostly of Caucasian South Africans (p<0.0001). The two groups were comparable in terms of age and duration of disease with no statistically significant differences seen (p=0.13 and p=0.44 respectively). Smokers/previous smokers vs. non-smokers reached near significance where the public sector comprised of more smokers/previous smokers (p=0.0620). Of the smokers/previous smokers, the public sector smoked for a mean of 27.5 years vs. a mean of 18.8 years in the private sector (p=0.0104). In terms of education level, the private sector consisted of 56% who attained tertiary education vs. 5% in the public sector (p<0.0001) and the public sector consisted of 6% with no education and 24% with primary school education compared to the private sector where all participants reached at least secondary school level (p<0.0001).

3.7.2 Body Composition

The differences in mean values for the private sector and public sector, with men and women analysed separately, are shown in Table 3.5. There was a significant difference in mean height between the two groups in females (1.57m in public sector vs. 1.62 in the private sector; p=0.0001). No overall differences between males and females were seen in mean weight, BMI and waist circumference except for the males, where a significant difference was seen in BMI (25.9kg/m2 in public sector vs. 30.3 in private sector; p=0.0461). Percentage body fat did not differ between the two sectors when comparing males and females separately nor when comparing the categories of percentage body fat for males and females separately (p=0.4891 and p=0.1979 respectively). Absolute fat mass and fat mass index in men did not differ (p=0.9688 and p=0.9020 respectively) when comparing private versus public sector. Absolute fat mass and fat-free mass did however differ in the females, where the private sector had a higher fat mass (p=0.0243) and fat-free mass (p=0.0134).

Table 3.5. Mean values for anthropometrical measurements for the public versus private sectors.

<table>
<thead>
<tr>
<th>Participants</th>
<th>Anthropometrical measurement (Mean values)</th>
<th>Public sector</th>
<th>Private Sector</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants</td>
<td>BMI (kg/m²)</td>
<td>29.8</td>
<td>29.1</td>
<td>0.748355</td>
</tr>
<tr>
<td>Females</td>
<td>Weight (kg)</td>
<td>76.2</td>
<td>76.4</td>
<td>0.729321</td>
</tr>
<tr>
<td></td>
<td>Height (m)</td>
<td>1.57</td>
<td>1.62</td>
<td>0.000067</td>
</tr>
<tr>
<td></td>
<td>BMI (kg/m²)</td>
<td>30.7</td>
<td>28.9</td>
<td>0.195674</td>
</tr>
</tbody>
</table>
### Anthropometrical Measurement (Mean values)

<table>
<thead>
<tr>
<th>Participants</th>
<th>Public sector</th>
<th>Private Sector</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WC (cm)</td>
<td>91.8</td>
<td>89.5</td>
<td>0.392367</td>
</tr>
<tr>
<td>TSF Average (mm)</td>
<td>19.1</td>
<td>21.5</td>
<td>0.176366</td>
</tr>
<tr>
<td>BSF Average (mm)</td>
<td>8.7</td>
<td>10.6</td>
<td>0.061523</td>
</tr>
<tr>
<td>SISF Average (mm)</td>
<td>16.1</td>
<td>17.3</td>
<td>0.553125</td>
</tr>
<tr>
<td>SSSF Average (mm)</td>
<td>19.2</td>
<td>19.0</td>
<td>0.979951</td>
</tr>
<tr>
<td>Sum of SF (mm)</td>
<td>63.0</td>
<td>68.3</td>
<td>0.450897</td>
</tr>
<tr>
<td>% Body fat</td>
<td>33.4</td>
<td>35.1</td>
<td>0.114519</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>20.9</td>
<td>24.7</td>
<td>0.024341</td>
</tr>
<tr>
<td>Fat-free Mass (kg)</td>
<td>40.8</td>
<td>44.4</td>
<td>0.013404</td>
</tr>
<tr>
<td>Fat Mass Index (kg/m²)</td>
<td>8.4</td>
<td>9.4</td>
<td>0.054861</td>
</tr>
<tr>
<td>Fat-free Mass Index (kg/m²)</td>
<td>16.4</td>
<td>16.9</td>
<td>0.144957</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>75.2</td>
<td>89.7</td>
<td>0.054479</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.70</td>
<td>1.72</td>
<td>0.553128</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>25.9</td>
<td>30.3</td>
<td>0.046054</td>
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<tr>
<td>WC (cm)</td>
<td>91.3</td>
<td>100.7</td>
<td>0.091148</td>
</tr>
<tr>
<td>TSF Average (mm)</td>
<td>9.1</td>
<td>11.6</td>
<td>0.332635</td>
</tr>
<tr>
<td>BSF Average (mm)</td>
<td>5.0</td>
<td>5.9</td>
<td>0.789268</td>
</tr>
<tr>
<td>SISF Average (mm)</td>
<td>12.9</td>
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<tr>
<td>SSSF Average (mm)</td>
<td>14.0</td>
<td>14.4</td>
<td>0.713258</td>
</tr>
<tr>
<td>Sum of SF (mm)</td>
<td>40.9</td>
<td>50.0</td>
<td>0.442264</td>
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<tr>
<td>% Body fat</td>
<td>21.1</td>
<td>24.5</td>
<td>0.616291</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>14.9</td>
<td>19.8</td>
<td>0.332635</td>
</tr>
<tr>
<td>Fat-free Mass (kg)</td>
<td>53.0</td>
<td>58.6</td>
<td>0.132751</td>
</tr>
<tr>
<td>Fat Mass Index (kg/m²)</td>
<td>5.2</td>
<td>6.8</td>
<td>0.367054</td>
</tr>
<tr>
<td>Fat-free Mass Index (kg/m²)</td>
<td>18.4</td>
<td>20.3</td>
<td>0.066149</td>
</tr>
</tbody>
</table>

BMI = Body Mass Index; WC = Waist Circumference; TSF = Triceps Skinfold; BSF = Biceps Skinfold; SISF = Supra-Ileac Skinfold; SSSF = Subscapular Skinfold; SF = Skinfold

### 3.7.3 Diet, Nutritional Supplements, Complementary and Alternative Medicines and Therapies

No differences were seen between the two groups in terms of their opinion regarding whether or not foods improved or worsened their symptoms of RA (p=0.0962 and p=0.5849 respectively) nor whether or not they avoided certain foods they believe worsened their symptoms of RA or
increased their intake of foods they believed could improve their symptoms (p=0.7034 and p=0.3377).

No differences were seen in the opinion regarding whether or not nutritional supplements and other forms of complementary and alternative medicines or therapies improved their symptoms of RA (p=0.7318), as well as the use of nutritional supplements (p=0.9964). A large difference was however seen in the overall use of non-prescribed nutritional supplements in the private sector (68%) vs. only 20% in the public sector (p<0.0001) with a higher use in the private sector of calcium (47% vs. 15%; p=0.0024), magnesium (18% vs. 3%; p=0.0215) and multivitamin and mineral supplements (47% vs. 15%; p=0.0024). No difference was seen in the use of prescribed nutritional supplements although there was a higher percentage of public participants who were prescribed calcium (91% vs. 15%; p<0.0001) and vitamin D (90% vs. 26% p<0.0001). A slight difference in the overall use of complementary and alternative medicines was seen with a trend of higher use in the private sector (24% vs. 13%; p=0.0514) and a higher use of glucosamine (50% vs. 12%; p=0.0116), and chondroitin (42% vs. 12%; p=0.0400) in the private sector. A definite difference was seen with a higher overall use of complementary and alternative therapies in the private sector (10% vs. 1%; p=0.0073). A large difference was also seen in whether or not the participants spent money on nutritional supplements and other forms of complementary and alternative medicines or therapies with 76% in the private sector and 20% in the public sector (p<0.0001).

3.7.4 Medication

The majority of the private sector participants (80%) had medical aid compared to only 3% in the public sector (p<0.0001) and 90% of those without medical aid or whose medical aid did not cover all their expenses in the public sector did not pay anything for their medication compared to 8% in the private sector (p<0.0001). Large differences were seen in the types of medication used (see Figures 3.28, 3.30, 3.32 and 3.34). The public sector used pain medication overall more frequently than the private sector (92% vs. 42%; p<0.0001) with a higher use of paracetemol in the public sector (97% vs. 57%; p<0.0001). A higher use of certain pain medication was however seen in the private sector, namely, tramacet (tramadol and paracetemol) (43% vs. 1%; p<0.0001), adcodol (paracetemol, codeine phosphate, caffeine and doxylamine succinate) (5% vs. 0%; p=0.0320) and dextroproxyphene (5% vs. 0%; p=0.0320). The private sector used anti-inflammatory medication overall more frequently than the public sector (72% vs. 57%; p=0.0447) with a higher use of arcoxia (etoricoxib) (8% vs. 0%; p=0.0031), piroxicam (6% vs. 0%; p=0.0161), coxflam (meloxicam) (44% vs. 0%; p<0.0001), and celebrex (celecoxib) (22% vs. 0%; p<0.0001). The public sector however had a higher use of diclofenac (98% vs. 17%; p<0.0001). A higher use of corticosteroids was seen in the public sector (84% vs. 52% p<0.0001). No difference was seen in the overall use of DMARDS. A higher use of certain DMARDS was however seen in the public sector, namely, Sulfasalazine (28% vs. 13%; p=0.0207), chloroquine (66% vs. 29%; p=0.0001),
and azathioprine (6% vs. 0%; p=0.0258). The private sector had a higher use of leflunomide (6% vs. 0%; p=0.0017). A large difference was seen in the use of biologic agents with 46% of the private sector compared to 0% of the public sector (p<0.0001).

3.7.5 Exercise
No differences were seen in exercise behaviour (p=0.2081), amount of exercise or intensity level of exercise (p=0.3599) between the two groups. There was however a difference in opinion regarding whether or not exercise improved their symptoms of RA, where the public sector was more likely than the private sector to answer ‘yes’ when asked if they think exercise can improve their symptoms (80% vs. 64%; p=0.0476).
CHAPTER 4: DISCUSSION
4. DISCUSSION

A satisfactory study population size was obtained, which came very near to the pre-calculated sample size required. Although the private sector participant numbers specifically, that were reached, were lower than the calculated number, this group was still large enough to detect significant differences between the private and public sectors.

The nutritional status of RA has previously been determined to be poor.\textsuperscript{46,84,102,104} This study looked at the body composition and anthropometrical status of RA patients and the results are very disturbing. Firstly, the presence of obesity and high waist circumference values are unacceptably elevated. These figures are much higher than the study conducted in Cape Town, South Africa by Mody et al\textsuperscript{111} in 1989 where obesity was seen in only 10.5\% of the RA patients. In this study population, obesity according to BMI, was seen in almost half of the participants and a FMI of >90\% percentile was seen in almost a third of non-obese participants according to BMI. Thus, when BMI and FMI were both used to classify obesity, the figures were even higher at more than half of participants being classified as obese. A possible reason for the increased obesity statistics compared to 1989 could be due to the overall increase of obesity in the general population worldwide.\textsuperscript{126} A number of reasons are thought to contribute to this increase including changes in diet (easily accessible food and a more palatable diet) and decreased physical activity due to increased reliance on cars and mechanical manufacturing.\textsuperscript{126} A review conducted in 2006 identified other possible reasons for the increase in obesity; namely insufficient sleep, endocrine disruptors (environmental pollutants which interfere with lipid metabolism), decreased rates of smoking (smoking suppresses appetite), and increased use of medications that can cause weight gain.\textsuperscript{113,126,127} Another reason for the high rates of obesity is that South Africa has a very high obesity prevalence in general, especially among Black women and Caucasian men.\textsuperscript{123,124} This could possibly also contribute to the development of RA in South Africa due to an increased susceptibility of obese individuals to develop RA.\textsuperscript{5} Central obesity was also present in this study. More than half of the participants had a waist circumference which showed a substantially increased risk for the development of metabolic complications and almost a quarter showed an increased risk. These statistics again mirror the general population in South Africa which has a high prevalence of central obesity.\textsuperscript{123,124} These findings are also consistent with the findings in other studies where central obesity was found in more than half the study population.\textsuperscript{73,109} In terms of body fat percentage, more than half of the participants and two thirds of women had an unhealthily high BF percentage classification. These statistics highlight a threatening problem in the body composition of these RA patients. It is worrying that in a national study conducted by the researcher and other authors in 2007\textsuperscript{128}, 68\% (n=15) of South African rheumatologists referred less than 10\% of their patients to a dietitian and 27\% (n=6) referred 10-30\% of their patients.\textsuperscript{128}
It is necessary to try to determine the reasons for the poor anthropometrical status in these patients in order to correct the problem and to provide improved treatment for these patients. The literature described earlier has indicated a number of reasons for the poor nutritional status seen in RA patients, the most obvious being the inability of some RA patients to exercise due to disability, the reduced range of movement they experience and pain.\textsuperscript{1,2,8,9} However, a high percentage of participants indicated that they exercised and more than half exercised at a self-reported moderate intensity for 150 to 300 minutes a week or more, which may, in the light of the high obesity statistics, be a case of over-reporting by the participants. Another reason for the poor nutritional status could be due to medication side effects. Corticosteroids have been shown to cause weight gain and the effect of DMARDS and biologics could possibly also have an effect on weight gain.\textsuperscript{8,33}

With regards to rheumatoid cachexia, it is very apparent that looking at BMI alone is not appropriate in RA patients because the concurrent presence of a low fat-free mass and a high fat mass seen in RA patients cannot be detected with BMI alone.\textsuperscript{73,109} This is illustrated in this population by the fact that all patients who presented with rheumatoid cachexia were classified according to BMI as underweight (1%), normal (7%) or overweight (3%) and not obese. These patients would appear to be in a reasonably good nutritional status when in fact they were very malnourished. The 2007 study by the researcher and other authors showed that 68% (n=15) of South African rheumatologists said that their patients were generally of normal weight and 32% (n=7) said their patients were overweight.\textsuperscript{128} These statistics highlight a possible discrepancy between the perceptions of rheumatologists regarding the nutritional status of their patients and the actual nutritional status of their patients.\textsuperscript{128} The 2007 study was however a national sample, whereas this study was a provincial sample and it is possible (and probably more plausible) that the Cape Metropolitan area in the Western Cape could have more obese RA patients compared to other provinces. In fact, the 1998 and 2003 SADHS studies both reported that overweight, obesity and mean waist circumference measurements seen in the general population were highest in the urbanized provinces of Western Cape, KwaZulu-Natal and Gauteng.\textsuperscript{113} A nationwide study on nutritional status in RA patients is needed to investigate if this is true for the RA population too.

When looking at the differences seen in the private and public sector, it is interesting to note that the private sector women were taller than those in the public sector. This could be due to the fact that in this study, the private sector participants are better educated than the public sector and it has been shown that taller men and women are those with the highest education level, while those without education are the shortest.\textsuperscript{113}

An increased risk of CVD already exists among patients with RA and a high prevalence of modifiable risk factors for CVD such as hypertension, smoking, obesity and high waist circumference values (indicating central obesity) was seen in this study population which could
potentially increase the risk for CVD even further. More than half of the population were smokers or previous smokers. Smoking is not only a risk factor for the development of heart disease but also may influence the risk of developing RA and may negatively influence the course of the disease. Brady et al found that when compared to controls, RA patients had higher mean BMI and waist circumference measurements and were more likely to be smokers. The mean absolute risk of CVD was significantly higher in the RA group (p=0.036) even after excluding smokers. This RA study has also shown a prevalence of high BMI and waist circumference values. Not only do the RA patients exhibit the presence of CVD risk factors, but many of them have a combination of CVD risk factors. A combination of hypertension together with high waist circumference, obesity or smoking was each seen in a third of participants. Since CVD is the leading cause of mortality in RA, it stands to reason that this is a problem which requires urgent attention. The monetary cost of RA is already high and with the additional co-morbidities, the cost of the burden of disease is exacerbated.

The effect of diet on the symptoms of RA have been said to be highly individualised and this has been confirmed in this study, with mixed results on perception of what improves or worsens the symptoms of the RA patients. An informal observation the investigator made when collecting the data is that most of the time, each individual felt quite strongly about whether or not diet affected their symptoms and which foods were responsible. Diet may have a role to play in alleviating symptoms but this is a very complex subject in RA. The improved symptoms seen in clinical studies may be due to the change from an unhealthy diet to a healthier diet with increased fruit and vegetable consumption and reduced saturated fats content. The perception of the participants that fruits and vegetables improve their symptoms may be due to this fact. The red meat, tomatoes, spices, etc. which participants said worsens their symptoms could be due to underlying and perhaps undiagnosed conditions such as gout. The effects of dietary manipulation require further studies to confirm the benefits of specific diets in order to make specific recommendations.

Patients with RA should follow an individualized, healthy, balanced diet. In general, the diet recommended for arthritis is similar to that of good health with special emphasis on cardiovascular risk prevention. Due to the increased risk for CVD and osteoporosis in RA patients, preventative dietary measures should be followed to prevent dyslipidaemia and enforce weight control. Nutritional supplementation should be considered in patients who struggle to meet their requirements through diet alone and in those on medications which have known drug-nutrient interactions such as folic acid supplementation with Methotrexate use. Those with osteoporosis for example, should meet their dietary recommendations for calcium intake from dietary sources where possible and calcium and vitamin D supplementation in older patients, particularly if housebound and/or in those with a poor dietary intake. Certain diets (such as fasting, elimination,
and elemental diets) have shown potential in improving symptoms but these diets cannot be regarded as standard dietary treatment. They may however be of use in certain individual patients.

The majority of the RA patients were taking nutritional supplements either prescribed or non-prescribed. The supplements which were prescribed most frequently by rheumatologists (folic acid, vitamin D and calcium) were appropriate in methotrexate and corticosteroid use in order to counteract the drug-nutrient interactions seen in these drugs and prevent possible side effects. Guzman-Clark et al reported that only 32% of patients on long term glucocorticoid treatment were prescribed calcium supplements. This study shows that almost all patients on corticosteroids were also prescribed calcium and vitamin D to prevent osteoporosis which is very satisfactory. It is well known that omega-3 FA supplementation reduces inflammatory markers and decreases the need for NSAIDS and DMARDS. Omega-3 FA were not prescribed by any of the rheumatologists but this is probably due to the fact that it does not have a code that can be used to claim the costs back from medical aid providers. It is however possible that they recommend it to their patients. The 2007 study by the researcher and other authors showed that sixty four percent (n=14) of South African rheumatologists indicated that they prescribe supplements. The three most common supplements that these rheumatologists prescribed/recommended were omega 3 FA (71%; n=10), calcium (57%; n=8) and vitamin B complex (29%; n=4).

The difference seen in the private and public sectors in the use of non-prescribed nutritional supplements, complementary and alternative medicines and alternative therapies (with a higher use in the private sector) is most likely due to the high costs of these supplements, medicines and therapies which those in the public sector cannot afford. A study conducted in Canada showed that high household income, high level of education and being food-secure were positively associated with supplement use and this could be true for this population too. The use of complementary and alternative supplements and therapies has become a growing and ever more popular field, especially within population groups suffering from a chronic disease such as RA. Fifteen percent of the participants reported using complementary and alternative medicines such as glucosamine, chondroitan and proanthocyanidin. The beneficial effects of these CAM have however not been conclusively confirmed. Some studies show that glucosamine and chondroitan may be beneficial in osteoarthritis. A recent meta-analysis has however shown no benefit. More studies are therefore needed to confirm this potential beneficial effect in osteoarthritis. Furthermore, no beneficial effect has been shown in RA patients. If further studies show a benefit in osteoarthritis, then there is the potential that patients with RA and concurrent osteoarthritis may see some benefit but this will need to be explored in experimental studies. Until studies are conclusive however, patients are wasting their money on expensive and seemingly ineffective CAM in addition to the
already high medical costs they incur. It is very important that RA patients are educated and informed on this issue and the dietitian has a very important role in achieving this.

Medication, such as what is used in this RA population (NSAIDs, Methotrexate, corticosteroids, etc.), can have an effect on nutritional status by altering nutrient absorption, metabolism, utilization or excretion of certain nutrients. RA patients are in particular vulnerable to these effects as they are at risk of developing drug induced deficiencies due to inadequate diets and increased nutritional needs due to chronic illness. It is very important that dietitians are aware of the drug-nutrient interactions which exist with the medication used in RA. Universities which offer dietetics need to ensure that training on RA is delivered in their courses and that they pay special attention to these drug-nutrient interactions.

In the public sector in South Africa, doctor’s consultations, medication and treatment is provided free of charge or at a minimal cost for those who cannot afford medical aid for private care. Those in the public sector therefore do not incur high costs for their treatment. Those on private care however incur very high expenses for the medication that medical aid does not cover as well as the expense of monthly medical aid payments which cover private doctors’ fees and can be thousands of rand per month. The differences in use of certain medications seen between the private and public sector are due to the costs of the medication and budgetary constraints in the public sector. Biologics are much more expensive than traditional DMARDs and therefore are not currently used in the public sector. This is an issue which needs to be addressed. Biologics have the potential to dramatically improve the quality of life for those who have failed at treating their disease with traditional DMARDs and should become less expensive in order for more patients to benefit. Patients, rheumatologists, government, medical aids and pharmaceutical companies need to work together to make this treatment accessible to all RA patients who need it. The consequences of RA include loss of employment, reduced social functioning and significant healthcare costs and the economic burden of RA is thought to be substantial for people with RA as well as the relevant health services. Perhaps if more patients were treated with the appropriate medication, a direct saving on long term healthcare costs and indirect savings with increased ability to work and function would warrant the spending of local governments on better medications. A cost-benefit and cost-effectiveness study is warranted to investigate this scenario.

In terms of medication use in the private sector, it must be mentioned that the high number of patients on tocilizumab and golimumab in this study population does not necessarily represent typical SA biologics use, but is influenced by fact that the rheumatologists in the private sector were participating in trials using these agents, which were not registered for use in SA at the time of the study. Tocilizumab is now registered as actemra and is available to SA patients.
The null hypothesis of this study was that there are no differences in terms of body composition, diet and medication use between the private and public sector participants. This null hypothesis can therefore be rejected as differences were seen between the two groups; mainly due to direct (costs of medication, supplements, etc.) and indirect (disadvantaged background, poor eating habits) socio-economic factors.

The main limitation to this study is that it was a descriptive study and the level of some of the evidence is therefore limited. The analytical component of the study does however strengthen the findings. Further limitations include the fact that no biochemical markers were measured to determine nutritional status. Although skinfolds are an accurate measure of calculating body composition, it would have been more accurate to use Dual X-Ray Absorptiometry (DEXA). DEXA could also have been used to measure bone density and therefore screen for and diagnose osteoporosis in these RA patients. DEXA however has little epidemiological applicability because of the high costs and methodological efforts required for its use in a study. The predictive equations derived from skinfold measurements provide good associations with fat mass estimation compared with the reference methods and are preferred in a research setting because of its lower costs and methodological effort. The smaller size of the private sector group was also a limitation but the study population was large in total and this smaller group was still large enough to detect significant differences between the two groups. Concerning the patient’ supplement intake of omega-3 FA, micronutrients and other forms of CAM, the exact doses and frequency of intake and whether or not the supplements were a combination of different nutrients (eg. omega-3 and omega-6 FA) was not recorded.
CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS
5. CONCLUSIONS AND RECOMMENDATIONS

RA is a devastating disease with a potentially profound effect on the quality of life of those who live with it. Any measure that can be taken in an attempt to improve their symptoms and quality of life should be addressed. The risk factors for CVD and the high obesity seen in this population are problems which need to be urgently addressed. The role of dietitians in this regard is vital. The fact that malnutrition in RA patients can be underlying and not obvious to the eye is all the more reason that all RA patients, not just the obese, should at least be assessed and further consulted if necessary by a dietitian. The dietitian should be involved in ensuring that the patient receives proper nutrition with enough protein and micronutrients and supplementation if appropriate and necessary. Reaching an ideal body composition and maintaining an ideal body weight will not only improve the symptoms of RA but also decrease the risk for developing cardiovascular disease and therefore improve their prognosis. Educating the patient on healthy eating and appropriate supplementation and addressing the problem of unproven CAM use is also very important. The successful, timely management of patients with RA depends on the involvement of a range of health care professionals, according to the individual patient’s needs. An intra-professional approach is very important and includes not only the dietitian but also physiotherapists and occupational therapists that can work out exercise regimens and improve the range of movement as well as increase physical activity levels. Support groups are another important part of improving the quality of life of persons with RA and can serve as an access to this patient group for targeted education and initiatives. Government, pharmaceutical companies, rheumatologists and medical aids should work together to create more awareness about RA and evidence-based practice in order to limit debilitation and to increase quality of life for these patients.

Recommendations for future studies include nationwide research on nutritional and anthropometrical status of RA patients in order to determine if the high obesity seen in this study is prevalent in the rest of the country. Future studies should also include biochemical markers to detect the micronutrient status of RA patients in SA as well as the dietary intake in order to determine a complete picture of the nutritional status of RA patients. Studies should look at the possibility that the presence of food allergies could exacerbate RA symptoms. Experimentally controlled studies relating to the effects of different types of diets (e.g. elimination, vegan, fasting, etc.) on the symptoms of RA and which patients are likely to benefit the most are needed. Another area for research is the effects of supplementation with antioxidants and other micronutrients as well as nutritional supplements such as chondroitin, glucosamine, gamma linolenic acid and proanthocyanidin.

In conclusion, this study highlights that it is very clear how important the role of the dietitian is in the management of RA and can undoubtedly improve the quality of life and symptoms, decrease overall medical costs and deliver improved standards of care for those living with RA.
References


34. Díaz-Borjón A. Guidelines for the use of conventional and newer disease-modifying antirheumatic drugs in elderly patients with rheumatoid arthritis. Drugs & Aging 2009; 26(4); 273-293.


82. Robert OH. Practical Applications of Fish Oil (omega-3 Fatty Acids) in Primary Care. JABFP 2005; 18: 28-36.


ADDENDA
Addendum A. Questionnaire – English

Questionnaire

BODY COMPOSITION OF RHEUMATOID ARTHRITIS PATIENTS AND THEIR PERCEPTIONS AND PRACTICES REGARDING DIET, NUTRITIONAL SUPPLEMENTS AND OTHER TREATMENTS.

A. Personal information

1. Date of birth: ___________________________________

2. Sex:  □ Female (F)  □ Male (M)

3. Rheumatoid Arthritis duration: ____________________________________________

4. Any other diseases/conditions present?  Yes (y)  No (n)
   4.1. If yes, specify:
   HPT    Hyperchol    DM    OA    Gastric    SE    HD
   ______________________________________________________________________________
   ______________________________________________________________________________

5. Any diagnosed food allergies/ history of food allergies?  Yes  No
   5.1. If yes, specify:
   Please tick appropriate box(es)
   Fish    Wheat    Other, specify:________________
   Seafood    Eggs
   Peanuts    Tree nuts
   Milk    Soya

6. Have you lost or gained any weight since you have been diagnosed with RA?  Yes  No
   6.1. If yes, brief weight loss/gain history:
   ______________________________________________________________________________
   ______________________________________________________________________________

7. Are you a smoker/ previous smoker?  Yes  No
   7.1. If yes, for how many years?
   ______________________________________________________________________________
   ______________________________________________________________________________

8. What is your highest level of education?
   Grade: ________ (1-12)
   Degree/Diploma (13)
   Postgraduate degree (14)
   No education (15)
B. Perceptions and Practices

1. Do you think certain foods *improve* your symptoms?  Yes (y)  No (n)  Don't know (d)

1.1. If yes, which foods do you think improve your symptoms?

**Please tick appropriate box(es)**

<table>
<thead>
<tr>
<th>Wholewheat products</th>
<th>Sugar</th>
<th>Dairy and dairy products (yogurt, cheese, etc.)</th>
<th>Fruit</th>
<th>Vegetables</th>
<th>Red meat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Do you think certain foods *worsen* your symptoms?  Yes  No  Don't know

2.1. If yes, which foods do you *think* worsen your symptoms?

**Please tick appropriate box(es)**

<table>
<thead>
<tr>
<th>Wholewheat products</th>
<th>Sugar</th>
<th>Dairy and dairy products (yogurt, cheese, etc.)</th>
<th>Fruit</th>
<th>Vegetables</th>
<th>Red meat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Do you *avoid* certain foods that you think might make your symptoms worse?  Yes  No

3.1. If yes, which foods?

**Please tick appropriate box(es)**

<table>
<thead>
<tr>
<th>Wholewheat products</th>
<th>Sugar</th>
<th>Dairy and dairy products (yogurt, cheese, etc.)</th>
<th>Fruit</th>
<th>Vegetables</th>
<th>Red meat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.2. If yes, do you replace that type of food with any other type of food or supplement in order to replace the nutrients of the food you have excluded?  Yes  No

3.3. If yes, specify:
4. Do you increase your intake of any specific foods to improve your symptoms?  Yes  No

4.1. If yes, specify:

- Whole wheat products
- Chicken & Poultry
- Refined carbohydrates (white bread, pastries, etc.)
- Fish
- Sugar
- Seafood (other than fish)
- Dairy and dairy products (yogurt, cheese, etc.)
- Spices
- Fruit
- Tomatoes
- Vegetables
- Alcohol, specify:__________________________
- Red meat
- Other, specify:__________________________

5. Do you think medication can improve your symptoms?  Yes  No  Don’t know

6. Do you use any medication to treat your Rheumatoid Arthritis?  Yes  No

6.1. If yes, which medications?

Please tick appropriate box(es)

- Pain medication (Paracetemol, Aspirin, Morphine, Codeine, etc.)
- Steroids (Cortisone, Prednisone etc.)
- NSAIDS (Diclofenac (Voltaren), Ibuprofen, Celecoxib, etc.)
- DMARDS (Methotrexate, Azathioprine, Chloroquine, Golimumab, Leflunomide Cyclphosphamide, Cyclosporin, etc.)
- Biologic agents

6.2. Is the medication prescribed by your doctor/ rheumatologist?  Yes  No

6.3. Do you always take the medication which is prescribed to you by your doctor/ rheumatologist?  Yes  No

6.3.1. If no, how often do you NOT take the medication? Specify:

6.4. Do you use any medication which has not been prescribed by your doctor/ rheumatologist?  Yes  No

6.4.1. If yes, specify:

7. Do you think nutritional supplements can improve your symptoms?  Yes  No  Don’t know

7.1. If yes, which nutritional supplements do you think improve your symptoms?

Please tick appropriate box(es)
8. Do you take any nutritional supplements to *treat* your Rheumatoid Arthritis?  Yes  No

8.1. If yes, specify:

<table>
<thead>
<tr>
<th>Please</th>
<th>tick</th>
<th>appropriate</th>
<th>box(es)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omega – 3 Fatty Acids</td>
<td></td>
<td>Selenium</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td></td>
<td>Zinc</td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td></td>
<td>Magnesium</td>
<td></td>
</tr>
<tr>
<td>Folic acid</td>
<td></td>
<td>Niacin</td>
<td></td>
</tr>
<tr>
<td>B – Carotenoids</td>
<td></td>
<td>Other, specify: ____________________________</td>
<td></td>
</tr>
<tr>
<td>Vitamin B complex</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

9. Have you ever heard of or know what *complementary and alternative medicines or therapies* (such as Glucosamine, Chondroitin, Gamma Linolenic Acid, Homeopathy, Chiropractor or Acupuncture) is?  Yes  No

9.1. If yes, Do you think *complementary and alternative medicines or therapies* can *improve* your symptoms?  Yes  No  Don’t know

9.1.1. If yes, which *complementary and alternative medicines or therapies* do you think can improve your symptoms?

<table>
<thead>
<tr>
<th>Please</th>
<th>tick</th>
<th>appropriate</th>
<th>box(es)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucosamine</td>
<td></td>
<td>Chiropractor</td>
<td></td>
</tr>
<tr>
<td>Chondroitin</td>
<td></td>
<td>Acupuncture</td>
<td></td>
</tr>
<tr>
<td>Gamma Linolenic Acid</td>
<td></td>
<td>Magnets</td>
<td></td>
</tr>
<tr>
<td>Thunder God Vine</td>
<td></td>
<td>Hydrotherapy</td>
<td></td>
</tr>
<tr>
<td>Valerian</td>
<td></td>
<td>Homeopathy</td>
<td></td>
</tr>
<tr>
<td>Zinaxin</td>
<td></td>
<td>Other, specify: ____________________________</td>
<td></td>
</tr>
<tr>
<td>Plant-Mineral Preparations</td>
<td></td>
<td>None of the above</td>
<td></td>
</tr>
</tbody>
</table>
10. Do you take any of the following complementary and alternative medicines/supplements?

Please tick appropriate box(es)

<table>
<thead>
<tr>
<th>Medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucosamine</td>
</tr>
<tr>
<td>Thunder God Vine</td>
</tr>
<tr>
<td>Chondroitan</td>
</tr>
<tr>
<td>Valerian</td>
</tr>
<tr>
<td>Gamma Linolenic Acid</td>
</tr>
<tr>
<td>Zinaxin</td>
</tr>
<tr>
<td>Plant-Mineral Preparations</td>
</tr>
<tr>
<td>Other, specify: _________________</td>
</tr>
<tr>
<td>None of the above</td>
</tr>
</tbody>
</table>

11. Do you use any of the following alternative therapies?

Please tick appropriate box(es)

<table>
<thead>
<tr>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chiropractor</td>
</tr>
<tr>
<td>Acupuncture</td>
</tr>
<tr>
<td>Magnets</td>
</tr>
<tr>
<td>Hydrotherapy</td>
</tr>
<tr>
<td>Homeopathy</td>
</tr>
<tr>
<td>Other, specify:</td>
</tr>
<tr>
<td>None of the above</td>
</tr>
</tbody>
</table>

12. How much do you spend on nutritional supplements per month?

Please tick appropriate box

<table>
<thead>
<tr>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nothing (1)</td>
</tr>
<tr>
<td>R0-100 (2)</td>
</tr>
<tr>
<td>R101-200 (3)</td>
</tr>
<tr>
<td>R201-300 (4)</td>
</tr>
<tr>
<td>R301-400 (5)</td>
</tr>
<tr>
<td>R401-500 (6)</td>
</tr>
<tr>
<td>R501-1000 (7)</td>
</tr>
<tr>
<td>R1001-2000 (8)</td>
</tr>
<tr>
<td>R2001-3000 (9)</td>
</tr>
<tr>
<td>R3001-4000 (10)</td>
</tr>
<tr>
<td>&gt;R4000 (11)</td>
</tr>
<tr>
<td>Other, specify:</td>
</tr>
</tbody>
</table>

13. How much do you spend on complementary and alternative medicines and therapies per month?

Please tick appropriate box

<table>
<thead>
<tr>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nothing (1)</td>
</tr>
<tr>
<td>R0-100 (2)</td>
</tr>
<tr>
<td>R101-200 (3)</td>
</tr>
<tr>
<td>R201-300 (4)</td>
</tr>
<tr>
<td>R301-400 (5)</td>
</tr>
<tr>
<td>R401-500 (6)</td>
</tr>
<tr>
<td>R501-1000 (7)</td>
</tr>
<tr>
<td>R1001-2000 (8)</td>
</tr>
<tr>
<td>R2001-3000 (9)</td>
</tr>
<tr>
<td>R3001-4000 (10)</td>
</tr>
<tr>
<td>&gt;R4000 (11)</td>
</tr>
<tr>
<td>Other, specify:</td>
</tr>
</tbody>
</table>

14. Do you have medical aid?  Yes  No

14.1. If yes, does the medical aid cover all your medication expenses?  Yes  No

14.2. If no, how much do you spend on medication per month?

Please tick appropriate box

<table>
<thead>
<tr>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nothing (1)</td>
</tr>
<tr>
<td>R0-100 (2)</td>
</tr>
<tr>
<td>R101-200 (3)</td>
</tr>
<tr>
<td>R201-300 (4)</td>
</tr>
<tr>
<td>R301-400 (5)</td>
</tr>
<tr>
<td>R401-500 (6)</td>
</tr>
<tr>
<td>R501-1000 (7)</td>
</tr>
<tr>
<td>R1001-2000 (8)</td>
</tr>
<tr>
<td>R2001-3000 (9)</td>
</tr>
<tr>
<td>R3001-4000 (10)</td>
</tr>
<tr>
<td>&gt;R4000 (11)</td>
</tr>
<tr>
<td>Other, specify:</td>
</tr>
</tbody>
</table>

15. Do you do any exercise?  Yes  No

15.1. If yes, what type of exercise do you do?
Please tick appropriate box(es)

- Resistance exercise (weights)
- Cardiovascular exercise (running, walking, swimming, cycling, etc.)
- Stretching
- Physio/OT exercises
- Pilates
- Yoga
- Other, specify: ________________________________

15.2. How often do you exercise?

Please tick appropriate box

- 1 x month (1)
- 2 x month (2)
- 3 x month (3)
- 1 x week (4)
- 2 x week (5)
- 3 x week (6)
- 4 x week (7)
- 5 x week (8)
- 6 x week (9)
- Everyday (10)

15.3. For how long at a time do you exercise?

Please tick appropriate box

- 10-20 mins
- 20-30 mins
- 30-40 mins
- 40-60 mins
- 60-90 mins
- >90 mins
15.4. Who suggested to you that you do exercise?

- Doctor/ Rheumatologist
- Myself/ Internal motivation
- Physiotherapist/ Biokineticist
- Dietitian
- Family or friends
- Other, specify:______________________________________

15.5. Do you do exercise specifically to improve your symptoms of RA?   Yes   No

15.6. If no, why do you do exercise?_________________________________________________

THANK YOU FOR YOUR PARTICIPATION ☺☺ ☺☺
**For Office Use Only:**

Comorbidities/ Medical history of note:

______________________________________________________________________________________
______________________________________________________________________________________
______________________________________________________________________________________

Prescribed Medication (Type & Dosage):

- MTX
- Folate
- Chloroquine
- Sulfasalazine
- Prednisone/Cortisone
- Voltaren
- Ibuprofen
- Paracetemol
- Codeine
- Asprin
- Vit D
- Ca
- Amitryptiline
- Radaq

______________________________________________________________________________________
______________________________________________________________________________________
______________________________________________________________________________________

<table>
<thead>
<tr>
<th>MEASUREMENT TYPE</th>
<th>MEASUREMENTS TAKEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td></td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td></td>
</tr>
<tr>
<td>Triceps skinfold (mm)</td>
<td></td>
</tr>
<tr>
<td>Biceps skinfold (mm)</td>
<td></td>
</tr>
<tr>
<td>Supra-ileac skinfold (mm)</td>
<td></td>
</tr>
<tr>
<td>Subscapular skinfold (mm)</td>
<td></td>
</tr>
</tbody>
</table>
Addendum B. Questionnaire - Afrikaans

Vraestel

LIGGAAM SAMESTELLING VAN RUMATOÏEDE ARTRITIS PASIENTE EN HULLE PERSEPSIES EN PRAKTYKE MET BETREKKING TOT DIEET, VOEDINGSAANVULLINGS EN ANDER BEHANDELINGS.

A. Persoonlike informasie

9. Geboorte datum: ________________________________
10. Geslag: □ Vroulik □ Manlik
11. Rumatoïede Artritis diagnosis datum: ________________________________
12. Enige ander toestande/ siektes teenwoordig? Ja Nee
   12.1. Indien Wel, Spesifiseer:
          HPT Hyperchol DM OA Gastric SE HD
          ____________________________________________

13. Enige gediagnoseerde voedsel allergië/ geskiednis van voedsel allergië? Ja Nee
   13.1. Indien Wel, Spesifiseer:
          Merk af asseblief die korrekte blok(ke)
          Vis Koring Spesifiseer: ____________
          Seekos Eiers                                            Ander,
          Grondboontjies Neute
          Melk Soja

14. Het u enige gewig verloor of opgetel sedert u diagnosis met RA? Ja Nee
   14.1. Indien Wel, kortlikse gewigsverlies/optel geskiedenis:
          ____________________________________________
          ____________________________________________

15. Is u 'n roker/ vorige roker? Ja Nee
   15.1. Indien Wel, vir hoeveel jaar?
          ____________________________________________
          ____________________________________________

16. Wat is u hoogste vlak van opvoeding?
    Graad: ____________________
    Graad/ Diploma
    Nagraadse Graad
    Geen opvoeding
B. Persepsies en Gewoontes

16. Dink u dat sekere kos u simptome kan verbeter? □ Ja □ Nee □ Weet nie

16.1. Indien Wel, wat se kos dink u sal jou simptome verbeter?

Merk af asseblief die korrekte blok(ke)

<table>
<thead>
<tr>
<th>Volkoring produkte</th>
<th>Vis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verfynde Koolhidrate (witbrood, pasteie, ens)</td>
<td>Seekos (Anders as Vis)</td>
</tr>
<tr>
<td>Suiker</td>
<td>Speserye</td>
</tr>
<tr>
<td>Suiwel en Suiwel produkte (jogurt, kaas, etc.)</td>
<td>Tamaties</td>
</tr>
<tr>
<td>Vrugte</td>
<td></td>
</tr>
<tr>
<td>Groente</td>
<td></td>
</tr>
<tr>
<td>Rooi vleis</td>
<td>Spesifiseer:__________________________</td>
</tr>
<tr>
<td>Hoender</td>
<td></td>
</tr>
</tbody>
</table>

17. Dink u dat sekere kos jou simptome vererger? □ Ja □ Nee □ Weet nie

Indien Wel, wat se kos dink u vererger jou simptome?

Merk af asseblief die korrekte blok(ke)

<table>
<thead>
<tr>
<th>Volkoring produkte</th>
<th>Vis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verfynde Koolhidrate (witbrood, pasteie, ens)</td>
<td>Seekos (Anders as Vis)</td>
</tr>
<tr>
<td>Suiker</td>
<td>Speserye</td>
</tr>
<tr>
<td>Suiwel en Suiwel produkte (jogurt, kaas, etc.)</td>
<td>Tamaties</td>
</tr>
<tr>
<td>Vrugte</td>
<td></td>
</tr>
<tr>
<td>Groente</td>
<td></td>
</tr>
<tr>
<td>Rooi vleis</td>
<td>Spesifiseer:__________________________</td>
</tr>
<tr>
<td>Hoender</td>
<td></td>
</tr>
</tbody>
</table>

18. Vermy u sekere kos wat u dink mag jou simptome vererger? □ Ja □ Nee

18.1. Indien Wel, wat se kos?

Merk af asseblief die korrekte blok(ke)

<table>
<thead>
<tr>
<th>Volkoring produkte</th>
<th>Vis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verfynde Koolhidrate (witbrood, pasteie, ens)</td>
<td>Seekos (Anders as Vis)</td>
</tr>
<tr>
<td>Suiker</td>
<td>Speserye</td>
</tr>
<tr>
<td>Suiwel en Suiwel produkte (jogurt, kaas, etc.)</td>
<td>Tamaties</td>
</tr>
<tr>
<td>Vrugte</td>
<td></td>
</tr>
<tr>
<td>Groente</td>
<td></td>
</tr>
<tr>
<td>Rooi vleis</td>
<td>Spesifiseer:__________________________</td>
</tr>
<tr>
<td>Hoender</td>
<td></td>
</tr>
</tbody>
</table>

18.2. Indien Wel, vervang u daadie tipe kos met enige ander tipe kos of aanvulling om die verlore nutriente te vervang? □ Ja □ Nee
18.3. Indien Wel, Spesifiseer:
______________________________________________________________

19. Verhoog u jou inname van enige spesifieke kos om jou simptome te **verbeter**? Ja  Nee

19.1. Indien Wel, Spesifiseer:

- Volkoring produkte  Vis
- Verfynde Koolhidrate (witbrood, pasteie, ens)  Seekos (Anders as Vis)
- Suiker  Speserey
- Suiwel en Suiwel produkte (jogurt, kaas, etc.)  Tamaties
- Vrugte  Spesifiseer:__________________________
- Groente  Spesifiseer:__________________________
- Rooi vleis  Spesifiseer:__________________________
- Hoender  Alkohol,

20. Dink u dat medikasie u simptome kan verbeter? Ja  Nee  Weet nie

21. Gebruik u enige medikasie om jou Rumatoïede Artritis te behandel? Ja  Nee

21.1. Indien Wel, watter medikasies?

**Merk af asseblief die korrekte blok(ke)**

- Pyn medikasie (Paracetemol, aspirin, morphine, codeine, etc.)
- Steroids (Cortisone, Prednisone etc.)
- NSAIDS (Diclofenac (Voltaren), Ibuprofen, Celecoxib, etc.)
- DMARDS (Methotrexate, Azathioprine, Chloroquine, golimumab, lefluNeemide Cyclphosphamide, Cyclosporin, etc.)
- Biologiese agente

21.2. Is die medikasie voorgeskryf deur jou dokter/ rumatoloog? Ja  Nee

21.3. Neem u gereeld die medikasie wat voorgeskryf is deur jou dokter/ rumatoloog altyd in? Ja  Nee

21.3.1. Indien Nie, hoe gereeld neem u die medikasie nie in nie? Spesifiseer:

21.4. Gebruik U enige medikasie wat nie voorgeskryf is deur jou dokter/ rumatoloog? Ja  Nee

21.4.1. Indien Wel, Spesifiseer:

22. Dink u dat **voedingsaanvullings** jou simptome kan **verbeter**? Ja  Nee  Weet nie

22.1. Indien Wel, wat se voedingsaanvullings dink u sal jou simptome kan verbeter?
Merk af asseblief die korrekte blok(ke)

Omega – 3 Vetsure
Calsium
Vitamien D
Folien suur
B – Caratonoids
Vitamien B kompleks
Selenium
Sink
Magnesium
Niasien
Ander,
Spesifiseer: ____________________________

23. Neem u enige voedingsaanvullings om jou Rumatoïede Artritis te behandel?  Ja  Nee
23.1. Indien Wel, Spesifiseer:

Merk af asseblief die korrekte blok(ke)

Omega – 3 Vetsure
Calsium
Vitamien D
Folien suur
B – Caratonoids
Vitamien B kompleks
Selenium
Sink
Magnesium
Niasien
Ander,
Spesifiseer: ____________________________

24. Het u al gehoor van, of weet u van komplimentere en alternatiewe medisyne of terapieë (soos Glucosamine, Chondroitan, Gamma Linolenic Acid, Homopatie, Kiropraktisyn of Akupunktuur) is?  Ja  Nee
24.1. Indien Wel, dink u dat komplimentere en alternatiewe medisyne of terapieë jou simptome kan verbeter?  Ja  Nee
24.2. Indien Wel, wat se komplimentere en alternatiewe medisyne of terapieë dink u kan jou simptome verbeter?

Merk af asseblief die korrekte blok(ke)

Glucosamine
Chondroitan
Gamma Linolenic Acid
Thunder God Vine
Valerian
Zinaxin
Plant-Minerale Preparations
Kiropraktisyn
Akupunktuur
Magnete
Hidroterapie
Homopatie
Ander,
Spesifiseer: ____________________________

Geen van bogenoemde
25. Neem u enige van die volgende komplimentere en alternatiewe medisyne/ aanvullings?

*Merk af asseblief die korrekte blok(ke)*

<table>
<thead>
<tr>
<th>Glucosamine</th>
<th>Valerian</th>
<th>Geen van bogenoemde</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chondroitin</td>
<td>Zinaxin</td>
<td></td>
</tr>
<tr>
<td>Gamma Linolenic Acid</td>
<td>Plant-Mineral Preparations</td>
<td></td>
</tr>
<tr>
<td>Thunder God Vine</td>
<td></td>
<td>Ander,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Spesifiseer:________</td>
</tr>
</tbody>
</table>

26. Gebruik u enige van die volgende alternatiewe terapieë?

*Merk af asseblief die korrekte blok(ke)*

<table>
<thead>
<tr>
<th>Kiropraktisyn</th>
<th>Homopatie</th>
<th>Ander,</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akupunktuur</td>
<td></td>
<td>Spesifiseer:__________________</td>
</tr>
<tr>
<td>Magnete</td>
<td></td>
<td>Geen van bogenoemde</td>
</tr>
<tr>
<td>Hidroterapie</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

27. Hoeveel spandeer u aan voedingsaanvullings per maand?

*Merk af asseblief die korrekte blok*

<table>
<thead>
<tr>
<th>Niks</th>
<th>R301-400</th>
<th>R2001-3000</th>
<th>R2001-3000</th>
<th>Ander,</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0-100</td>
<td>R401-500</td>
<td>R3001-4000</td>
<td>R3001-4000</td>
<td></td>
</tr>
<tr>
<td>R101-200</td>
<td>R501-1000</td>
<td>&gt;R4000</td>
<td>&gt;R4000</td>
<td></td>
</tr>
<tr>
<td>R201-300</td>
<td>R1001-2000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

28. Hoeveel spandeer u aan komplimentere en alternatiewe medisyne en terapieë per maand?

*Merk af asseblief die korrekte blok*

<table>
<thead>
<tr>
<th>Niks</th>
<th>R301-400</th>
<th>R2001-3000</th>
<th>R2001-3000</th>
<th>Ander,</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0-100</td>
<td>R401-500</td>
<td>R3001-4000</td>
<td>R3001-4000</td>
<td></td>
</tr>
<tr>
<td>R101-200</td>
<td>R501-1000</td>
<td>&gt;R4000</td>
<td>&gt;R4000</td>
<td></td>
</tr>
<tr>
<td>R201-300</td>
<td>R1001-2000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

29. Het u 'n mediese fonds? Ja Nee

29.1. Indien Wel, dek die mediese fonds al jou medikasie uitgawes? Ja Nee

29.2. Indien Nie, hoeveel spandeer u aan medikasie per maand?

*Merk af asseblief die korrekte blok*

<table>
<thead>
<tr>
<th>Niks</th>
<th>R301-400</th>
<th>R2001-3000</th>
<th>R2001-3000</th>
<th>Ander,</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0-100</td>
<td>R401-500</td>
<td>R3001-4000</td>
<td>R3001-4000</td>
<td></td>
</tr>
<tr>
<td>R101-200</td>
<td>R501-1000</td>
<td>&gt;R4000</td>
<td>&gt;R4000</td>
<td></td>
</tr>
<tr>
<td>R201-300</td>
<td>R1001-2000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

30. Doen u enige oefening? Ja Nee
30.1. Indien Wel, watter tipe oefening doen u?

*Merk af asseblief die korrekte blok(ke)*

- Weerstand oefeninge (gewigte)
- Kardiovaskulere oefening (hardloop, stap, swem, fietsry, ens.)
- Strek oefeninge
- Fisio/OT oefenings
- Pilates
- Yoga

Ander, Spesifiseer: ________________________________

30.2. Hoe gereeld doen u oefening?

*Merk af asseblief die korrekte blok(ke)*

<table>
<thead>
<tr>
<th>1 x maand</th>
<th>1 x week</th>
<th>4 x week</th>
<th>Elke dag</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 x maand</td>
<td>2 x week</td>
<td>5 x week</td>
<td></td>
</tr>
<tr>
<td>3 x maand</td>
<td>3 x week</td>
<td>6 x week</td>
<td></td>
</tr>
</tbody>
</table>

30.3. Vir hoe lank op ‘n slag oefen u?

*Merk af asseblief die korrekte blok(ke)*

- 10-20 mins
- 20-30 mins
- 30-40 mins
- 40-60 mins
- 60-90 mins
- >90 mins
30.4. Wie het oefening aan jou voorgestel?

- Dokter/ rumatoloog
- Self/ Interniese motiveering
- Fisioterapeut/ Biokinetikus
- Dieetkundige
- Familie of vriende
- Ander, Spesifieer:______________________________________

30.5. Oefen u spesifiek om jou simptome van RA te verbeter?   Ja   Nee

30.6. Indien Nie, waarom oefen jy?_________________________________________________

DANKIE VIR U DEELNAME 😊
**For office use only:**
Comorbidities/ Medical history of Neete:

Prescribed medication (Type & Dosage):
- MTX
- Folate
- Chloroquine
- Sulfasalazide
- Prednisone/Cortisone
- Voltaren
- Ibuprofen
- Paracetemol
- Codeine
- Aspirin
- Vit D
- Ca
- Amitryptiline
- Radaq

<table>
<thead>
<tr>
<th>MEASUREMENT TYPE</th>
<th>MEASUREMENTS TAKEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td></td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td></td>
</tr>
<tr>
<td>Triceps skinfold (mm)</td>
<td></td>
</tr>
<tr>
<td>Biceps skinfold (mm)</td>
<td></td>
</tr>
<tr>
<td>Supra-ileac skinfold (mm)</td>
<td></td>
</tr>
<tr>
<td>Subscapular skinfold (mm)</td>
<td></td>
</tr>
</tbody>
</table>
Addendum C. Consent form – English

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT:
Body composition of rheumatoid arthritis patients and their perceptions and practices regarding diet, nutritional supplements and other treatments.

REFERENCE NUMBER: ___________

PRINCIPAL INVESTIGATOR:
Louise Lombard
Registered Dietician
Master of Nutrition student

ADDRESS:
Division of Human Nutrition
Faculty of Health Sciences
Stellenbosch University
Tygerberg Campus

CONTACT NUMBER:
021 913 6504
0829022281

Dear participant

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is entirely voluntary and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the Committee for Human Research at Stellenbosch University and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

- The study will be conducted at Tygerberg Hospital, Groote Schuur Hospital and at a few private practices in the Cape Metropolitan area. There will be a total of about 250 participants.
- The study aims to determine the body composition of rheumatoid arthritis patients in the private and public health sector in the Cape Metropole as well as their perceptions and practices regarding the use of diet, nutritional supplements, medication, complementary and alternative medicines/therapies and exercise in the treatment of the disease. This will gather important and useful...
information that will help rheumatologists, dietitians and any other healthcare professional in treating rheumatoid arthritis optimally.

- You will need to answer a few questions that the researcher will ask you about your diet, the use of nutritional supplements, medication, any other complementary and alternative medicines or therapies you may be using and exercise.
- Then we will be measuring your weight, height, waist and hip circumference and skinfolds. The skinfolds are measured by using callipers that look like tongs. It might pinch a little but it will not hurt you. The measurements will be taken by a professional and qualified dietician in a private and confidential room where no one will be able to see you.
- We will also need to access your medical records, with your permission, in order to obtain information about your medical history, other health conditions and the medication you are on.
- The questionnaire will only take approximately 10-15 minutes to complete and approximately 15 minutes for the measurements to be taken. The total amount of time will therefore not be longer than 30 minutes.

**Why have you been invited to participate?**

- You have been invited to partake in this study because you have rheumatoid arthritis.

**What will your responsibilities be?**

- You will need to sign this consent form which details all the particulars of the study as explained to you and state that you give your permission for us to gather the information and use it for the research study.
- You will need to answer the questions as explained to you above and allow us to take the measurements.

**Will you benefit from taking part in this research?**

- You will not benefit financially from this research project, but you will benefit in an indirect way since your participation will be of paramount importance in gathering the much needed information that rheumatologists, dieticians and other healthcare professionals need to treat rheumatoid arthritis optimally and make a difference in the lives of RA patients.

**Are there in risks involved in your taking part in this research?**

- There are no risks involved.

**Who will have access to your medical records?**

- Only the researcher will have access to your medical records.
- The information collected will be treated as confidential and protected and your identity will always remain anonymous.

**What will happen in the unlikely event of some form of injury occurring as a direct result of your taking part in this research study?**

- There are no risks involved in partaking in this research project.

**Will you be paid to take part in this study and are there any costs involved?**

- No you will not be paid to take part in the study. There will be no costs involved for you, if you do take part.

**Is there anything else that you should know or do?**

- You can contact Lisanne du Plessis at tel 021 9389175 if you have any further queries or encounter any problems.
- You can contact the Committee for Human Research at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by your study doctor.
- You will receive a copy of this information and consent form for your own records.
Declaration by participant
By signing below, I (name)………………………………………… agree to take part in a research study entitled “Body composition of rheumatoid arthritis patients and their perceptions and practices regarding diet, nutritional supplements and other treatments”.

I declare that:

• I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
• I have had a chance to ask questions and all my questions have been adequately answered.
• I understand that taking part in this study is voluntary and I have not been pressurised to take part.
• I may choose to leave the study at any time and will not be penalised or prejudiced in any way.
• I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (place) ................................................. on (date) ....................... 2011.

Signature of participant

Signature of witness

Declaration by investigator

I (name) ................................................................. declare that:

• I explained the information in this document to ..........................................
• I encouraged him/her to ask questions and took adequate time to answer them.
• I am satisfied that he/she adequately understands all aspects of the research, as discussed above.
• I did/did not use a interpreter. (If a interpreter is used then the interpreter must sign the declaration below.

Signed at (place) ................................................. on (date) ....................... 2011.

Signature of investigator

Signature of witness

Declaration by interpreter

I (name) ............................................................. declare that:

• I assisted the investigator (name) ................................................ to explain the information in this document to (name of participant) ........................................ using the language medium of Afrikaans/Xhosa.
• We encouraged him/her to ask questions and took adequate time to answer them.
• I conveyed a factually correct version of what was related to me.
• I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her question satisfactorily answered.
Signed at *(place)* ........................................... on *(date)* ...........................................2011..

.............................................................. ..............................................................
Signature of interpreter                      Signature of witness
Addendum D. Consent form - Afrikaans
DEELNEMERINLIGTINGSBLAD EN -TOESTEMMINGSVORM

TITEL VAN DIE NAVORSINGSPROJEK:
Liggaam samestelling van Rumatoïede artritis pasiente en hulle persepsies en praktyke met betrekking tot dieet, voedingsaanvullings en ander behandelings.

VERWYSINGSNOMMER: ___________

HOOFNAVORSER:
Louise Lombard
Geregistreede Dieetkundige
Meester Voeding student

KONTAKNOMMER:
021 913 6504
0829022281
ADRES:
Divisie Menslike Voeding
Fakultyd van Gesondheidswetenskappe
Stellenbosch Universiteit
Tygerberg Kampus

U word genooi om deel te neem aan ’n navorsingsprojek. Lees asseblief hierdie inligtingsblad op u tyd deur aangesien die besonderhede van die navorsingsprojek hierin verduidelik word. Indien daar enige deel van die navorsingsprojek is wat u nie ten volle verstaan nie, is u welkom om die navorsingspersoneel of dokter daaroor uit te vra. Dit is baie belangrik dat u ten volle moet verstaan wat die navorsingsprojek behels en hoe u daarby betrokke kan wees. U deelname is ook volkome vrywillig en dit staan u vry om deelname te weier. U sal op geen wyse hoegenaamd negatief beïnvloed word indien u sou weier om deel te neem nie. U mag ook te enige tyd aan die navorsingsprojek onttrek, selfs al het u ingestem om deel te neem.

Hierdie navorsingsprojek is deur die Etiek Komitee oor Gesondheidsnavorsing van die Universiteit Stellenbosch goedgekeur en sal uitgevoer word volgens die etiese riglyne en beginsels van die Internasionale Verklaring van Helsinki en die Etiese Riglyne vir Navorsing van die Mediese Navorsingsraad (MNR).

Wat behels hierdie navorsingsprojek?

- Die studie sal uitgevoer word by Tygerberg Hospitaal, Groote Schuur Hospitaal en by ’n paar privaat praktyke in die Kaapse Metropolitaanse gebied. Daar gaan omtrent ’n totaal van 250 deelnemers wees.
- Die studie se doel is om die liggaam samestelling van Rumatoïede artritis pasiente in die privaat en publieke gesondheids sektor in die Kaapse Metropolitaan te ondersoek asook hulle persepsies en praktyke met betrekking tot dieet, voedingsaanvullings, medikasie, komplimentere en alternatiewe medisyne of terapieë en oefening in die behandeling van die siekte. Dit sal belangrik en nuttige informasie insamel wat rumatoloë, dieetkundiges en enige ander gesondheids professioneel sal help in die optimale behandeling van Rumatoïede artritis.
- Dit is nodig dat u ’n paar vrae beantwoord wat die navorser gaan vra oor u dieet, gebruik van voedingsaanvullings, medikasie, komplimentere en alternatiewe medisyne of terapieë dat U dalk gebruik en beoefening.
- Ons gaan dan u gewig, lengte, middelomtrek en velvoue mates neem. Die velvoue word gemeet met ’n kaliper wat soos ’n tang lyk. Dit gaan dalk ’n bietjie knyp maar dit sal jou nie seer maak nie. Die meetings gaan deur ’n professionele en gekwalifiseerde dieetkundige geneem word in ’n privaat en konfidensiële kamer waar niemand jou sal kan sien nie.
- Ons gaan ook met jou toestemming, toegang tot jou mediese rekords nodig hé om die informasie oor jou mediese geskiedenis, ander gesondheidskondisies en die medikasie wat u neem te verkry.
Die vraestel sal net omtrent 10-15 minute neem om te voltooi en ongeveer 15 minute om die meetings te neem. Die totale tydperk sal dus nie langer as 30 minute duur nie.

Waarom is u genooi om deel te neem?

- U is genooi om deel te neem aan hierdie studie omdat u Rumatoïede artritis het.

Wat sal u verantwoordelikhede wees?

- U sal hierdie toestemmingsvorm moet teken wat al die besonderhede van die studie soos vir jou verduidelik is en verklaar dat u toestemming gee vir ons om die informasie saam te stel en te gebruik vir die navorsing studie.
- U sal die vrae moet antwoord soos bo verduidelik en ons die meetings laat neem.

Sal u voordeel trek deur deel te neem aan hierdie navorsingsprojek?

- U sal nie finansieel voordeel trek van hierdie navorsing projek nie maar U sal wel in ’n indirekte manier voordeel trek aangesien U deelneme van kardinale belang is in die versameling van informasie wat baie nodig is vir rumatoloë, dieetkundiges en enige ander gesondheids professionele om Rumatoïede artritis optimaal te behandel en ’n verskil te kan maak in die lewens van RA pasiente.

Is daar enige risiko’s verbonde aan u deelname aan hierdie navorsingsprojek?

- Daar is geen risiko betrokke.

Wie sal toegang hê tot u mediese rekords?

- Slegs die navorser sal toegang hê tot u mediese rekords.
- Die informasie wat versamel is sal konfidensieel behandel word en U identiteit sal altyd anoniem bly.

Wat sal gebeur in die onwaarskynlike geval van ’n besering wat mag voorkom as gevolg van u deelname aan hierdie navorsingsprojek?

- Daar is geen risikos betrokke in die deelneme van hierdie navorsing projek.

Sal u betaal word vir deelname aan die navorsingsprojek en is daar enige koste verbonde aan deelname?

- U sal nie betaal word vir deelname aan die navorsingsprojek nie. Deelname aan die navorsingsprojek sal u niks kos nie.

Is daar enigiets anders wat u moet weet of doen?

- U kan Lisanne du Plessis kontak by tel 021 9389175 indien u enige verdere vrae het of enige probleme ondervind.
- U kan die Etiek Komitee oor Gesondheidsnavorsing kontak by 021-938 9207 indien u enige bekommernis of klagte het wat nie bevredigend deur u studiedokter hanteer is nie.
- U sal ’n afskrif van hierdie inligtings- en toestemmingsvorm ontvang vir u eie rekords.

Verklaring deur deelnemer
Met die ondertekening van hierdie dokument onderneem ek, (naam) ........................................................., om deel te neem aan ’n navorsingsprojek getiteld “Liggaam samestelling van Rumatoïede artritis pasiente en hulle persepsies en praktyke met betrekking tot dieet, voedingsaanvullings en ander behandelings”.

Ek verklaar dat:
Ek hierdie inligtings- en toestemmingsvorm gelees het of aan my laat voorlees het en dat dit in 'n taal geskryf is waarin ek vaardig en gemaklik mee is.

Ek geleentheid gehad het om vrae te stel en dat al my vrae bevredigend beantwoord is.

Ek verstaan dat deelname aan hierdie navorsingsprojek vrywillig is en dat daar geen druk op my geplaas is om deel te neem nie.

Ek te eniger tyd aan die navorsingsprojek mag onttrek en dat ek nie op enige wyse daardeur benadeel sal word nie.

Ek gevra mag word om van die navorsingsprojek te onttrek voordat dit afgehandel is indien die studiedokter of navorser van oordeel is dat dit in my beste belang is, of indien ek nie die ooreengekome navorsingsplan volg nie.

Geteken te (plek) ........................................ op (datum) ......................... 2011.

............................................................................   .........................................................................
Handtekening van deelnemer Handtekening van getuie

Verklaring deur navorser
Ek (naam) ......................................................... verklaar dat:

• Ek die inligting in hierdie dokument verduidelik het aan .................................................................

• Ek hom/haar aangemoedig het om vrae te vra en voldoende tyd gebruik het om dit te beantwoord.

• Ek tevrede is dat hy/sy al die aspekte van die navorsingsprojek soos hierbo bespreek, voldoende verstaan.

• Ek ’n tolk gebruik het/nie ’n tolk gebruik het nie. (Indien ’n tolk gebruik is, moet die tolk die onderstaande verklaring teken.)

Geteken te (plek) ........................................ op (datum) ......................... 2011.

............................................................................   .........................................................................
Handtekening van navorder Handtekening van getuie

Verklaring deur tolk
Ek (naam) ......................................................... verklaar dat:

• Ek die navorser (naam) ......................................................... bygestaan het om die inligting in hierdie dokument in Afrikaans/Xhosa aan (naam van deelnemer) ................................................................. te verduidelik.

• Ons hom/haar aangemoedig het om vrae te vra en voldoende tyd gebruik het om dit te beantwoord.

• Ek ’n feitlik korrekte weergawe oorgedra het van wat aan my vertel is.
• Ek tevrede is dat die deelnemer die inhoud van hierdie dokument ten volle verstaan en dat al sy/haar vrae bevre digend beantwoord is.

Geteken te (plek) ................................................. op (datum) ................................. 2011.

............................................................................   .........................................................................

Handtekening van tolk                     Handtekening van getuie
Addendum E. Ethics approval from Health Research Ethics Committee of Stellenbosch University

14 December 2010

Mrs L Lombard
Department of Human Nutrition
3rd Floor, Clinical Building

Dear Mrs Lombard

Body composition of rheumatoid arthritis patients and their perceptions and practices regarding diet, nutritional supplements and other treatments.

ETHICS REFERENCE NO: N10/027/02

RE: AMENDMENT 1 APPROVAL

Thank you for your letter of 14 December 2010, requesting ethical approval for Amendment 1 and submitting revised documentation, as listed below.

1. Questionnaires December 2010 Version 2

Amendment 1 was considered by the chairperson

On behalf of the Committee, I am pleased to confirm an approval for the amendment on the basis described in the documentation as revised.

Yours faithfully,

MS CARLI SAGER

RESEARCH DEVELOPMENT AND SUPPORT
Tel: +27 21 938 6140 / E-mail: carli@sun.ac.za
Fax: +27 21 931 3302

14 December 2010 12:57