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Developing a Customised Programme of Exercise to Reduce Fatigue and Improve Societal Participation in Kuwaiti Patients with Multiple Sclerosis

A thesis presented for the degree of

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Declaration

I confirm that the thesis is my own work: and that all published or other sources of material consulted have been acknowledged in notes to the text or the bibliography. I confirm that the thesis has not been submitted for a comparable academic award.

Dedication

To my parents, wife and children
with
love, thanks and gratitude
for their support and patience

Acknowledgements

I must thank all patients who participated in this study.

My deepest thanks and gratitude also goes to my supervisor, Professor Anand Pandyan, School of Health and Rehabilitation, Keele University, for his time, endless support and guidance. I am also indebted to Professor Clive Hawkins and Dr Seema Kalra Department of Science and Technology in Medicine, Keele University, for their help and insightful remarks.

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Abbreviations

ADL: Activities of daily living

AT: Aerobic training

BI: Barthel Index

BBS: Berg balance scale

CNS: Central nervous system

CT: Combined training

EDSS: Expanded Disability Status Scale

ET: Endurance training

EX: Exercise

FSRI: Fawziya Sultan Rehabilitation Institute

FSS: Fatigue Severity Scale

HADS: Hospital Anxiety and Depression Scale

MFIS: Modified Fatigue Impact Scale

MS: Multiple Sclerosis

MVC: Maximal voluntary contraction

PP: Primary progressive

PRT: Progressive Resistant Training

QoL: Quality of life

RCT: Randomised, controlled trial

RT: Resistance training

SP: Secondary progressive

TUG: Timed Up and Go

VO2-max: Maximal oxygen consumption

Contents

Chapter 1.

Abstract

Background: It is now widely accepted that physical training therapy is more reliable and effective than medication in improving fatigue in patients with Multiple Sclerosis (MS). However, efforts are still being made to maximise the benefits of training and hence increase independence and optimise the levels of daily functioning in those patients. The present research is a step in that direction. Towards this end, a 12-week training programme with new design guidelines has been developed and tested on a group of fatigued Kuwaiti MS patients with no previous training experience.

Method: This was a mainly quasi controlled study (ABA design) with an independent assessor studying the effects of 12-week period of exercise on fatigue measure using the Modified Fatigue Impact Scale (MFIS). In addition to fatigue, a range of both quantitative and qualitative data were collected and these were: Expanded Disability Status Scale (EDSS), , Hospital Anxiety and Depression Scale (HADS), Barthel index (BI), Berg Balance Scale (BBS), Timed Up and Go (TUG), the 10-metre walk, the 6-minute walk, and the 9-Peg-hole test. Handgrip strength, knee, elbow and hip flexion and extension and shoulder adduction were also assessed. Two short and semi-structured interviews were administered to obtain additional information on the impact of fatigue on the participants and their attitude towards training.

The training programme consisted of 3x30-minute weekly sessions of resistance or combined training. Initially, combined training consisted of 15 minutes of treadmill walking, followed by 2 sets of 9 stretching and strengthening exercises, 15-20 repetitions. For resistance training, participants performed 3 sets of 15-20 reps of stretching and strengthening exercise. In week

7 onward, treadmill walking time was increased by 5 minutes, and resistance training sets were increased by one.

Results: We recruited 26 patients (mean age 37.54, 8 males and 18 females). Following the 12-week training programme, tests showed significant improvements in fatigue, fine mobility and static and dynamic balance (TUG); short duration walking speed (10m test); exercise tolerance (6-minute walk); balance and fear of fall (BBS); left and right shoulder flexion and adduction, and left and right elbow, knee and hip flexion and extension (MMT). All these gains were still maintained four weeks after the training intervention had been terminated. However, there was no significant effect of training on anxiety and depression (HADS); mobility disability (EDSS); personal basic functional activities (B1); fine motor coordination and finger dexterity (9-HolePeg) and hand grip (JAMAR). Results of the study also show that support for Kuwaiti MS patients is lacking and that the rigid cultural norms place those patients under a great deal of unnecessary stress and pressure

Conclusion: MS patients with mild to moderate disabilities can gain immensely from individualised and customised resistance and combined training programmes. There is good reason to suggest that their gains can be increased even further with improved attitude towards training. Societal stressors are a significant confounder and these need to be addressed before an randomised controlled trial is carried out.

Chapter 1: Introduction

1.1. Statement of the problem

Multiple Sclerosis (MS) is a chronic, progressive and degenerative disease that affects the central nervous system, CNS (Mumford et al., 1992). To this day, no curative treatment for MS has been found, and its sources and causes remain unknown (Compston and McDonald, 2005). The disease is usually associated with a wide range of impairments including, muscle weakness (Ng et al., 2004), sensory dysfunction (Thoumie and Mevellec, 2002), movement incoordination (Cattaneo et al., 2002), spasticity (Paisley et al., 2002), anxiety, depression, and fatigue (Schwid et al., 2002). Of these, fatigue is often described as one of the most common and debilitating symptom (Chatterton et al., 2006). It is reported to have a negative impact on the patient's ability to perform physical or mental activities (Flensner and Lindencrona, 2002), bring a lower quality of life (Amato et al., 2001), lead to unemployment (Jarandhan and Bakshi, 2002); cause distress and psychological disorders (Colosimo et al., 1995; Kroencke et al., 2000); generate low levels of motivation and self-esteem (Fisk et al., 1994), and result in disability and neurological impairment (Schwartz et al., 1995). To combat fatigue, a variety of psychological, psychosocial and pharmacological interventions have been traditionally prescribed (Krupp, 2003), and patients were, until recently, advised to avoid unnecessary physical activities so that they preserve the little energy they have in order to perform essential every day activities, and/or for fear that unnecessary physical effort might provoke MS symptoms and relapses (Solari et al., 1999). However, as the exact causes of MS fatigue are not known, the effect of conventional therapies has been modest and even controversial (Bethoux, 2006; Krupp, 2003).

Contrary to the traditional view that physical training for MS patients might exacerbate fatigue and provoke other symptoms of the illness (Freeman et al., 1997; Ponichtera, 1993), it is now widely accepted that exercise has no deleterious effect on patients with mild to moderate disability (Taylor et al., 2006), and that many of those patients can actually benefit from exercise in terms of reduced fatigue, increased independence and levels of daily functioning (Rasova et al., 1006), and improved quality of life (Turner et al., 2009; Romberg et al., 2005). Nevertheless, findings of studies on the impact of exercise on MS fatigue are somewhat confusing (Dalgas et al., 2010). For, whereas some researchers find little or no positive impact of exercise (Van den Berg et al., 2006; Klieff and Ashburn, 2005), others report positive results though with different levels of improvement (Rasova et al., 2006; Oken et al., 2004). Indeed, given the fact that no consensus has been reached on the definition of fatigue or on a core set of outcome measures to be implemented in experimental trials, it is not surprising that those confusing findings are obtained. Added to the question of lacking consensus, it is to be noted that in almost all studies on exercise for MS fatigue, the intensity of exercise is not clearly described in terms of customisation and duration (Dalgas et al., 2008). Furthermore, although patients' abilities and needs as well as their perceptions of exercise and what they feel about it are important determinants of the outcomes (Dodd et al., 2006), researchers hardly pay any attention to those perceptions, feelings and needs. There is also the possibility that some participants in some trials are not fatigued or are already engaged in supervised or unsupervised physical training activities. All these failings in experimental designs can, no doubt, result in biased and distorted outcomes. Hence, there remains the question as to whether or not it would be possible to maximise the benefits of physical training if concerns over those shortcomings were addressed. The present research is an attempt to answer this question.

1.2. Importance of the research

In the literature on MS, the negative effects of the disease on the patients' activities of daily living, and hence their mood and quality of life, are widely reported. Because physical activity is usually restricted in many of those patients, their social and recreational activities are compromised, the reduced sense of control they experience can lead to depression and exacerbations, cardiovascular diseases and other illnesses can develop as a result of immobility, and they become more and more dependent on others for help. Those patients may have more than one reason to avoid un-necessary physical effort. The most obvious of those reasons is that they may be trying to conserve energy for essential tasks and also minimise the potential risk of exertion. The irony is that contrary to the understanding of those patients, reducing physical activity can lead to harmful physiological and psychological consequences, and optimising it can be an effective strategy in coping with their condition. In fact, it is now widely accepted that exercise has no harmful effects and that it can increase independence in MS patients and improve their mood and quality of life. If we manage to persuade those patients to engage in physical activity and, at the same time, succeed at maximising the benefits of exercise, this will be one of greatest achievements. The present study is a step in that direction.

1.3. Study aims and objectives

The present study has two objectives, one is primary, and the other is secondary. The former is to assess the effects of a supervised training programme on fatigue in a sample of MS patients. The latter is to explore the attitude of those patients towards physical training and the impact of fatigue on their daily living activities. Closely related to the former objective is to assess the impact of training on muscle strength, gait and functional performance in the participants. To achieve these objectives, a number of aims have to be identified and met.

1. Developing an appropriate and informed exercise protocol.
2. Determining the set of outcome measures to be employed.
3. Implementing the training programme and evaluating its effects.

Information obtained through an exploratory pilot study together with that obtained from a wide range of secondary data sources, including specialised journals, articles and experimental studies, enabled the present writer to make informed decisions as to: the type, duration and intensity of the training programme to be implemented, the study sample, and data collection tools and analysis. These issues are considered in some detail in Chapter 5, and the rationale behind the decagons made throughout the study is given in different parts of the paper. Meanwhile, it suffices to note that the present study wanted to identify participants who were fatigued, had no prior training experience, were involved in the decision making process as to the type of exercise they wished to perform, and training activities customised to their abilities and needs. Also, for the purpose of the study, both quantitative and qualitative data were obtained through a range of self-report questionnaires, functional tests and semi-structured interviews.

1.4. Scope of the study

This study investigates the relationship between exercise and MS fatigue from a biopsychosocial perspective. The primary aim was to develop an intervention for reducing fatigue. The secondary aims were to investigate the effect of exercise on other impairments, activities in daily activities and social participation. Whilst there is a significant body of research on exercise in MS in a western population there is almost no research within a

Kuwaiti (or Arab) population. In this context the experimental studies planned to be conducted in Kuwait will draw on the lessons learnt from the studies carried out in the Caucasian populations.

1.5. Thesis structure

The present research project is reported in eight chapters. Following this introductory chapter, focus in Chapter 2 is on general issues pertaining to MS. In particular, emphasis is on the nature, possible causes, prevalence, types, symptoms, diagnosis and treatment of MS. A case for the potential benefits of physical training for MS patients is also presented. The chapter concludes with a discussion on barriers to physical activities in MS patients. Chapter 3 entitled, “Literature Review” is focused on MS fatigue, the main theme of the present study. The chapter begins with a discussion on the definition and nature of MS fatigue. Different fatigue measurement scales are then considered and contrasted. The position taken by the present study is that MS fatigue is a multi-faceted rather than a unidimensional symptom. Hence, argument is made in favour of the Modified Fatigue Impact Scale (MFIS) as a reliable measure. The argument is followed by a review of studies on different physical exercise modalities targeting the symptom. The main features of those experimental studies are described, their findings are presented, and lessons learned from them are highlighted. Such lessons should inform the present study and enable the writer to propose a novel approach to physical training to address the MS fatigue problem, and also, put the proposed approach to the test. Perceptions of two samples of patients, a British and a Kuwaiti, about MS fatigue and their attitude towards exercise are explored in Chapter 4. The methodology employed for the purpose of the present research is described in Chapter 5. Results obtained through the utilised data collection instruments are presented in Chapters 6 and 7. The former chapter is concerned with quantitative data obtained through questionnaires and functional measures, and the latter with qualitative information obtained through interviews. Conclusions of the study, critique of the work carried out and suggestions for future directions are presented in Chapter 8.

1.6. Search strategy

To enable the present writer to establish the theoretical framework for this study, a comprehensive literature review activity was performed. For the purpose, four databases (MEDLINE, CINHAL, PEDro, and Sport Discuss) were searched using the following key words on their own or combined with “AND” or “OR”:

1. Multiple Sclerosis
2. MS
3. Demyelination Autoimmune Diseases
4. Autoimmune Diseases of the Nervous System
5. Fatigue
6. Fatigue*
7. Fatigability
8. Muscle Fatigue
9. Lethargy
10. Tiredness
11. exercise therapy
12. Physiotherapy
13. occupational therapy
14. functional therapy
15. physical therapy
16. $therapy
17. physical$
18. physio$
19. training$

20. function$
21. activities of daily living
22. disability of function
23. disability
24. rehabilitation

1 or 2 or 3 or 4
4 or 5 or 6 or 7 or 8 or 9 or 10
11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24

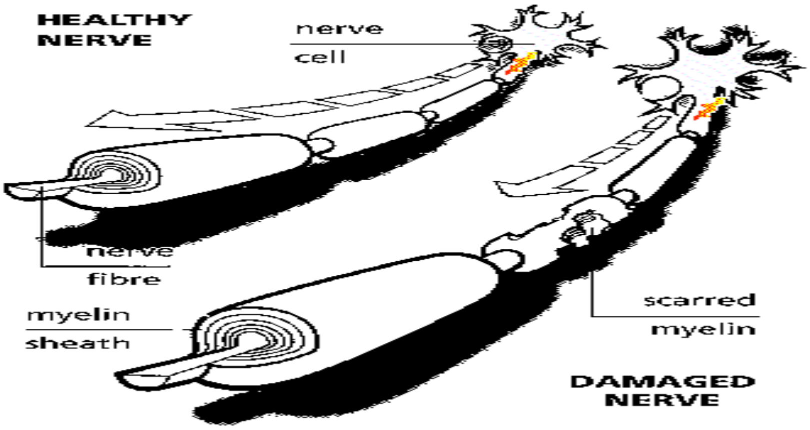
In all, 518 articles have been retrieved, and they were all screened on title and abstract. Many of those papers were discarded because they were duplicates and repetitive. The number of papers left for close inspection was 248. These papers were classified into two groups that serve two different purposes. The first group (n=135) provide general information on MS (i.e. aetiology and epidemiology of the disease, its nature, types, symptoms and treatment). Some papers in this group also present a case of the potential benefits of physical training for MS patients. Main findings of these research papers are presented in Chapter 2. The second group of papers (n=113) are focused only on issues related to MS fatigue and the physical training interventions that target this particular symptom. Reference to these papers is made in Chapter 3 where they are examined in some detail.

Chapter 2: Background

2.1. What is MS?

All our actions from thinking to moving, seeing and breathing are controlled by the central nervous system (CNS) which consists of the brain and the spinal cord (McReynolds et al., 1999). The CNS is made up of billions of nerve cells with fibres, known as axons, extending from those cells to connect them together. Axons are surrounded by a sheath of fatty protein (called myelin) that protects them and makes it possible for messages to be communicated throughout the brain and the body quickly and without interruption (Tyldesley and Grieve, 1996). However, it sometimes happens that the myelin sheaths are damaged or even destroyed in that hard patches or scars (scleroses) develop in multiple areas (Lindsay and Bone, 2004). This condition is called, “multiple sclerosis” (MS), and it results in slowing down or even blocking the nerve messages (Figure 2.1). As a result of this process, varied symptoms that may change over time and vary from one patient to another are triggered in different parts of the body (Lindsay and Bone, 2004). More than often, such symptoms interfere with a range of bodily functions (Heeson et al., 2006), restrict the patient’s ability to engage in physical activities, and result in important consequences for living a full life (Mitchell et al., 2005).

Figure 2.1: Healthy and damaged nerves



Although we now know what causes the symptoms of MS, the causes of the illness, itself, remain a mystery. To complicate things even further, MS has a variable and unpredictable time course of progression (McReynolds et al., 1999). For example, although symptoms such as sensory and cognitive disturbances are somewhat common among MS patients, these can vary greatly across individuals and episodes, and they can make the MS experience a very unique one to each patient (Lindsay and Bone, 2004). Also, whereas it has been found that gradual repair of the damaged tissue and some recovery of functioning is possible in some cases, damage in other cases may occur more quickly than it can be repaired, and the condition may decline sharply over time as more and more damage accumulates (Robinson et al., 2000). It is, indeed, this progressive, variable, and unpredictable nature of the disease that makes MS difficult to manage and, at the same time, interesting with respect to illness representation and coping (Cameron et al., 20002).

2.2. The Aetiology of MS

A number of explanations as to the possible causes of MS have been suggested over the years. In the main, such explanations are genetically and/or environmentally based. As to the genetic factors, evidence from genome analysis shows that genes on at least two chromosomes make a person more likely to develop MS (O'Connor, 1999). In particular, it has been found that a group of genes in chromosome 6, which is associated with the immune system, increase the probability of acquiring the disease (Compston and Coles, 2008). In fact, it is widely believed that MS is an autoimmune disease (Robinson et al., 2000). By that, it is meant that the immune system perceives myelin as an intruder and attacks it. Evidence also suggests that the risk of acquiring MS is higher among the close relatives of a person with the disease than the general population (O'Connor, 1999, Compston, 2002). However, although some studies indicate that MS is likely to occur in generations of families, other studies show that the disease is not hereditary (Ebers et al., 2000).

As to the environmental factors, research shows that MS is prevalent in countries farther away from the Equator (Ebers et al., 1998, Burgess, 2002).For example, whereas it is uncommon in countries such as the Ecuador and Malaysia, it is more common in Britain and Scandinavia (Hauser, 1994). Research has also shown that people born in areas of low prevalence who migrate to areas of high prevalence develop an increased risk of acquiring MS in their new environment. However, such risks diminish if the person moves after the age of 15. This suggests that exposure to environmental factors early in life (e.g. sunlight, diet, sanitation) may predispose a person to develop MS in later years. In this respect, decreased exposure to sunlight has been linked with higher risks of developing MS (Marrie, 2004). There also appears to be a connection between one's lifestyle and likelihood of him/ her acquiring MS. For instance, it has been found that individuals from middle and upper socio-economic classes are more affected by the disease than individuals from other social groups (O'Connor, 1999). A link between MS and viral infections or sexually transmitted diseases has also been suggested (De Sousa et al., 2002).

2. 3. The Epidemiology of MS

Early studies put the numbers of those affected by MS in the world at 1.1 million individuals (Sadovnik and Ebers, 1993). But more recently, it has been reported that those numbers have more than doubled to reach the 2.5 million figure (MS Trust, 2007). It is also noted that the disease is more common in cool temperature climates (i.e. in countries with close proximity to the North Pole or the South Pole) and rare in tropical and semi-tropical countries (Ebers et al. 1998). With reference to the United Kingdom in particular, it is reported that the number of those with MS is somewhat between 85,000 (Robinson et al., 2000) and 100,000 individuals (Thomas et al., 2009) and that approximately 2,500 cases are identified every year (Robinson et al., 2000). According to reports complied in the United Kingdom at the turn of the millennium, prevalence rates varied between 125 per 100,000 people in England and 200 per 100,000 people in Scotland, with Surrey in the south of England having the lowest prevalence and Orkneys in the north of Scotland the highest (MS ,2000) (115 and 224 per 100,000 inhabitants consecutively). Regional variations in the United Kingdom are in line with early research findings in New Zealand where the highest incidents of the disease were found in the southern part of the country, which is cold and close to the south pole (Skegg et al., 1987). Although results similar to these are interpreted by some writers as an indication of a possible correlation with latitude from the equator (Erbes et al., 1998), others suggest that diagnostic miscalculations and methodological differences may be responsible for reported variations between countries and geographic regions (Forbes et al., 1999). In this respect, a more recent study in New Zealand shows that MS levels in the relatively warm northern part of the country may be much higher than previously reported (Chancellor et al., 2003).

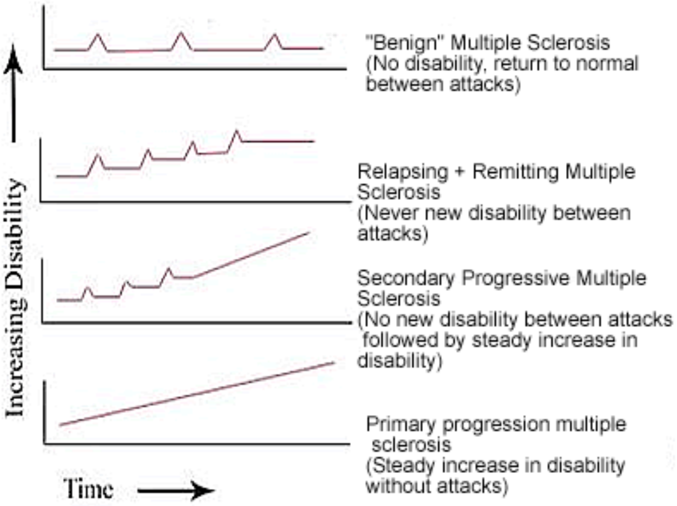
Research has also shown that females are twice more likely to be diagnosed with MS than males (Mohr and Cox, 2001). Reasons for this phenomenon are unknown (Compston, 1998). Further, whereas women tend to be diagnosed young, men are usually diagnosed when they are over 40 (McReynolds et al., 1999).There is also evidence that unlike women, men are likely to develop more severe MS forms (Burgess, 2002). On the whole, however, it has been found that people are usually diagnosed with MS in their productive years, i.e. between the ages of 20 and 40 (Schultz et al., 2004, McCole, 2005). But, in some cases, people have been diagnosed with MS at the age of infancy or when they are in their seventies (Burgess, 2002).

As to whether or not there is a relationship between MS and life expectancy, it has been found that those with the disease generally have a normal life expectancy (Reynolds et al., 1999). However, individuals in the advanced stages of MS may be more susceptible than others to general health dangers such as pneumonia and serious infections (Antonak and Livneh, 1995). This implies that those patients in particular should be encouraged to keep fit and remain physically active. On the question of MS and ethnicity, although the disease affects all racial groups, it is still most frequent in white people (O'Connor, 1999). However, it is argued that geography rather than the racial makeup that is related to higher incidence (Robinson et al., 2000).

2.4. Types of MS

Progression of MS and its symptoms follow different patterns and are highly unpredictable. In fact, unpredictability of the disease is often described as the most anxiety provoking issue among patients (Silcox, 2003). This being so, it is not surprising that the clinical profile and the MS experience is different for everyone (McReynolds et al., 1999). For instance, whereas some patients may regularly experience a number of symptoms that get worse very quickly, others may experience only mild symptoms or no symptoms at all over a long period of time (De Sousa et al., 2002). Despite this problem, researchers still found it possible to distinguish between four broad types of the disease (Figure 2.2.). Generally speaking, the differences between the four recognised types would suggest that differences in illness perceptions may exist.

Figure 2.2: Types of MS. Source: Department of Work and Pension, 2008.



2.4.1 Benign MS

This type of MS accounts for between 15 and 20 per cent of cases and is characterised by infrequent, very mild or relatively minor attacks separated by long periods with no symptoms. Also in this form, the disease progresses slowly, it is even hardly perceptible (Rumrill, 1996), and patients usually experience a full recovery (Reynolds et al., 1999). However, the term, “benign”, does not necessarily indicate how the MS will progress in the future. For example, it has been found that individuals who were initially diagnosed as having benign MS had developed significant disabilities later in the lives (Robinson et al., 2000).

2.4.2 Relapsing- Remitting MS

This is when patients show symptoms of MS (relapse) but then their condition improves and the symptoms between the attacks becomes stable (remission). It is the most common type of MS (Gross and Sinaki, 1987), particularly among young patients (Robinson et al., 2000). Exacerbations may include a number of symptoms, and they are often several months apart. During the attack of MS, symptoms may worsen and it might a few days before they gradually start to improve over a few weeks (Robinson et al., 2000, McReynolds et al., 1999). In the early stages of the disease in particular, some attacks may have a little lasting effect, with a complete or almost complete remission. However, in some cases, attacks may result in permanent loss or reduction in functioning.

2.4.3 Secondary Progressive MS

The majority of individuals with relapsing-remitting MS are likely to start having attacks that last for a longer period of time with remissions between those attacks becoming smaller

(Mohr and Goodkin, 1999). This is known as secondary progressive MS. Early in this stage, disability is hardly noticeable after the attacks, but any problems the patient might already have can gradually start getting worse. For example, mobility becomes more and more restricted and even damage to the cerebellum might occur (Lindsay and Bone, 2004, Silcox, 2003).

2.4.4. Primary progressive MS

Primary progressive MS affects nearly 20% of MS patients, particularly those who get the disease after the age of forty (Robinson et al., 2000). In primary progressive MS, symptoms start getting worse after the first attack, remissions do not occur, patients become gradually and increasingly inactive and disabled, and within a few years or even a few months, loss of sensory performance and serious disability can occur. This type of Ms is also associated with feelings of despair and perceived loss of control (McReynolds et al., 1999).

Apart from the four types of MS mentioned above, reference is sometimes made to an extremely rare form, called “fulminating” or “malignant”. This is an aggressive and persistent form of MS that can render the patient totally incapacitated, and it may even result in death within a few months (Gross and Sanaki, 1987, McReynolds et al., 1999, Robinson et al., 2000).

2.5. Symptoms of MS

Knowing that the central nervous system is highly specialised and that different areas of that system control different functions, it is not surprising that MS has a wide range of symptoms and signs (Reynolds et al, 1999). Depending on the MS form of their condition, it is not also surprising that different patients may experience different symptoms at different stages and times (Buljevac et al., 2003). On the whole, however, researchers have identified marked differences between MS patients and healthy subjects in terms of increased fatigue, depression, cardiovascular disease risks, and decreased function, muscle strength, muscle activation, health related quality of life, VO2max, bone density and daily activity levels (Dalgas et al., 2008; Kersten and McLellan,1996).

Some MS symptoms are, nevertheless, more common than the others. Common symptoms include: fatigue, weakness, depression, anxiety, anger, cognitive impairment, incontinence, and walking and concentration problems (Feinstein, 2004). Less common symptoms include: disinclination, delirium, psychosis, apathy, dementia, emotional and behavioural disturbances (Feinstein, 2004), blurred/double vision, pain at the back of the eye, tingling, ringing in the ear, nerve pain in the face (Compston and Coles, 2002) and sexual problems (McReynolds et al., 1999). Evidently, patients' response to the disease and the kind of help or care they need are determined by the nature of the symptom and its level of severity. For instance, unlike patients with a relapsing or remitting form of the disease who may need little help, those with more progressive forms may require constant attention, and they may become more dependent on others for help (Cheung and Hocking, 2004). It is, however, to be noted that because MS is an unpredictable disease, it becomes difficult to determine the exact pattern of any specific symptom or establish when it will occur and how it will develop (Petajan et al., 1996). Nevertheless, an understanding of the MS symptoms will, no doubt, increase our awareness about their impact on patients and enable us to suggest a care plan (Hadjimichael et al., 2008). In particular, this study is concerned with fatigue as it is often viewed as the most disabling symptom that affects MS patients (this is discussed in Chapter 3). Other factors related to this symptom, particularly muscle weakness, depression and anxiety are considered below.

2.5.1. Weakness

Weakness, or the reduced ability to generate maximal force (Taylor et al., 2006), is often described as another MS major impairment that can lead to disability in people with MS (Frankel, 2001; Ponichtera et al., 1992), depression, anxiety, and hopelessness (White and Dressendorfer, 2004). It also explains why many MS patients limit their daily activities, especially those that require physical effort (White et al., 2000). Weakness and fatigue are closely linked and the one often affects and worsens the other (Kent-Braun et al., 1997). Other MS symptoms can be also affected by weakness. For instance, weak legs can lead to problems with mobility and balance (McCullagh, 2006).

According to some studies, the primary cause of weakness in MS is reduced or interrupted transmission of messages by the nerve damaged as a result of demyelination or axonal degeneration (Ng et al., 2004; White and Dressendorfer, 2004). Other studies show that when muscles are not used, secondary changes to muscles mass occur, and these changes contribute to the weakness of the muscles (Lambert et al., 2000; Ng et al., 2004). In effect, at least as far as MS patients are concerned; lack of physical activity would mean that their condition can get even worse. Put differently, when those patients do not use an already weakened muscle, that muscle will be weakened even further (Fargoso, 2008).

2.5.2. Depression

It has been noted earlier that MS is an unpredictable disease that is characterised by periods of relapse and remissions. This being so, it is to be expected that patients need to make constant behavioural changes in response to their illness and as a means of coping with or adapting to the uncertainties that accompany it. Among other things, depression becomes a possible consequence of such adaptations and changes (MS, 2010). As a matter of fact, there is compelling evidence that every other MS patient will experience at least one episode of clinical depression after getting the disease (McGuigan and Hutchinson, 2005; La Rocca, 2000; Sadovnick et al., 1991). Other studies have found that up to 57 % of MS patients can be depressed at any one time (Shubert and Foliart, 1993) compared to only 6% of the general population(Roth and Fonagy, 1996). The rate could be even higher as it has been found that one in four patients with MS had unrecognised and untreated symptoms of depression (McGuigan and Hutchinson, 2005). There is also evidence that the rate of depression among MS patients is higher than that in other progressive diseases such as osteoarthritis and systemic lupus erythematosus (Creed, 1990). Although research is inconclusive as to when depression exactly occurs, high levels of it are often associated with progressive forms of the disease. It is also generally accepted that it equally affects both males and females (Beal et al, 2007).

Research shows that depression affects MS patients in different ways. In the main, it has been found that MS patients suffer from insomnia and loss of appetite and experience symptoms such as anger, anxiety, irritability, hopelessness (Minden and Schiffer, 1991). Depression in those patients also involves a persistent feeling of sadness accompanied by a sense of low self esteem and guilt (Strenager et al., 1992). It is also reported that some MS patients may even contemplate suicide. According to Turner et al., (2006), as many as 30 % of MS patients have suicidal thoughts at one stage during the course of the illness. It has been also found that suicide rate in MS patients is approximately twice that of the general population (Bonnum et al., 2005). In itself, this suggests that it is rather important for service providers to identify MS patients who are affected by depression so that they can provide them with the support they need.

Researchers fail to agree on the exact source or cause of depression in MS patients. One reason for the controversy is that depression affects patients in different ways (Minden and Schiffer, 1991). Another is that some of the symptoms used to assess it (e.g. insomnia and lack of concentration) are also characteristic of MS (Mohr and Goodkin, 1999). Nevertheless, there is evidence that a relationship exists between depression and disability. For some researchers, this is interpreted to mean that depression occurs in response to specific disease processes and neurological damage (Lynch et al., 2001; Packenham, 1999; Reynolds et al., 1999). On the other hand, there is also evidence that depression can be significantly reduced through counselling and other psychological interventions (Mohr et al., 2001). For some researchers, this means that lack of social support and inability to cope with the illness are at least partially responsible for depression in MS patients (Packenham, 1999). However, there is also the view that depression in MS patients can be attributed to a multitude of factors rather than only to one factor. Proponents of this view suggest that it may be caused by a combination of psychological reactions to illness, disease processes and neurological damage (Mohr and Cox, 2001). But regardless of its cause, most researchers agree that depression results in low self-esteem and reduced energy (Mohr et al., 2001; Robinson et al., 2000; Vercoulin et al., 1996).

2.5.3. Anxiety

Anxiety is yet another common MS symptom that is closely related to depression. In fact, as it is the case with depression, rates of anxiety in MS patients have been found to be higher than those in the general population (Rumrill, 1996) with a prevalence rate of between 19-34% (Srenager et al, 1994). In a study by Feinstein et al., (1999), it was even found that anxiety in MS patients has a higher prevalence rate than depression. The researchers also found that although the disease profiles were similar in their male and female subjects, the rate of anxious women to anxious men was 8:1. They further note that patients who are both anxious and depressed are more somatically preoccupied, socially dysfunctional and may contemplate suicide more than other patients. Research also shows that patients with increased levels of depression are more likely to experience anxiety and less likely to adhere to medication (Mohr and Cox, 2001). This may have a negative impact on their quality of life and daily living activities. It has been also found that anxiety can exacerbate other MS symptoms (Mohr et al., (2000).

2.6. Diagnosis of MS

Diagnosing MS is a complex process that may take a considerably long period of time. Lovelend (1999) quotes many MS patients as having to wait for years before a diagnosis was made. According to Burnfield and Burnfield (1982), this is because the initial symptoms are vague and confusing for both the patient and the neurologist. Traditionally, a neurologist may not confirm diagnosis before the occurrence of two attacks involving different areas of the central nervous system and separated by a period of at least one month. Diagnosis may also involve testing samples of cerebrospinal fluid for abnormalities or electrodes placed on the head to measure the time the brain takes to receive and process information. More recently, magnetic resonance imaging has been utilised for diagnostic purposes (Rolak and Fleming, 2007).

2.7. Measuring MS disability

Two measures of disability and disease progression in MS are widely used, the MS Functional Composite (MSFC), and the Expanded Disability Status Scale (EDSS), (Polman and Rudick, 2010). The MSFC consists of three components that measure upper limbs function, walking speed and cognitive performance, by using a 9-hole peg test, 25 foot timed walk and the Paced Auditory Serial Addition Test (Cutter et al., 1999). By contrast, the EDSS measures neurological impairment across eight functional systems based on a standard neurological examination, walking speed and the symptom history of the patient (Kurtzke, 1983). It has a complex scoring system with scores ranging from 0 (normal neurological examination) to 10 (death). Scores 1 to 3 indicate minimal disability, 3 to 5 moderate disability, and 6 to 9.5 denote severe to more severe disability (Appendix 1). According to Francis et al., (1991), one major limitation of the EDSS is that scores of 4 and above are mainly determined on basis mobility, which means that the scale is insensitive to cognitive and upper limb disabilities. Despite this limitation, the EDSS is widely used in research trials and clinical practice (Sharrack and Hughes, 1996), and it is even described as the gold-standard measure (Kragt et al., 2006).

2. 8. Treatment of MS

Despite ongoing research, no cure has been found for the MS condition, and the gradual progression of the disease and the decline in function in MS patients remain almost inevitable (Lindsay and Borne, 2004). This being so, existing treatments remain largely aimed at slowing the progression of the disease and relieving the various symptoms which arise during the course of the condition. Traditionally, steroid therapy and immunomodulating drugs have been used to treat relapses and reduce their rate and severity (Blasier, 2008, Burgess, 2005). However, although it is true that some of these drugs have been used with some success in treating a number of symptoms, they do not reverse the disease progression or suit all patients. It is also to be noted that traditional therapies remain highly controversial because of the unacceptable side-effects they can cause (Hernandez-Reif et al., 1998). The adverse side-effects include: increased spasticity, nausea, depression, myelgia, fever, headache (Huntley and Ernst, 2000), flu-like symptoms, fatigue, muscle ache, and fever (Lublin et al., 1996). It has been also reported that they can affect blood count levels, provoke stiffness and insomnia (Walther and Hohlfeld, 1999). To state the obvious, such side-effects can have a negative impact on physical and social functioning and decrease the patient's quality of life (Huntley and Ernst, 2000). In recent years, shortcomings of pharmacological interventions have led many researchers and patients to turn to complementary or alternative therapies. In fact, it has been reported that two thirds of MS respondents use alternative therapies because they think that they have not gained much from drugs (Hayes and Cox, 2000). In particular, there has been a growing interest in physiotherapy as a tool to relieve MS symptoms and improve functionality, mobility and quality of life.

2.9. Exercise and MS

Given the progressive nature of MS and its debilitating and unpredictable symptoms, it is not surprising that MS patients usually feel weaker and more depressed than the general population (Romberg et al., 2004). It is not also surprising that those patients are less active than the others and are even often reluctant to engage in simple physical activities (Dalgas et al., 2008). This is either because they feel they need to preserve the little energy they have in order to perform essential every day activities, and/or for fear that unnecessary physical effort might provoke MS symptoms and relapses (Rietberg et al, 2004). It does; however, appear that many of those fears are unfounded or over-exaggerated. In fact, as we shall see later in the discussion, there is evidence that MS patients can actually benefit from physical training.

It has been suggested that physical activity on part of the MS patient would lead to increased body temperature (Petajan and White, 1999), which would, in turn, lead to the exacerbation of the MS symptoms (White et al., 2000). In a study by Guthrie and Nelson (1995), it was found that an increase of 0.5 degree centigrade in body temperature can block nerve impulse conduction in demyelinated fibres and trigger fatigue. However, the authors note that the effect is only temporary. Other researchers have also found that when sensory symptoms were provoked after a bout of exercise, they settled within a short period of time (Smith et al., 2006). On the other hand, there is evidence that increased core and skin temperature did not actually provoke any MS symptoms (Mulcare et al., 2001). Nevertheless, at least as far as heat sensitive patients are concerned, it has been suggested that pre-exercise cooling techniques or training in a shoulder deep pool of water can enhance performance and reduce subjective feeling of fatigue (Petajan and white, 1999).

Fears have also been expressed that exercise might increase spasticity and MS related fatigue. However, although rare cases of spasticity have been recorded in patients undertaking graded exercise tests (Mostert and Kesserling, 2002), there is no evidence that such cases were the result of training (Rietberg et al., 200$). Similarly, at least as far as patients with mild to moderate disability are concerned, there is no evidence to suggest that training has a negative impact on fatigue.

Weakness and respiratory problems in MS patients have been another area of concern for researchers. Yet again, there is no evidence that training would influence the primary cause of weakness, i.e. the reduced central activation (Rasova et al., 2005). In fact, it has been found that inactivity would result in secondary changes to muscle mass (De Haan et al., 2000). As regards patients with respiratory problems, although it is acknowledged that they might encounter breathing difficulties during training, it has been found that their condition can improve if they are given respiratory muscle training prior to the exercise intervention (Fry, 2000).

In summary, contrary to the traditional view that physical training for MS patients might provoke the symptoms of the illness, exercise has been gaining recognition as a tool that has the potential to address major impairments. In fact, plethora of evidence exists in the literature on the benefits of exercise for MS patients with mild to moderate disability in terms of improved muscle activity (Gutierrez et al., 2005; Romberg et al., 2004), improved aerobic capacity (Rasova et al., 2006; Rampello et al., 2007); improved function (Klieff and Ashburn, 2005; Van den Berg, 2006); and improved quality of life (Stuifbergen et al., 2006; Motl et al., 2007). In Chapter 2, studies on the effects of exercise therapy on MS related fatigue will be reviewed in some detail.

2.10. Barriers to physical activity

It has been noted above that MS patients are usually less active than healthy individuals. This is due to the functional limitations and reduced abilities caused by the disease. With the passage of time, these patients find it more and more difficult to adjust to uncertainties and bodily changes, the level of their physical activity and mobility diminishes even further, and their muscles get weaker as a result of disuse and deconditioning (Motl et al., 2009). Hence, it is not surprising that the quality of life in those patients and their mental and physical health are adversely affected (Putman et al., 2006). In fact, some parts of the world, especially in Western Europe and North America, physical activity has now become an important component of MS management and rehabilitation programmes and patients are usually advised to remain physically active at the onset of the disease in order to increase their functional reserve. To persuade and encourage those patients to engage in physical training, it is rather important that barriers to exercising are explored. By "barriers", it is meant "the subjectively perceived costs inherent in undertaking health behaviour" (Becker and Stuifbergen, 2004: 75).

A review of literature on barriers to exercising clearly indicates that the impact of these barriers is more noticeable in MS patients than in healthy individuals. However, although it is true that the majority of MS patients often rate fatigue and impairment as the two main obstacles to exercising, research shows that barriers to health practices are also often related to factors that are not directly associated with the disease itself (Becker and Stuifbergen, 2004). Based on the "Incapacity Status Scale" which provides a measure of functional disability due to MS (Kurtzke, 1981), those barriers can be classified into three groups: those related to the psychological make-up of the patient and his/her personal circumstances (i.e.

intrapersonal barriers), those associated with the patient's relationship with other people (interpersonal barriers), and those to do with the environment. These and other barriers associated with the disease are shown in Table 2.1.

Beginning with interpersonal factors, it is often argued that the experience, attitude and behaviour of health and care professionals play a pivotal role in shaping patients' perception of physical activities. For example, it is reported that patients are less likely to engage in health promoting activities if they feel that they do not receive the proper screening, treatment and attention they need (Putman et al., 2003). They are also less likely to be physically active when they are denied the necessary advice, counselling or information. For instance, it is to be expected that the respiratory and cardiovascular systems are compromised in patients who smoke or have weight control problems. Unless a counselling service is available and tailored to meet the specific needs of those patients (in this case advice on smoke cessation and nutrition), they may still find it difficult to engage in or appreciate physical training (Rimmer, 1999; Nosck, 2008). Lack of encouragement and support from family and friends, social stigmatisation, concerns over appraisal by others, and negative exercise experience are also reported as reasons for decreased physical activity among MS patients. On the other hand, it is reported that patients who used to exercise before diagnosis as well as those with a positive post-diagnosis training experience are more determined than others to remain physically active (Borkoles et al., 2007).

Table 2.1. Barriers to exercising. Adapted from Becker and Stuifbergen, 2004.

a) Disability related factors	d) Intrapersonal factors
1. Fatigue	1. Lack of time
2. Impairment	2. Safety concerns

b) Interpersonal factors 1. Lack of information 2. Lack of support from family and friends 3. Lack of support from health professionals 4. Communication problems 5. No one to provide help c) Environmental factors 1. Problems with facilities 2. Bad weather	3. Interference with duties and responsibilities 4. Financial problems 5. Lack of interest 6. Embarrassment 7. Low self-esteem 8. No faith in training 9. Transportation

Other barriers to physical training can be directly related to the patient's personal circumstances and demographic characteristics. For example, some patients noted that they refrained from exercising because they do not have enough time or because it interferes with other duties and responsibilities. Others described high training costs and transportation as major obstacles to training. It is also reported that young and inexperienced patients as well as those with a modest level of education may find it difficult to obtain or understand information about training programmes and services (Rimmer, 1999; Stuifbergen and Becker, 1994). Patients' attitude towards exercise and their expectations about the outcomes are also powerful predictors of engaging in training. For example, they are less likely to undertake exercise if they lack faith in their abilities or feel that the training programme is not rewarding or too much demanding (Becker and Stuifbergen, 2004).

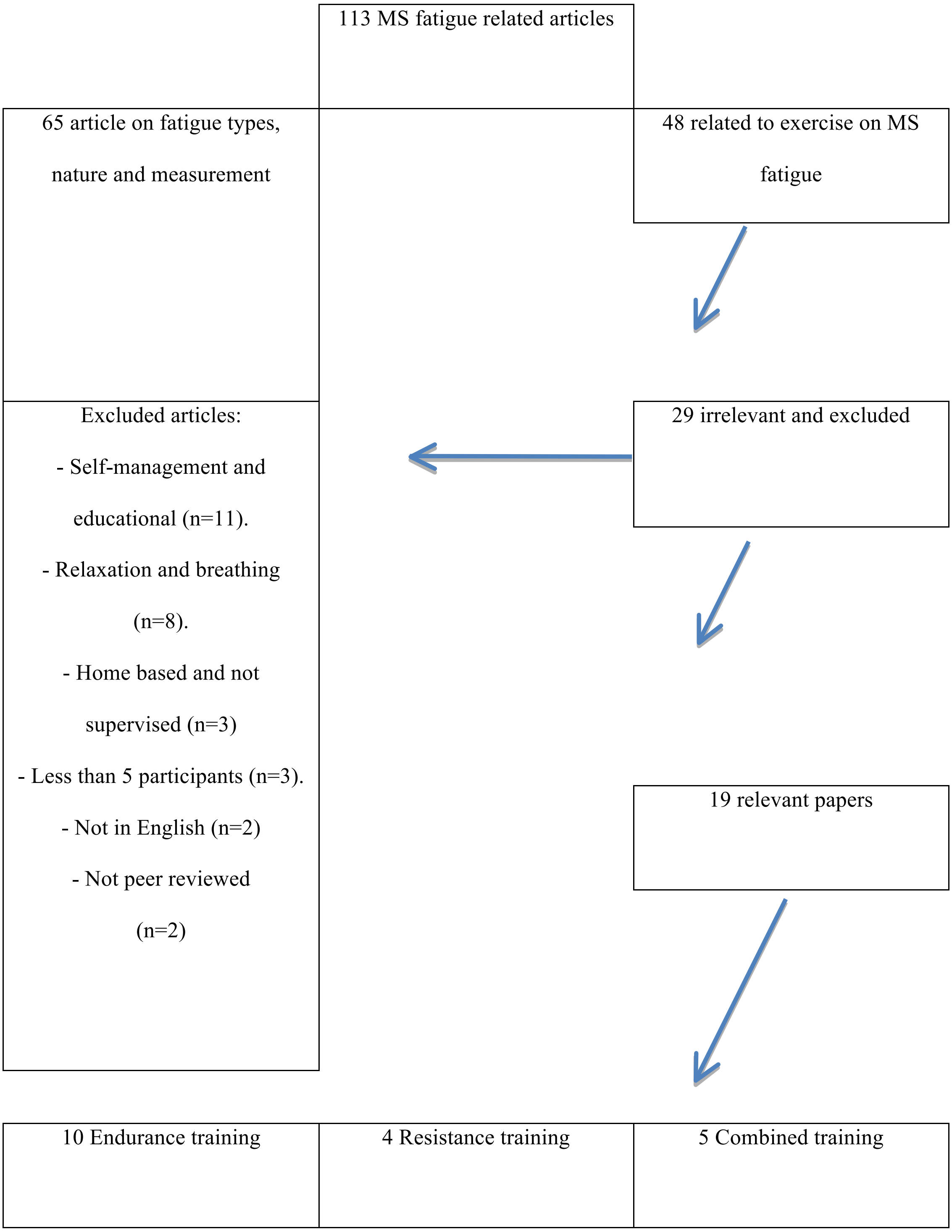
The final set of barriers to participation in exercise programmes is termed "environmental". One example of these barriers is adverse weather conditions (e.g. rain, strong wind and high or low temperature) that make it difficult for patients with disabilities to venture out because of concerns for personal safety. Other examples pertain to training facilities, exercising equipment and accessibility. To say the least, patients may be denied a training opportunity when training venues and programmes are not available, in the first place. The same thing can be said when training facilities are too busy, inappropriate for the patients' disability needs or lacking in specialised equipment. Even when training venues are available and properly equipped, this does not necessarily mean that they can be accessed with ease. For example, some may not have sufficient parking slots, the routes to others may be long or unsafe, and patients may find it difficult to access rest places (Rimmer, 1999; Becker et al., 1989; Borkoles et al., 2008).

Chapter 3: Literature review

3.1. Introduction

It was noted in the opening chapter that literature search revealed 113 MS fatigue related papers and articles. Of those, 65 had discussions on the nature of MS fatigue, its types, related symptoms and measurement tools. All were read, contrasted and summarised. The remaining 48 research papers had discussions on exercise targeting MS related fatigue. A number of these papers were excluded from analysis because they did not meet the operational definition of therapeutic exercise. By that, it is meant that exercise was not prescribed, it did not comprise voluntary muscle contraction or body movement, and the aim of training was not to improve function or reduce fatigue (Taylor et al., 2007). Papers were also excluded if they were not peer-reviewed or published in a language other than English or involved less than five participants in the exercise programme. This left 19 papers that were closely read and considered for analysis (Figure 3.1). Before describing those papers and presenting the findings of the review, it is important that we establish what fatigue is and how it can be measured.

Figure 3.1 Study selection flowchart



3.2 MS fatigue

It is not unusual that some people experience periods of heightened tiredness and exhaustion at some point during the day. Yet, more than often, such an experience is not disabling; it may have little, if any, impact on our physical wellbeing; and we usually recover after a period of rest. However, when we talk about fatigue in MS, we have in mind a completely different type of experience and feeling. What makes MS fatigue different from other types of fatigue or exhaustion is that it is characterised by the sudden loss of energy, the inability to continue an activity, and the relatively long recovery time (Table 3.1). MS fatigue can also affect the patient's disability and physical, social and occupational well being and bring a lower quality of life (Chwastiac et al., 2005; Jarandham and Bakshi, 2002); interfere with work and/or home life (O'Connor, 1999); lead to unemployment; cause distress and psychological disorders; and have a negative impact on the patient's ability to perform physical or mental activities (Stuifbergen and Rogers, 1997). Fatigue is also associated with a sense of loss of control over one's environment; low levels of motivation and self-esteem; and neurological impairments (Bethoux, 2006; Bakshi, 2003).

Although fatigue is common in MS patients, researchers do not agree on a single and unified definition of the symptom. In fact, rather than define it, they tend to describe it in broad and vague terms (Bethoux 2006; Flechenecker, 2006). Examples of those descriptions include: "a piercing feeling of weakness, lack of strength and energy, or total exhaustion" (Kumork and Piezchala, 2006); "a state of exhaustion distinct from depressed mood or physical weakness" (Krupp, 2003); "difficulty initiating or sustaining voluntary effort" (Chaudhuri and Behan, 2004); and "a subjective lack of physical and/or mental energy that is perceived by the individual or the care-giver to interfere with usual or desired activity" (Multiple Sclerosis Council, 1998).

Despite disagreement among researchers on a unified definition of fatigue, they still agree that it is the most debilitating and the most common symptom of the disease. However, research shows that the rates of MS patients who suffer from fatigue are somewhat varied. For, according to some studies, it was reported by 75 to 90 per cent of MS patients with at least 50% of them stating that it was their worst problem (Fisk et al., 1994). Schwartz et al., (1996) find that fatigue is reported by the majority (77%) of patients. Giovannoni (2006) puts the rate at roughly 80%, and in agreement with Forwell et al (2008), he notes that half of those patients describe fatigue as the 'most annoying' symptom. Bakshi, (2003), notes that 40% of patients with MS describe fatigue as the most disabling symptom. Somewhat different estimates are given by Kumork and Piezchala (2006) who state that fatigue is experienced by 40 to 90% of people with MS and other neurological disorders. What is disturbing, however, is that fatigue in MS remains elusive and the exact causes of the symptom and the course it may take are still not well-defined. In the main, this is because of the complexity of factors that contribute to it as well as the lack of defined biological markers (Forwell et al., 2008).

In their discussions on MS, researchers often make reference to different types or categories of the symptom. For example, there are the notions of "central" and "peripheral" fatigue (i.e. whether fatigue is generated in the CNS or in the peripheral tissues) (Chaudhuri and Behan, 2000); "acute" and "chronic persistent" fatigue (i.e. fatigue appearing only recently or being present for more than six weeks for 50% of the time) (Multiple Sclerosis Council, 1998);

“localised” and “global” fatigue (Bakshi, 2003); fatigue as opposed to fatigability (Comi et al., 2001); and “mental” and “physical” fatigue (Flenser Lindencrona, 2002). Other writers talk about more than two types of fatigue. Linyzer (1998) mentions four: objective, subjective, systematic, and asthenic. Coulthard and Vollmer (1995) identify eight types: that caused by sleep disturbance, fatigue related to diet, normal fatigue, deconditioning fatigue, fatigue caused by depression, fatigue resulting from disability, fatigue due to neuromuscular problems, and fatigue unique to MS. However, two broad types of fatigue are encountered most frequently in the literature: primary fatigue (PF) and non-primary or secondary fatigue (NPF). The former refers to the type of fatigue that is related directly to the MS disease process (Forwell et al., 2008) particularly the hardening or scarring of the myelin sheath (McReynolds et al., 1999), inflammation, disturbances in the neuroendocrine system related to fatigue (Kos et al., 2008), or immune dysfunction (Robinson et al., 2000). By contrast, NPF is thought to be influenced by other MS symptoms such as reduced muscle strength and endurance, spasticity, pain, sleep disturbances, cardiac and/or respiratory problems, physical disability, cognitive impairment, and poor mobility (Forwell et al., 2008; Bakshi, 2003; Colombo et al., 2000; McReynolds, 1999; O’Connor, 1999; Clark et al., 1992). Other possible contributors to fatigue include ambient temperature, medication, infections and inadequate diet (MS, 2010). There is also evidence that increased perception of fatigue can be the result of anxiety and depression (Kos et al., 2008). In this connection, it is often noted that because MS symptoms are subjective, vague and hard to measure, fatigue is sometimes misinterpreted as laziness. In itself, this can be a factor in the depression experienced by MS patients (McReynolds et al., 1999; Vercoulin et al, 1996).

In one study conducted by Forwell et al., (2008), it was found that non-primary fatigue was present in 36 of the 50 participants who completed the study (72% of the sample). Of those 36 patients, 34 had a multiple of factors that contributed to fatigue. The most common factors were: sleep problems (58%), mobility limitations (52%), and depression (40%). It was also found that patients isolated with primary fatigue had lower fatigue scores. These findings led Forwell et al., 2008 to the conclusion that in order for MS fatigue to be studied and managed properly, non-primary fatigue factors should be identified and ameliorated before focusing on primary fatigue. In another study, Giovannoni (2006) found that the levels of fatigue in patients with benign MS were the same as the in patients with the non-benign form. However, other studies show that fatigue is not an indicator of the severity of MS (Fisk et al., 1994). Furthermore, although some studies indicate that fatigue occurs during the early stages of the disease, others claim that it is more prominent during the advanced stages (Bergamachi, 1997; Krupp, 1988).

3.3. Measuring MS fatigue

In the early studies on MS, fatigue was rarely recognised as a symptom of the illness, its severity, prevalence or impact on patients were not an issue of concern (Schwid et al., 2000), and it was even thought to have a basically psychological origin (Kurtzkie, 1961). It was not until the 1980s when that thinking began to change. That was when the results of a cross-sectional survey of 656 MS patients revealed that fatigue was present in 78% of those surveyed (Freal et al., 1984). Even more, 50% of the sample equated fatigue with an exacerbation and described it as the most worrying symptom that affected their daily living activities and quality of life. In another study by Murray (1985), 96% of surveyed MS patients listed fatigue as a symptom, over three quarters described it as an abnormal feeling of tiredness, and 40% mentioned that it was a worrying and major problem. It is to be noted, however, that the studies by Freal and Murray did not include healthy controls. This limitation was recognised by Krupp et al., (1988) who interviewed 32 MS patients and 33 healthy adults with the aim of trying to assess the characteristics of MS fatigue and establish the connection between this symptom, physical activity, neurological disability and depression. Results of the study showed that fatigue was more severe in MS patients than in healthy controls. For example, fatigue was reported to interfere with physical functioning by 79% of the MS group and 28% of the healthy controls. It has been also found that MS fatigue can be triggered quite easily and is worsened by heat (Table 3.1). However, the researchers found no relationship between fatigue and neurological disability measured by the Expanded Disability Status Scale (EDSS).

Table 3.1: Characteristics distinguishing fatigue in MS patients and healthy controls. **Source**: Krupp et al., (1988).

Characteristic	MS %	Control	P
Heat worsens it	92	17	<0.001
Prevents sustained physical Functioning	89	0	<0.001
Comes on easily	82	22	<0.001
Interferes with physical functioning	79	28	<0.001
Interferes with responsibilities	67	0	<0.001
Causes frequent problems	63	17	<0.001

The findings of Krupp et al., (1988) triggered more interest in MS fatigue and formed the basis for Fatigue Severity Scale (FSS), one of the earliest fatigue measurement tools. Over the years, large numbers of scales that purport to measure fatigue have been proposed. Dittner et al (2004) identify thirty such scales and classify them into two major groups, unidimensional scales, and multidimensional scales (Tables 3.2a and 3.2b). The former group are designed to arrive at a single score, are relatively brief, easy to administer and more suitable for relatively large studies. On the other hand, the latter group are usually longer and provide more detailed quantitative and qualitative information which makes them suitable for identifying specific aspects of fatigue" (op.cit).

Regardless of their types, fatigue measurement scales have been designed to assess fatigue in different clinical settings. Hence, if a particular measure is proven suitable in a specific clinical condition, this does not necessarily mean that it would be suitable in other groups of patients with different illnesses or experiences. Moreover, not all scales provide evidence of sensitivity to change, some even fail to provide information on reliability, and others have not been validated. Even when some are validated, it is more likely that validation takes place between MS patients and healthy individuals, not between fatigued and non-fatigued patients (Flachenecker et al., 2002). Added to this, many scales do not even make an attempt to investigate the possible effect on fatigue of some important factors such as the age, gender, culture or socioeconomic condition of respondents (Dittner et al., 2004). Indeed, unidimensional or otherwise and validated or not, all fatigue measurement instruments are often suspected of failing to provide a proper and accurate assessment of the symptom (Ford et al., 1997). One reason for their failings is that they often ask respondents to rate fatigue even without defining it (Schwid et al., 2002). Another is that questions put to participants are influenced by the developers' conception of fatigue and answers given are, in turn, determined by the respondent's interpretation of the questions being asked. Furthermore, results obtained through questionnaires are likely to be biased because respondents are usually asked to make retrospective judgements over a long period of time (Schwid et al., 2002). Despite these limitations, self-report questionnaires remain the most appropriate method of measuring MS fatigue (Comi et al., 2001). The question is: which is the most appropriate fatigue assessment approach, the unidimensional or the multidimensional?

In research on MS fatigue, the Fatigue Severity Scale (FSS) has, until recently, been the most popular and frequently used scale. This scale is often branded as a typical unidimensional measure that does not distinguish between motor and cognitive fatigue (Comi et al., 2001, Ford et al., 1998), and is more focused on the physical aspects of the symptom possibly because these are more likely to be stressed by MS patients (Schreurs, 2002, Braley et al., 2010). The FSS consists of only 9 items scored on a seven-point Likert scale. In itself, this makes it easy to administer and analyse and, at the same time, may explain why it is frequently used in MS research and clinical trials (Comi et al., 2001). Other reasons for the popularity of the FSS include its sensitivity to change in clinical conditions over time (Krupp et al., 1989), good concurrent validity and high internal consistency (Pepper et al., 1997). Despite that, the FSS is not without critics.

Contrary to claims made by the developers of the FSS, there is the view that it has limited face validity as a measure of the severity of fatigue (Schwid et al., 2002). Similar concerns are voiced by Petajan et al., (1996) who note that although the FSS was found to distinguish between fatigue experienced by individuals with a medical condition and fatigue experienced by healthy controls, it still failed to show sensitivity to change over time. They further note that the assumption made by statement 4 in the scale (i.e. "fatigue interferes with my physical functioning") would be accepted by patients regardless of what they would be feeling at the time of assessment. In the main, however, critics of the FSS often stress its limitations as a unidimensional approach to measuring fatigue.

Dittner et al., (2004) observe that although unidimensional scales (particularly the FSS) may be useful in screening tests, multidimensional scales are more useful when used as outcome measures in clinical trials. In agreement with this view, the majority of writers find no good reason to suggest that MS fatigue is a single entity. Rather, for those writers, in order for fatigue to be better understood, it has to be considered as a multidimensional symptom (Kos et al., 2008; Pener et al., 2007). In fact, it is not unusual that recent studies on MS fatigue have long discussions on different types, divisions or subdivisions of the symptom with the two main aspects, the mental (or cognitive) and the physical (or motor), being the most frequently visited. Distinction between different components of fatigue is rather important because a patient may feel physically exhausted but mentally alert or he/she may experience different levels of mental and physical fatigue. In itself, this would mean that different types of fatigue may require different intervention therapies (Ford et al., 1998). From this viewpoint, a multidimensional instrument to measuring fatigue becomes the ideal alternative. One such instrument that is now gaining popularity is the Modified Fatigue Impact Scale, MFIS, (Tellez et al., 2005).

Until recently, not much was mentioned in the MS literature about the MFIS. Lately, however, the MFIS has become one of the most widely used fatigue measurement instruments and is currently described as the most reliable of those tools (Tellez et al., 2005; Flachenecker et al., 2002). This tool, which was originally proposed by the American MS Council for Clinical Practice (1998), is a modified version of the 40-item Fatigue Impact

Scale, also known as the Fisk Fatigue Severity Scale (Schwid et al., 2002). Compared to the short 9-item FSS which has a physical focus, the MFIS is more descriptive of fatigue and it consists of 21 items scored on a 0 (never) to 4 (almost always) Likert scale with the total score ranging between 0 and 84 (Appendix 2). 9 of those items are intended to analyse the physical status, 10 the cognitive status, and 2 the psychosocial function (Flachenecker et al., 2002). Put differently, this scale recognises the widely accepted principle of fatigue being a multi-faceted symptom in which different aspects play different roles (Tellez et al., 2005). Added to this, the MFI is reported to have proven high internal consistency as well as validity and reliability in assessing the impact of fatigue on daily living activities and the physical, cognitive and psychosocial domains on MS. It is also easy to use and has good reproducibility (MS Council, 1998; Comi et al., 2001; Flachenecker et al., 2002; Tellez et al., 2005). Indeed, the MFIS addresses a major weakness in quantitative investigation in that it addresses the psychosocial experience of the patient (Mohr et al., 1999). For these same reasons, it is utilised for the purpose of the present research.

No matter how reliable the fatigue measurement scale is, there remains the view that, on their own, self-report questionnaires may not reflect or capture the real experience of the symptoms. For example, there is good reason to suggest that patients' beliefs can influence their perceptions of fatigue, and also, their attitude towards physical activity (e.g. exercise) and its outcomes (Mohr et al., 1999). There is also the argument that fatigue is shaped and influenced by a wide range of factors including, depression, stress, pain, motivation, self-efficacy, social impact, psychological consequences, sleep disturbances, patient’s behaviour and level of activity (Braley et al., 2009; Dodd et al., 2006; Dittner et al., 2004; Comi et al., 2001; Fisk et al., 1994; Schwartz et al., 1993). Because these factors are not fully explored by self-report questionnaires, and also because information about them is better obtained through qualitative data collection techniques, e.g. interviews (Bethoux, 2006; Mohr et al., 1999), it is suggested that our understanding of fatigue would be improved if we used quantitative methods in conjunction with qualitative analysis (Bethoux, 2006; Dodd et al., 2004; MS Council, 1998). In fact, because qualitative analysis has been proven successful in evaluating fatigue and in patients with other neurological conditions (McBurney, 2003), there is now growing interest in applying this form of analysis in conjunction with quantitative analysis in MS research, particularly the areas of physical training and fatigue (Dodd et al., 2006). In this respect, the MS Council (1998) suggests that researchers seek answers to important questions such as: whether fatigue is related to muscle weakness or is precipitated by stress or physical activity, how it progresses during the day, factors that contribute to it and its impact on daily living activities and relationship with other people. Dodd et al., (2006) add that qualitative information obtained on the effect of exercise on patients can provide researchers with insights for developing and implementing training programmes and enable them to identify factors that hinder or facilitate MS patients' participation in health promoting activities. With this in mind, the present study employs both quantitative and qualitative data collection methods.

Table 3.2a. Unidimensional fatigue scales. (Source: Dittner et al., 2004: 160-161)

Scale	Assessed area	Scale items	Scale type	Factors number	Target population	Internal consistency	Test reliability	Cut off score	Sensitivity to change
The Brief Fatigue Inventory (BFI)	Severity	9	11-point Likert	1	Cancer	0.96	-	-	-
Cancer-Related Fatigue Distress Scale (CREDS)	Impact	20	11-point Likert	1	Cancer	0.97	-	-	-
Daily Fatigue Impact Scale (DFIS)	Impact	8	5-point Likert	1	General medical	0.91	-	-	-
Fatigue Severity Scale (FSS)	Impact and functional outcomes	9	7-point Likert	1	Chronic medic	0.88	0.84	3/4	Yes
Functional Assessment of Cancer Therapy Fatigue (FACT-F)	Severity and impact	13	5-point Likert	1	Cancer	0.93	0.90	-	-
Global Vigour and Affect (GVA)	Severity	8	Visual analogue	2	Psychiatric	-	-	-	Yes

May and Kline Adjective Checklist	Phenomenology and severity	16	9-point Likert	1	Non-clinical	-	-	-	-
Pearson Byars Fatigue Feeling Checklist	Severity	26	Checklist	1	Non-clinical	-	-	-	-
Rhotten Fatigue Scale	Severity	1	10-point Likert	1	General medical	-	-	-	-
Schedule of Fatigue and Anergia	Phenomenology and severity	10	5-point Likert	1	Primary care and CFS	-	-	1/2 or 2/3	-

Table 3.2b. Multidimensional Fatigue Scales. (Source: Dittner et al., 2004:162-164).

Scale	Assessed area	Scale items	Scale type	Factors number	Target population	Internal consistency	Test reliability	Cut off score	Sensitivity to change
Cancer Fatigue Scale	Phenomenology and severity	15	5-point Likert	3	Cancer	0.88	0.69	18/19	-
Checklist of Individual Strength (CIS)	Phenomenology and severity	20	7-point Likert	4	CFS	0.90	-	-	Yes
Fatigue, Anergia, Consciousness, Energised and Sleepiness Adjectives (FACES)	Phenomenology and severity	50	4-point Likert	5	Energy-deficient states	0.72-0.97	-	-	-
Fatigue Assessment Instrument (FAI)	Phenomenology, severity and impact	29	7-point Likert	4	General medical	0.70-0.91	0.29-0.69	-	-
Fatigue Descriptive Scale	Phenomenology, severity and frequency	12	Yes/no	5	MS	-	-	-	
Fatigue Impact Scale (FIS)	Impact	40	5-point Likert	3	MS	0.93	-	-	-

HR-Related Fatigue Scale (HRFS)	Intensity and impact	56	5-point Likert	3	HIV	0.94	0.43	3/4	-
Fatigue Questionnaire (FQ)	Severity	11	Yes/no or 4-point Likert	2	CFS	0.88-0.90	-	-	-
Fatigue Symptom Checklist (FSCL)	Severity, impact and direction	13	11-point Likert	3	Cancer	70.94	0.35-0.75	-	-
Multidimensional Assessment of Fatigue (MAF)	Severity, impact and distress	16	Visual analogue and 10-point Likert	5	Rheumatoid arthritis	0.93	-	-	-
Multidimensional Fatigue Inventory-20 (MFI-20)	Phenomenology, severity and impact	20	7-point Likert	5	General medical			-	-
Multidimensional Fatigue Symptom Inventory (MFSI)	Phenomenology and severity	30	5-point Likert	5	Cancer	0.85-0.96	>50	-	-
Piper Fatigue Scale (PFS)	Phenomenology and severity	76	Visual analogue	7	Cancer	0.85	-	-	-

Profile of Fatigue- Related Symptoms (PFRS)	Phenomenology and severity	54	7-point Likert	4	CFS	0.96	0.97	-	-
Revised Piper Fatigue Scale	Phenomenology and severity	22	10-point Likert	4	Cancer	0.97	Yes	-	-
Revised Swedish Occupational Fatigue Inventory	Phenomenological and severity	20	7-point Likert	5	Non-clinical	0.92	-	-	-
Schwartz Cancer Fatigue Scale (SCFS)	Phenomenology and severity	28	5-point Likert	4	Cancer	0.97	-	-	-
Visual Analogue Rating of Physical and Mental Energy	Severity	2	Visual analogue	2	Non-clinical	-	-	-	-
Visual Analogue Scale for Fatigue (VAS-F)	Severity	18	Visual analogue	2	General medical	0.91-0.96	-	-	Yes

3.4. Exercise and MS fatigue

In 3.1, it has been noted that literature search has revealed 19 relevant studies on the effect of exercise on fatigue. These can be classified into three groups: endurance training (ET, n=10 studies), resistance training (RT, n=4 studies), and combined training (CT, n=5 studies).The first training modality, ET, is described as moderate intensity exercise that involves the use of skeletal muscle groups and mainly aims at improving mobility and cardiovascular fitness (Newman et al., 2007). Examples of this type of training include treadmill walking and stationary cycling. On the other hand, resistance training is primarily aimed at improving muscular strength and functional capacity (Dalgas et al., 2008). As regards CT, this refers to two or more exercise types, mainly ET and RT training activities). In recent years, attention has been paid to another form of exercise therapy known as aquatic training which involves carrying out training activities in a water pool. The rationale behind this form of training is that water will prevent body temperature from increasing and, as such, enable trainees to complete or prolong or training activities (Broach and Dattilo, 2001). In the discussion below, all 19 papers on exercise in MS fatigue are described and assessed. Assessment includes judgement as to the characteristics of participants, trial design and length, outcome measures, and rate of reporting on the effect of the training intervention. By contrasting different trials, the present writer should be able to identify and explain areas of strength or weakness in research on exercise for MS fatigue.

3.4.1. Endurance training

The effects of an eight-week bicycling, walking and stretching training programme on balance, fatigue, depression and QoL in MS patients, were investigated by Cakit et al., (2010). Patients were included in the study if they had a definite relapsing remitting or secondary progressive MS, an EDSS score of 6 or below, and the ability to stand upright unaided for a minimum of three seconds. Individuals were excluded if they had an acute exacerbation immediately before or during the training programme, were actively involved in physical therapy treatment or had participated in regular training activities four weeks before the trial, were unable to cycle a static bike, or had persistent fatigue or depression. The 45 patients who took part in the study were divided equally into three groups; a supervised exercise training group an unsupervised home-based training group and a control group. Only 33 of the 45 participants completed the trial: 14 in the supervised exercise training group, 10 in the home-based training group, and 9 in the control group. In the exercise training and home-based training groups, three patients dropped out because of acute exacerbations, and another three for undisclosed or work related reasons. Of the control group, three dropped out for unknown reasons, and three were discharged because of acute exacerbation. The training group had two training sessions a week. Each session began with static bicycle ergometer training, 15 sets of repetitions, followed by 5 minutes walking and 20-25 minutes of balance exercise. The home-based group received the same training as the exercise training group but without cycling, and they were contacted twice a month by phone to monitor their performances and adherence level. Tests were carried out at baseline and immediately at the end of the training programmes, and they included the Becks Depression Index (BDI) to measure depression, the Timed Up and Go (TUG) test to assess dynamic balance, the 10m walk to assess walking speed, the Falls Efficacy Scale (FES) to assess fear of falling, the short form – 36 (SF-36) to assess QoL, and the FSS to measure fatigue. Results of the study showed no improvement in the control group but moderate to good improvement in the training group in gait, depression, balance, and fatigue.

A randomised controlled study by Oken et al., (2004) sought to determine the effects of a structured yoga intervention and an aerobic exercise on the cognitive function, fatigue, mood and QoL in MS patients. For the purpose of this study, they recruited 96 MS patients with an EDSS score of 6 or less. Patients were excluded if they had cardiovascular problems or any other illness that might prevent them from training. However, the researchers note that although they initially planned to exclude subjects 'taking any medication known to affect CNS function or subjects with significant psychiatric diseases', they were forced to abandon their plan because they were 'unable to recruit subjects with such exclusions' (p.2059). To say the least, concomitant medication can be a confounding factor. After screening patients for medical problems, a series of tests were performed including Profile of Mood States, State-Trait anxiety Inventory to test the intensity of feelings of anxiety, short form-36 (SF-36) Health- related QoL, and Multidimensional Fatigue Inventory (MFI). The authors note that they have deliberately chosen to employ the MFI scale. In their view, this is because unlike the popular FSS, the MFI accounts for both physical and mental fatigue. Following the baseline tests, participants were randomly assigned to one of three groups; the yoga training group (YT, n=26), the aerobic exercise training group (ET, N = 21), and a waiting list control group (C, n=22). Yoga classes were held once a week and each class lasted for 90 minutes.

Aerobic training consisted of bicycling on recumbent or dual-action stationary bicycle. It was held once a week and participants were instructed to exercise at the 2 to 3 or very light to moderate intensity on the modified Borg Rate of Perceived Exertion scale. They were also instructed to continue cycling until they were ready to stop because of fatigue. Both the YT and the ET groups were also encouraged to exercise at home. Outcome assessments were performed at the end of the six-month long trial period. Results of the study showed no significant effect on either of the primary outcome measures of cognitive function or alertness. However, the researchers report that the exercise intervention and the yoga intervention produced significant improvements in measures of fatigue (in the ET, physical fatigue 13.2 ± 4.6 at baseline, 10.8 ± 4.0 at the end of the study, mental fatigue 8.3 ± 4.8 at baseline, 7.8 ± 4.4 at the end of the study, and in the YT group, physical fatigue 13.9 ± 3.5 and 12.1 ± 4.4 at baseline and at the end of the study consecutively and for mental fatigue, 11.4 ± 4.7 baseline, and 10.7 ± 4.0 at the end of the study).However, the authors note that the "yoga and exercise classes were significantly modified from the usual community classes " to account for some of the limitations MS patients may have (p.2063). For this reason, they suggest that the results of their study may not be generlisable to typical community yoga or exercise classes. They further note that although subjects in their study were almost all women, the results can be generalised to men. However, they do not provide any justification for their claim.

Impact of an 8-week aerobic training programme on immune-endocrine factors, coordinate functions and QoL in MS patients was assessed by Schultz et al., (2004). To be included in the study, patients had to pass a 30 minute stepwise incremental cycle ergometry test, provided they had a definitive MS condition and scored below 5 on the EDSS. Patients on immune-modulatory treatment were also included unless they had received medication (e.g. interferon) the day before the endurance test. Individuals were excluded if they were suffering from an acute relapse or had severe cognitive deficits or signs of any psychiatric disease. Patients who were eligible to take part in the study (n=39) were randomly assigned either to a bicycling training group (ET, N=23) or a control group (C, n=16). At the baseline and also at the end of the study, a number of measures were employed. These were; the SF-36 and the Hamburg Quality of life Questionnaire in

Multiple Sclerosis (HAQUMAS) to assess QoL, the Profile of Mood States (POMS) to assess affect and mood, HADS to assess depression, the MS Self-Efficacy Scale to assess self-efficacy, and the MFIS to measure fatigue. Members of the ET group had two sessions of bicycle ergometry training a week, thirty minutes a session. Training activities were tailored to their individual abilities. Results of the study showed improvement in the training group in both muscle coordination and disease specific quality of life, but no significant differences were found on the SF-36, POMS, HADS or the Self-Efficacy Scale. The authors conclude Moreover, the training programme had no significant impact on fatigue (MFIS total 23.0 ± 15.4 pre-trial and 21.1 ± 15.0 post trial, $p = 0.33$).

A non-controlled experiment was conducted by Klieff and Ashburn (2005) to investigate the effect of aerobic exercise on the mobility and function in a small group of MS patients. Participants in the trial were eight females aged between 33 and 61 with moderate disability and an EDSS score between 4 and 6. Patients with mild or severe disability or those who had a recent exacerbation or a major medical problem were excluded from the study. Individuals who were unable to cycle a static bike were also excluded. Six of the participants used walking aids. A number of outcome measures were used to assess participants at baseline and at the end of the three month trial. The 10m walk and the 6 Minute Walk (6-MWT) were used to assess walking velocity and endurance respectively, the Gulick Scale was used to establish patients' perception of their disability, as well as the kind of help they needed with their basic daily activities, the FSS to measure fatigue, and the Guys Neurological Disability Scale (GNDS) to measure various aspects of disability, including mood, vision, speech, swallowing, and upper and lower limb function. The training intervention was aimed at enabling subjects to reach their "aerobic training zone "which involved working out 60-80% of their working heart rate. The authors note that because they were concerned that training three times a week might worsen MS related fatigue, they decided to provide training only twice a week. Initially, the first few sessions lasted for 15 minutes each, but they were gradually increased to reach 30 minutes over the first two weeks. Two participants dropped out of the trial, one due to a leg injury and the other because of a relapse. Results of the study showed significant improvement on the GNDS with the mean score reducing from 13 to 9 (p=0.026), and the 6-MWT with the mean distance increasing from 200m to 261m. With reference to fatigue, the FSS failed to reach significance (p=0.058).

Newman et al., (2007) investigated the effects of a four-week treadmill training programme on aerobic fitness and fatigue in MS patients with mild to moderate disability (EDSS scores of the participants are not reported). Patients were included in the study if they were able to walk 10m in less than 60 seconds (with or without walking aids) and use a treadmill safely without support from a physiotherapist or partial body weight support harness. Those who had an exacerbation within eight week before the study or comorbidities that would make it unsafe for them to train were excluded. At baseline and at the end of the study, walking effort was measured by oxygen consumption during treadmill walking at comfortable speed, the Guy's Neurological Disability Scale (GNDS) and the Rivermead Mobility Index (RMI) were used to assess functional mobility, and the FSS was used to measure fatigue. Three of the 19 participants who were originally recruited for the trial dropped out for reasons unrelated to their illness or training, and only 16 patients completed the training programme. Participants were given three training sessions a week. Each session was up to 30 minutes of treadmill training at 55-85% of age predicted maximum heart rate. The researchers report that their short training programme resulted in significant improvements in walking speed and endurance (with the mean 10m time reduced 15.6 seconds to 13.9 seconds, and the 6 -minute walk increased from 88.2m to 94.3m. Changes in reported fatigue levels at baseline and at the end of the trial were not significant (p= 0.178).

In a randomised crossover controlled study, Van Den Berg et al., (2006) investigated the effects of a four week treadmill training programme on mobility and fatigue in MS patients. Patients were included in the study if they had a confirmed diagnosis of MS, were able to walk 10m in less than sixty seconds with or without hands on support, and had the ability to walk on the treadmill with or without assistance. Individuals were excluded if they had a relapse during the two month before the study or suffered from a medical condition that might have a negative impact on their ability to exercise. Sixteen patients took part in the study, and they were allocated either to an immediate training group (n = 8) or a delayed training group (n = 8). Following assessment at baseline, the immediate group received training for four weeks, whereas members of the delayed group acted as controls. After the four weeks period, participants were reassessed, the delayed group underwent training and the final assessment took place after the intervention. Tests used to assess participants included a 10m timed walk, a 2 minute walk, the Rivermead Mobility Index and the FSS. The supervised treadmill walking intervention consisted of three training sessions per week. Walking duration was increased as tolerated up to a maximum of 30m and participants were encouraged to perform at an intensity of 55-85% of age predicted maximum heart rate. Results of the study showed a significant increase in the walking speed in both the immediate and the delayed training groups, a non-significant increase in endurance and no changes in fatigue scores. However, follow up tests showed that training effects went back towards baseline scores. The authors note that the small sample size, short duration of the intervention and rise in environmental temperature during the trial period might have affected their results.

Rasova et al., (2006) examined the effects of different training techniques on muscle performance; fatigue, depression and cardio-respiratory fitness in patients with MS. Patients were excluded from the study if they had an exacerbation during the last four weeks before the study or an acute manifestation of other disease or injury. Individuals included in the study were those who showed no sign of progression of their illness for three months before the experiment, were able to walk independently with or without crutches up to 20m, and had an EDSS score of 6.5 or below. Participants ($n = 95$) were allocated to one of four groups on the basis of 'next patient, next group'. Over the period of 8 weeks, the first group ($n = 24$) received neurophysiologically based therapy (operating on the principles of sensory-motor adaption and learning). They were given two training sessions a week, each lasting up to one hour. The second group ($n = 26$) were given training on a bicycle ergometer, twice a week. In this group, patients with lower levels of disability (EDSS ≤ 3) started training for a period of 5-10 minutes and increased the time gradually up to 20-30 minutes. Patient with a higher level of impairment (EDSS > 3 and ≥ 6.5) started training for a period of 2 minutes and increased to 10-15 minutes. Training speed was approximately 60 RPM, and activities were interrupted in case of an increase in muscle weakness, spasticity or pain. The third group ($n = 19$) also trained twice a week, and they were given a mixed training programme consisting of aerobic exercise (received by the first group) and neurophysiologically based therapy (given to the second group). Members of the fourth group ($n = 16$) were asked to keep their normal daily habits unchanged. The following tests were used to assess patients at baseline and at the end of the study; the Multiple Sclerosis Quality of Life (to assess QoL), the Modified Fatigue Impact Scale (MFIS to measure fatigue), and the Beck Depression Inventory Scale (to assess depression). Respiratory function and physical fitness were also assessed using spirometric parameters on a bicycle ergometer. According to the researchers, results of the study showed improvements in the neurological impairment only in the physiotherapy group and the physiotherapy and exercise group. However, all three training programmes had a positive impact on both depression and fatigue. In light of their study, the researchers suggest that rather than considering subjective fatigue as a limit of load within rehabilitation, it should be the principal point of therapeutic interest. The authors conclude by suggesting that it is rather important for MS patients to undergo a physiotherapeutic programme. In their view, such a programme should be specific to the patient's symptoms and disease progression and applied during the early stages of the disease.

A randomised crossover controlled study was conducted by Rampello et al., (2007) to compare the effects of aerobic training (AT) and neurological rehabilitation (NR) on walking capacity, health related quality of life and fatigue in patients with MS. Participants in the study were 19 patients aged between 20 and 51 and had a mild to moderate disability with an EDSS score of 6 or below. Patients were excluded if they had a relapse within the four weeks before the study, were receiving or had recently received steroid therapy, had a medical condition that would preclude them from participation, or had engaged in a regular exercise programme within two months before the study. Participants in the study were assigned either to an AT exercise group or to a parallel 8 week NR group. Tests were carried out immediately before and after intervention. The disease specific Multiple Sclerosis Quality of Life-54 questionnaire was used to assess health related QoL, the MFIS was used to measure fatigue, a flow pyrometer was used to assess pulmonary function, and the 6MWT was used to assess walking capacity. Over the period of 8 weeks, participants in the AT group received three weekly sessions of training on a leg cycle ergometer. Each session lasted for 30 minutes. On the other hand, the NR programme consisted of three weekly sessions of respiratory exercises and stretching exercise. Each session lasted for 60 minutes. Of the 19 patients who initially took part in the study, only 11 were able to complete the overall crossover controlled parallel study. Four of those who dropped out complained of exercise induced fatigue and breathlessness, and the other four had a relapse. Results of the study showed no change over time in the neurological status of the participants as measured by the EDSS. There were also no changes in lung function and respiratory muscle strength in participants in the two training groups. However, within group analysis showed significant improvements in walking distance (p= .02)and walking speed (p=.02)after the AT programme but not after the NR programme. AT was also found to have a positive effect on health related quality of life, and patients who were most disabled tended to benefit more from AT than from NR. No differences were found between AT and NR in effects on fatigue. The authors admit that their study had a major limitation in that a large number of participants failed to complete the study, which suggests that a type II error might have occurred.

Petajan et al., 1996, carried out an RCT aimed at determining the impact of aerobic training on the quality of life, mood and fatigue in MS patients. Forty six MS patients (15 males and 31 females) took part in the trial. All participants had EDSS score of 6 or less, no medical condition that would preclude their participation in the trial, and none had been involved in a physical activity programme for at least six months prior to the trial. Participants were randomly assigned to an exercise group (EX) or a non- exercise 'control' group (NE). Members of the EX group (n=21) took part in a supervised programme of aerobic training (arm and leg ergometry) for 15 weeks, three sessions a week. Each session lasted for 40 minutes of aerobic training followed by 10 minutes stretching. The 25 patients of the NE group agreed to keep their physical activity at its normal level throughout the entire period of the trial. A graded exercise test and psychological instruments were administered to all participants at baseline, weeks 5 and 10 and the end of the trial. Fatigue was assessed using the Fatigue Severity Scale (FSS). Compared with the NE group, the EX group showed significant improvements in terms of overall fitness, ambulation, mobility and body care. Members of the EX group also demonstrated a non-significant trend toward decreased bad moods. As regards fatigue, although the results showed no significant effect on the FSS, the researchers note that there had been a trend toward improvement. They further note that the training group received more attention than the control group. This is, according to them, a factor that might have affected the study outcomes. Nevertheless, they remain convinced that MS patients can benefit from aerobic exercise, and they suggest encouraging those patients to engage in this type of training.

A four week training programme was designed by Mostert and Kesselring (2002) to investigate the effects of aerobic training on aerobic fitness, fatigue and health perception and activity level in MS patients. Individuals fulfilling the inclusion criteria (n = 26) were randomly assigned either to an exercise group (EX, n = 13) or a control group (C, n = 13). Patients were included if they had a confirmed diagnosis of clinical definite MS with an EDSS score of 1-6.5, had no acute exacerbations during the two months before the study, no disease history or medical conditions that would prevent them from taking part in the experiment and were able to pedal a free standing bicycle ergometer. A battery of tests was administered on participants at baseline and at the end of the study. Spasticity of lower extremities was measured using the modified Ashworth Spasticity Scale, maximum aerobic capacity was determined by using an incremental graded exercise test, heart rate was measured by Polar system, BAECKE Activity Questionnaire was used to measure three dimensions of physical activity (work related activity, sport related activity and leisure time related activity), SF-36 to determine self perception of health status, and the FSS to measure fatigue. The training programme consisted of 5 x 30 minute sessions a week of bicycle exercise with individualised intensity. At the end of the study, the training group showed an increase in the activity level and remarkable improvements of the aerobic threshold and social functioning indexes of the SF-36. The researchers also note that there was a tendency for reductions in fatigue (-14%) in the training group. They also note that compliance to the training programme was quite low (65%).

Table 3.3. Endurance training

Study	Design	Sample	Disability (EDSS)	MS course	Duration /weeks	Frequency (Day/Week)	Training programme	Fatigue Scale	Dependent variables	Main findings
Cakt et al., 2010 (1)	RCT	EX(1): 14 EX(2): 10 C: 9	6.0	RR SP	8	2	EX1: Ergometer bicycling 15 sets of 2min of pedalling. Walking and stretching. EX2: As EX1 but home-based and without bicycling	FSS/4-5	Progressive resistance training, depression, QOL, fatigue.	Improvements in fatigue, gait and depression particularly in the supervised training group.
Oken et al., 2004 (2)	RCT	EX: 21 Yoga EX: 26 C: 22	< 6	NR	26	1	Ergometer bicycling and yoga. Until fatigue or personal goals are reached. Exercise at home encouraged.	MFI	Fatigue, mood, QOL, cognitive function.	No significant impact on depression. Significant impact on vitality and fatigue
Schulz et al., 2004 (3)	RCT	EX: 23 C: 16	<5.0	RR SP PP	8	2	Aerobic bicycle training. 30 min training with max intensity.	MFIS/38	QOL, fatigue, coordinative and psychological function.	Improvement in diseases-specific quality of life. No effect on fatigue.

Kileff & Ashburn, 2005 (4)	NC	EX:8	4-6	NR	12	2	Ergometer bicycling. Cycling steadily increased from 15 min to 30 min over the first four sessions.	FSS/4-5	Mobility, function, disability, fatigue	Significant improvements in disability and mobility. A trend toward an effect on fatigue.
Newman et al., 2000 (5)	NC	EX:19	NR	NR	4	3	Treadmill training: max 30min with up to 3 rest periods	FSS/4-5	Endurance , fatigue	Significant improvement in endurance and walking speed. Reported fatigue levels remained unchanged..
Van Den Berg et al., 2006 (6)	RCCT	EX:8 C: 8	NR	NR	4	3	Treadmill walking: max 30min with up to 3 rest intervals. Intensity increased by increasing walking speed.	FSS/4-5	Mobility, fatigue	Significant improvement in walking speed and endurance. A return to baseline scores at week 12 after training had ceased .No significant changes in fatigue scores.
Rasova et al., 2006 (7)	QE	EX 36 PT: 24 EX+PT : 19 C: 16	<6.0	NR	8	2	Ergometer bicycling.2-10 min increased progressively to reach 30min	MFIS? 38	Disability, depression, QOL, physical fitness, fatigue.	Improvement in neurological impairment in the PT and PT and ET groups. Significant reduction in depression and fatigue in those two groups in addition to the ET group

Rampello et al., 2007 (8)	RCCT	EX: 19 (11 completed the cross-over study)	<6	NR	8 (AT) 8(NR)	3 (AT) 3(NR)	30min Ergometer bicycling. 60min of respiratory and stretching exercises	MFIS/38	Walking capacity, fatigue, QOOL.	Significant impact of aerobic exercise on walking distance and speed. Most disabled patients tend to benefit from training. Insignificant effect on health related QOL. No effect on fatigue.
Patajan et al., 1996 (9)	RCT	EX:21 C: 25	<6.0	NR	15	3	- Arm & leg ergometry. 40min (including 10m warm up & cool down period).	FSS/4-5	Daily function. fatigue, mood, disability.	No significant improvement or change in depression anger or psychosocial factors. No effect of the intervention on FSS
Mostert & Kesserling., 2002 (10)	RCT	EX: 13 C: 13	1-6.5	RR CP RP	4	5	Ergometer bicycling. 30 min	FSS/4-5	QOL, health perceptions, social interaction, fatigue.	Significant improvement in aerobic threshold, vitality and social functioning. No significant impact on fatigue

C, Control group; CP, Chronic Progressive; EDSS, Expanded Disability Status Scale; EX, Exercise Group; FSS, Fatigue Severity Scale; MFI, Multidimensional Fatigue Inventory; MFIS, Modified Fatigue Impact Scale; NC, Non-controlled; NR, Not Reported; PP, Primary Progressive; PT, Physiotherapy; QE, Quasi Experiment; QOL, Quality of Life; RCCT, Randomised Controlled Crossover Trial; RCT, Randomised Controlled Trial; RR, Relapsing Remitting.

3.4.2. Resistance training

MS patients' perceptions about Progressive Resistant Training (PRT) and the factors that might hinder or facilitate participation have been investigated in a qualitative study by Dodd et al., (2006). Participants in the study were seven females and two males aged between below 65. All participants had to demonstrate an ability to walk 200m without assistance, and also, produce a signed consent form from their doctor stating that it was safe for them to engage in PRT. Patients were excluded if they had recently participated in a PRT program or engaged in a physical therapy treatment. They were also excluded if they had an exacerbation immediately before or during the ten-week long training programme.

Training sessions were held twice a week, and they targeted lower and upper extremities, three for the legs and another three for the arms, with patients completing two sets of 10-12 repetitions of each exercise. Each exercise session lasted for nearly one hour followed by 30 minutes to give participants time to cool down and socialise over light refreshments. Soon after the programme, semi-structured interviews were conducted to explore participants' perceptions of PRT and of participating in the study. Participants were also asked to evaluate the benefits of PRT on a 10cm visual analogue scale. On the whole, feedback from participants showed that physical, social and psychological benefits were gained as a result of the training. With reference to fatigue in particular, most participants noted that they felt less fatigued after the programme. However, a few negative but minor outcomes such as aches and pains that had no effect on the training programme were reported. Encouragement, enjoyment, socialisation, knowledge of exercise, positive attitude, determination and seeing signs of progress were all given as reasons behind completing the programme.

Dodd et al., 2011, investigated the effect of a ten-week PRT programme on the walking function and muscle performance in MS patients. Participants in the study were randomly assigned either to a training group (n=36) or a control group (n=35). Patients were included in the trial if they were 18 years or over old, had a confirmed diagnosis of relapsing remitting MS, received medical clearance to take part in the trial, and had mild to moderate walking disabilities (an Ambulation Index score of 2,3 or 4). Patients were excluded from the research if they had benign or progressive relapsing MS, an exacerbation during the two months before the trial, a serious unstable medical condition, or participated in a PRT programme during the six months that preceded the training programme. Twice a week, the training group performed a number of exercises targeting the lower limb muscle (namely, leg press, knee extension, calf raise, leg curl and reverse leg press). Training intensity consisted of two sets of 10-12 repetitions of each exercise. The weight lifted was increased when two sets of 12 repetitions of an exercise could be completed. The two exercise sets were separated by a 2-minute rest period. To control for the social aspects involved in the PRT programme, the control group participated in a purely social programme for one hour each week. After completing the 10-week intervention programme, participants were asked not to continue with training until after the follow-up assessment session (after 12 weeks). Outcome measures were recorded at baseline and at weeks 10 and 22. Changes in walking endurance were measured using the two-minute walk test (2MWT), and changes in muscle strength were determined by the amount of weight lifted in a single seated leg press. Changes in health-related quality of life were assessed using the WHOQoL-Bref, which is a 26-point scale that measures the domains of physical and psychological health as well as social relationships. The MS Spasticity Scale-28 was used to measure changes in muscle stiffness, and the MFIS was used to assess fatigue. As to the results, although PRT did not lead to improved walking performance, it still improved muscle endurance. Further, it did have a significant short-term effect on physical fatigue (-3.9 units, 95% CI -6.6-1.3) and total fatigue (-5.9 units, 95% CI-11.3-0.5) compared with the control group. The authors reported a high compliance rate (92%) to the training programme. The study's major limitation is that only patients with relapsing remitting MS were included.

White et al., 2004, evaluated the effects of an eight-week progressive resistance training programme on lower extremity muscle strength, gait kinematics and self-reported fatigue and disability in MS patients. Participants in the trial (n=8: one male and seven females) were engaged in light physical activity for three months prior to the training programme. EDSS scores of participants ranged between 2.5 and 5.5. Patients using MS disease modifying drugs were included, but those who had cardiovascular, thyroid or gout disorders were excluded. The training programme consisted of two weekly training sessions. Each session was up to 30min.At the beginning of each session, participants performed a warm-up set (5 reps at 40% of maximal voluntary contraction , MVC on each machine)Subjects performed one set of 6-10 repetitions at 5% of MVC during the first two weeks and one set of 10-15 repetitions at 70% MVC in subsequent sessions . Before and immediately after the training programme, an isokinetic dynamometer was used to assess the isometric strength of the quadriceps, hamstring, plantaflexor and dorsiflexor muscle groups. A 25-ft walking test and a three minute step test were used to measure ambulatory function, and the MFIS was used to assess fatigue. Following the training programme, significant improvements were observed in muscle strength as well as in gait kinematics. Following the training programme, significant improvements were recorded in knee extension, plantar flexion and stepping performance. As regards self-reported fatigue, the average score was 32 at baseline but it went down to 26 after training (p=0.05).

Dalgas et al., 2010, used an RCT design to examine the effects of progressive resistance training (PRT) on fatigue, mood and quality of life in MS patients. Participants in the trial were 38 adults who were randomly assigned either to the exercise group (n=19) or the control group (n=19). Of those participants, seven dropped out of the intervention group, one because of back pain as a result of training, and the other six for reasons that were not related to the intervention. Criteria for inclusion in the trial were: definite relapsing-remitting MS; EDSS score between 3.0 and 5.5; ability to walk up to 100 meters; age 18 years or over; and acceptance of diagnosis and treatment. Patients were excluded if they: suffered from dementia or alcoholism, had a pacemaker implanted or a serious medical condition, were pregnant, had an MS exacerbation during the last eight weeks prior to the trial, or had taken systematic resistance training within the last three months that preceded the intervention. The PRT intervention was performed twice a week over a twelve-week period, and it targeted the lower extremities. Each session began with a 5-minute warm up on a stationary bicycle. Participants were then asked to perform five different exercises: leg press, knee extension, hip flexion, hamstring curl and hip extension. During the first two weeks, participants performed three sets of 10 repetitions at a load of 15RM, weeks 3 and 4 three sets of 12 repetitions at a load of 12 RM, weeks 5 and 6 four sets of 12 repetitions at a load of 12 RM, weeks 7 and 8 four sets of 10 repetitions at a load of 10 RM, weeks 9 and 10 four sets of 8 repetitions at a load of 8 RM, and weeks 11 and 12 three sets of 8 repetitions at a load of 8RM. During the intervention, one participant dropped out because training worsened his back pain condition, and six more patients quit due to circumstances not related to the intervention. Data obtained from the remaining 31 patients (training group, n=15, control group, n=16) were used for analysis. The two groups of participants were compared at the start and the end of the intervention, and also, at a twelve-week follow up point. Mood was assessed using the Major Depression Inventory, quality of life was assessed using the SF36, and fatigue was measured using the FSS and the MFI scales. AS regards the results, significant improvements were recorded in the training group (p= <0.05). Significant improvements were also reported in the physical component of the SF-36 in the exercise group (p= <0.05), but no significant differences were recorded in the mental component between the two groups(p=0.09).With reference to the effect of resistance training on fatigue, significant improvements were recorded in the FSS score (p= <0.05), and also, in the general fatigue score of the MFI scale((p= <0.05). However, the authors note that they have chosen a design in which social interaction might have influenced the results. Moreover, it is to be noted that participants in this study were a group of relapsing-remitting MS patients with low EDSS scores. This being so, it would be reasonable to suggest that such patients would tolerate and benefit from resistance training.

Table 3.4. Resistance training

Study	Design	Sample	Disability (EDSS)	MS course	Duration/ weeks	Frequency (Day/Week)	Training programme	Fatigue Scale	Dependent variables	Main findings
Dodd et al., 2006 (11)	NC	EX:9	NR	NR	10	2	Three exercises for the legs and three for the arms. Two sets of 10-12 repetitions of each exercise	Semi-structured in-depth interviews	Perceptions about PRE, fatigue.	Physical, psychological and social benefits reported. Reduced fatigue reported by 7/8 of the sample.
Dodd et al., 2011 (12)	RCT	EX: 36 C: 35		RR	10	2	Exercise targeting lower limb muscles. Intensity consisted of two sets of 10-12 repetitions of each exercise	MFIS	Walking function, muscle performance, fatigue	Increased muscle endurance and small improvements in QOL. Significant short term effect on fatigue.

White et al., 2004 (13)	NC	EX:8	2.5-5.5	RR	8	2	Progressive resistance training (lower extremities). First two weeks: one set of 6-10 repetitions. Last six weeks: one set of 10-15 repetitions	MFIS/38	Lower extremity strength, ambulatory function , fatigue, disability	Significant improvements in muscle strength, gait kinematics and fatigue.
Dalgas et al., 2010 (14)	RCT	EX: 15 C: 16	3-5.5	RR	12	2	5-machine exercise(lower extremities)	FSS/4-5 MFI-20	QOL, depression, fatigue.	Significant effect on fatigue. Long-term effect also recorded on depression and QOL.

C, Control group; CP, Chronic Progressive; EDSS, Expanded Disability Status Scale; EX, Exercise Group; FSS, Fatigue Severity Scale; MFI, Multidimensional Fatigue Inventory; MFIS, Modified Fatigue Impact Scale; NC, Non-controlled; NR, Not Reported; PP, Primary Progressive; PT, Physiotherapy; QE, Quasi Experiment; QOL, Quality of Life; RCCT, Randomised Controlled Crossover Trial; RCT, Randomised Controlled Trial; RR, Relapsing Remitting ;SP, Secondary Progressive.

3.4.3. Combined training

Surraka et al., (2004) conducted a RCT study to investigate the effects of a twenty six week combined endurance and resistance training program, on motor fatigue of knee flexor and extensor muscles in Multiple Sclerosis (MS) patients. Participants in the study were 95 male and female patients with a mild to moderate disability and an EDSS score between 1 and 5.5. Patients were excluded from the trial if they had taken part in any regular or intensive training activity during the last three months before the trial. Patients were also excluded if they had a relapse within four weeks before the baseline tests or a muscoskeletal disorder that would not allow them to complete the programme. At baseline, subjective fatigue was assessed using the FSS, ambulatory ability was assessed by means of a 500m walking test, and motor fatigue of knee flexor and extensor muscles was assessed during a static 30-s maximal sustained muscle contraction. Measures were taken again at week three and week 26 at the end of the programme. Participants were assigned either to an exercise group (n=47) or a control group (n=48). The first three weeks of the training programme consisted of ten supervised exercise sessions, five resistance and five aerobic. Each resistance training session consisted of 10 minutes warming up followed by ten exercises of circuit type with 10-15 repetitions. The aerobic training sessions covered different forms of gymnastic exercises in shoulder-deep water, and each session lasted for 45 minutes, including 10-15 minutes warming up and cooling down period. After the three week supervised training period, participants were asked to continue training at home for another 23 weeks, and they were instructed to keep a diary in which they recorded the duration and intensity of exercise, as well as general information about their condition. Patients' progress and adherence were monitored by regular phone contact. 88 patients (44 in each group) completed the programme, with women scoring a 25% adherence rate higher than men. The results showed that whereas associations were observed with changes in extension fatigue index and EDSS score and mean extension torque, no changes were detected in fatigue index or aerobic or strength exercise activity, mean Ambulatory Fatigue Index, mean FSS or in mean flexion torque. Motor fatigue was reduced in knee flexion (p=0.0014) and extension (ns) only in female, not male exercisers. The authors are of the view that lack of exercise effect in men is not necessarily related to the amount of training. Rather, in their view, reasons related to MS or to individual physiology may explain the difference in exercise effect between males and females. As noted above, this trial lasted for a relatively long period of time and no measures were taken between week three and week 26 when the programme was terminated. This means that some positive effects of exercise might have been hidden because of the progression of the disease. Nevertheless, the authors do agree that they should have applied their test measures more frequently.

Another randomised controlled pilot study was carried out by McCullagh et al., (2008). The aim of the study was to explore the effects of a three-month combined aerobic and arm-strengthening training programme on the Quality of Life (QoL) and fatigue in MS patients. For the purpose of the research, 30 MS patients with mild disability were recruited and randomly allocated either to an exercise training (ET) group or a control (C) group. Of those individuals, only 24 completed the study, ET group, n=12 and C group, n=12. Subjects eligible for participation were those with no history of cardiac, cognitive or psychological conditions and those who had a definite diagnosis of MS and were independently mobile without the use of aids. Exercise training classes were held twice a week, and participants exercised independently once a week. Each session consisted of 2 x 5 minutes warm up and cool down period and 40 minute of training. Training activities included treadmill walking/running, cycling, stair master training, arm strengthening and outdoor walking. Rather than using specific heart rate as a target in training, patients were encouraged to maintain their level of exertion between ‘fairly low’ and ‘somewhat hard’. Members of the control group were visited by a psychotherapist once a month and they were asked to maintain their normal daily life activities. Fatigue was measured using the MFIS, a graded exercise test was used to measure exercise capacity, and QoL was assessed using the Functional Assessment of Multiple Sclerosis scale (FAMS) as well as the Multiple Sclerosis Impact Scale – 29 (MSIS-29). Measures were taken at baseline, at the end of the three month exercise period, and three months after training had been terminated. Based on the measures taken at three months the exercise group showed significant improvements in exercise capacity, QoL (FAMS but not the MSIS-29), and fatigue (MFIS: -13 (-20, -3) versus 1 (-4, 4.5)). At six months, the significant differences in the change scores for both the FAMS and the MFIS were still observed (p=0.002 and p=0.02 respectively).

Smith et al., (2009) investigated the effects of an eight week long endurance and resistance training programme on perceived control over fatigue in MS patients. Participants in the trial were 10 patients (8 females and 2 males) who had a confirmed diagnosis of MS and were able to walk short distances without assistance. To gauge participants’ attitude towards exercise and find out whether their perceptions of fatigue change over time, semi-structured interviews were performed at baseline, mid-way during the programme, and at the end of it. Training sessions were held three times a week. Each session lasted for one hour. The individually tailored programme consisted of a wide range of activities, including cycling, treadmill walking/running, jumping, balance, stair climbing, foam standing and strengthening. Findings of the study show that exercise outcomes are often determined by the individual’s level of perceived control over fatigue.

There are also indications that fluctuations in the patient's perceived level of control are influenced by emotional and environmental changes.

Effects of a12-week aquatic exercise programme on the QoL and fatigue in patients with primary progressive (PP) or secondary progressive (SP) MS were investigated by Roehrs and Karst (2004). For the purpose of their non-controlled study, the researchers recruited 31 patients. Six of those recruits withdrew before the exercise intervention and another six dropped out during training, two due to exacerbations, one due to an infection and three because they lacked motivation. Patients below the age of 19 and those with severe cognitive impairments were excluded from the study. Inclusion criteria in the study required the availability of a care-giver to provide assistance when needed, clearance for exercise participation from a neurologist and a clinical course consistent with PP and SP. The EDSS scores of the participants ranged between 1.5 and 8. Outcome measures performed at baseline and at the end of the trial period were the Medical Outcome Study Short Form-36 (SF-36) and the Multiple Sclerosis Quality of Life Inventory to assess QoL, and the MFIS to measure fatigue. Participants were given two sessions a week, one hour a session. Training activities were individualised based on the ability of participants and water temperature was maintained between 83˚F and 85˚F, and they consisted of balance, endurance, strengthening and stretching activities. Of the 19 participants who completed the study, five attended between 25% and 49% of the training classes and another six scored between 50% and 74% rate of attendance. Results of the study showed significant improvements in the QoL domains of social functioning and on fatigue (Pre-test 48.7 ± 12.1, Post-test 43.5 ± 15.0, $p = 0.035$).

Fargoso et al., 2008, evaluated the effect of a 20-week, three days a week training exercise programme on nine female and one male fatigued MS patients aged between 20 and 49 years. None of the participants enrolled for the trial had serious cardiac or respiratory problems, none was undergoing treatment for fatigue, and they were all allowed to continue with any treatment (including physiotherapy and immunomodulators) they were receiving. Patients with moderate to severe weakness of respiratory muscles were excluded. At entry and at the end of the training programme, fatigue was assessed using the Chadler Fatigue scale. The training programme was as follows: 4 weeks x 60 minutes a session of stretching, 10 weeks of stretching for 15min followed by exercise with light weight for 30min then another 10min of stretching, and 6 weeks x 90min a session divided equally between stretching, resistance, and conditioning exercises that included walking and short running periods. All exercises were adapted to each participant's special limitations. One female participant dropped out of the programme because she lacked motivation. Results of the study showed significant improvements in cardio circulatory parameters as well as a significant decrease in fatigue scores (46+- 6.3 at baseline, 39.4+-3.4 at the end of the programme, p=0.01). The authors conclude by suggesting that reduction in fatigue may be caused by improvement in cardio-circulatory parameters and that, at least in part, physical inactivity may cause fatigue.

Table 3.5. Combined training

Study	Design	Sample	Disability (EDSS)	MS course	Duration/ weeks	Frequency (Day/Week)	Training programme	Fatigue Scale	Dependent variables	Main findings
Surakka et al., 2004 (15)	RCT	EX: 47 C: 48	1-5.5	All	26	First 3 wks: 5 aerobic and 5 resistance. Last 23 wks 1 :aerobic and 3-4 resistance	First 3 weeks: 30min aerobic training and 10 exercises for whole body and 10-15 repetitions resistance training. Last 23 weeks: One 30min aerobics exercise and eight resistance exercises	FSS/4-5	Fatigue, muscle strength	Endurance and resistance training reduced motor fatigue in female participants, but not in males.
McCullagh et al., 2008 (16)	RCT	EX: 12 C: 12	NR	RR SP	12	2	Combined training (treadmill walking/running, cycling, stair-master training, arm-strengthening, outdoor walking). 40 min training and 10 min warm up and cool down.	MFIS/38	Fatigue, QOL	At months three and six, a significant effect of combined training on fatigue and QOL was still observed.

Smith et al., 2009 (17)	NC	EX: 10	NR	NR	8	3	One hour long individually tailored exercise which included aerobic, strengthening and stretching activities.	Qualitative study (interpretive description)	Exercise, fatigue perception	Patients' level of perceived control over fatigue plays a pivotal role in determining exercise outcomes
Roehrs & Karst., 2004 (18)	NC	EX: 19	1.5-8	PP SP	12	2	Individualised aquatic training: balance activities, stretching, endurance training, strengthening. One hour	MFIS/38	Health-related QOL, fatigue	Significant improvements in QOL and in fatigue
Fragoso et al., 2008 (19)	NC	EX:10	6.0	RR SP	20	3	Gradual exercise adapted to the specific abilities of each patient. 4weeks x60min stretching. 10 weeks x 15min stretching followed by 30min exercise with light weight and other 10min stretching.	Chalder's Fatigue Scale	Fatigue	Fatigue can be significantly improved with gradual and indivilduaised endurance and resistance training exercises

							6 weeks x 90min divided equally between stretching, resistances, and walking and running.			

C, Control group; CP, Chronic Progressive; EDSS, Expanded Disability Status Scale; EX, Exercise Group; FSS, Fatigue Severity Scale; MFI, Multidimensional Fatigue Inventory; MFIS, Modified Fatigue Impact Scale; NC, Non-controlled; NR, Not Reported; PP, Primary Progressive; PT, Physiotherapy; QE, Quasi Experiment; QOL, Quality of Life; RCCT, Randomised Controlled Crossover Trial; RCT, Randomised Controlled Trial; RR, Relapsing Remitting ;SP, Secondary Progressive

3.5. Discussion

To facilitate our discussion, the findings of the three training modalities considered above are summarised below in terms of participants in those studies, type of training, programme duration and intensity, and the measures employed.

3.5.1. Study participants

Although all participants in the 19 studies of the review fulfilled a clinical diagnosis in order to be eligible to take part in the training programmes, a huge diversity among studies exists with regard to the numbers of participants and their characteristics. To begin with, some studies recruited large numbers of participants (for example, between 46 and 95 patients in Oken et al., 2004, Rasova et al., 2006; Petajan et al., 1996; Dodd et al., 2011; Surakka et al., 2004. Other studies comprised a small or a relatively small sample size between 8 and 10 participants in Klieff and Ashburn, 2005; Dodd et al., 2006; White et al. 2004; Smith et al., 2009; Fargoso et al., 2008 and not more than 19 in Newman et al., 2000; Rampello et al., 2007; Fargoso et al., 2008. In itself, this can limit the statistical power to detect any differential effects of the intervention. Moreover, although it is widely accepted that the rate of MS female patients to male patients is 2 to 1, (see section 2.4), gender bias can be observed in some studies. For example, 7 females and 1 male took part in the study by White et al., 2004; 8 females and 2 males Smith et al., 2009 , and only one male compared to 9 females in Roehrs and Karst, 2004. In other words, it would be difficult to claim that findings of biased studies can be generalised. Also in the reviewed studies, three include all or three MS course types (Schultz et al., 2004; Mostert and Keeserling, 2002; Surakka et al., 2004), three include two types (McCullagh et al., 2008; Roehrs and Karst, 2004; Fargoso et al., 2009), another three include only the relapsing remitting type (Dodd et al, 2011; White et al., 2004; Dalgas et al., 2010), and the rest make no reference to the MS course. Indeed, it would be unrealistic to assume that patients with more progressive forms of the illness or those with restricted mobility would tolerate exercise or benefit from it the same way as the others. Added to this, EDSS scores are generally within the range between 1 and 6.5. Only one study (Roehrs and Karst, 2004) included severely disabled patients (EDSS up to 8.5). This indicates diverse disabilities and severities of the disease among participants. However, three studies had fixed EDSS scores: 2.5-5.5 in White et al., 2004, 3- 5. 5 in Dalgas et al., 2010, and 4-6 in Klieff and Ashburn, 2005. Added to this, a close look at demographic information in the studies described above shows that only very few older patients are included in the trials. This might give the impression that old age is a barrier to exercise. Nevertheless, at least one study that included relatively old participants (Newman et al., 2007) shows that those individuals can actually benefit from exercise and tolerate it. These variations may explain why different results were obtained by different researchers.

3.5.2. Exercise modality

From the review above, it is clear that endurance training has received more attention than resistance training. Beginning with the first type of training modality, three out of the ten endurance training studies in the review showed significant improvements in fatigue as a result of training (Oken et al., 2010; Rasova et al., 2006; Mostert and Keeserling, 2002), two showed a trend toward improvement (Cakit et al., 2010; Klieff et al., 2005), and the remaining five showed no improvement Schultz et al., 2004; Newman et al., 2000; Rasova et al., 2006; Rampello et al., 2007; Petajan et al., 1996). On the other hand, more positive results have been obtained from resistance training, with three studies revealing significant improvements (Dodd et al., 2011; White et al., 2004; Dalgas et al., 2010) and study (Dodd et al., 2006) showing reduced fatigue levels. Similarly, positive results appear to be obtained when both endurance and resistance training activities are combined in that significant improvements have been reported in three combined training studies (McCullagh et al., 2008; Roehrs and Karst, 2004; Fargoso et al., 2008) and reduced fatigue levels in two studies (Surakka et al., 2004; Smith et al., 2009). It is to be noted that the study by Smith et al., 2009, is a qualitative study and that reductions in the level of fatigue were, according to the authors, dependent on the patient's perception of exercise and the illness, with positive attitudes generating more favourable results. However, results obtained from combined training studies do not clearly show whether one training modality (i.e. endurance or resistance) is superior to the other. Nevertheless, it seems that both training modalities are well-tolerated and that patients benefit from both types of training because they complement each other.

3.5.3. Duration and intensity

Studies in the present review vary considerably in terms of duration, frequency and intensity. For example, in studies evaluating ET, intervention periods range between 4 and 26 weeks, 2-3 weekly training sessions are applied within the range of 30-40 minutes. But, although some short-term interventions show positive effect on fatigue (Cakit et al., 2010; Rasova et al., 2008; Mostert and Keeserling 2002), others have no effect on the symptom(Shultz et al., 2004; Newman et al., 2000; Van den Berg et al., 2006; Rampello et al., 2007). The same applies to long or relatively long term intervention: significant improvement in fatigue in a 26-week long intervention (Oken et al., 2004), no effect in a 15 week-long intervention (Petajan et al., 1996), and a trend toward improvement in a 12-week long intervention (Cakit et al., 2010). Intervention periods in RT and CT also vary between 8 weeks and 26 weeks and training sessions are held 2-5 times a week. However, although all these studies have reported improvement in fatigue, the levels of those improvements remain unclear. On the whole, it can be said that it would be difficult to draw clear-cut conclusions on optimal exercise duration frequency and intensity. At the same time, it would be possible to arrive at general conclusions and recommendations based on the findings of the reviewed studies.

As regards ET, there is evidence that well-functioning patients can benefit from arm-ergometry, arm-leg ergometry and treadmill walking. During the early stages of training, it is suggested that intensity of 50%-70% of VO2-max corresponding to 60%-80% of maximum heart rate appears to be suitable. Exercise sessions lasting for 30 minutes each also appear to be effective. As to exercise intensity, it would be appropriate if it is customised against the RPE scale (on the patient's level of disability) and training volume increased progressively either by increasing the session time or by adding an extra training day. A rest period of one day between exercise sessions and a maximum of four sessions a week are recommended. With reference to RT, it would more appropriate in the initial stages of training to use training machines (closed kinetic chains) instead of free weights (open kinetic chains) as the former method is easier to control rather than the latter. Intensity of 15 repetitions maximum (RM) would be also appropriate. This should be progressively increased to between 8-10RM. Also in the beginning of training, one to three sets would be sufficient, but they may be increased to three or four sets of every exercise if the patient can manage. It is necessary that patients have a rest period of between two and four minutes between sets and exercises to allow time for the muscle to recover between exercises. In order for treatment to be more effective, training activities must be designed in a way to activate working muscles but avoid overload that can result in conduction block. It is also recommended that exercise is planned in a way so that large muscle groups are targeted before small muscle groups. All major muscle groups, including the trunk muscles, should be exercised. What has been said about ET and RT also applies to CT. However, it would be appropriate if the training programme included equal proportions of resistance and endurance training activities.

3.5.4. Fatigue measures

In eight of the 19 studies under investigation, fatigue was assessed using the MFIS. Seven of those studies showed improvement in fatigue after training((Shultz et al., 2004; Rasova et al., 2006; White et al., 2004; Dodd et al. 2011; McCullagh et al., 2008; Roehrs and Karst, 2004; Oken et al., 2004), and only one showed no change in fatigue levels (Rampello et al., 2007). The FSS was used in seven studies. Three of those showed positive effect of training on fatigue, (Cakit et al., 2010; Klieff and Ashburn, 2005; Surakka et al., 2004), and in the other four (Van den Berg et al., 2006; Mostert and Keeserling, 2002; Newman et al., 2000; Petajan et al., 1996) , no changes in fatigue levels were recorded. The Chadler Fatigue Scale was employed in one study (Fargoso et al., 2008), two studies utilised semi-structured interviews for the purpose of assessment (Dodd et al., 2006; Smith et al., 2009), and both the MFIS and the FSS were used in one study (Dalgas et al., 2010). All last four studies showed improvements in fatigue after training. However, as noted in 3.4, FSS is often described as an effective tool to measure the social consequences of fatigue but not its intensity.

Although no adverse effects of training on fatigue have been reported in any of the studies under investigation, not much is mentioned about drop-outs in the training groups. For example, there were six drop-outs in Klieff and Ashburn., 2005; Petajan et al., 1996;

Mostert and Keeserling, 2002 (two dropouts each), and only small numbers of participants completed trials (Rampello et al., 2007; Roehrs and Karst, 2004). In some other studies, there were also losses to follow-up assessment. Hence, an adverse effect of fatigue in one or more than one of those studies is not to be discounted. It is also to be noted that in studies with control groups, individuals in those groups are usually given less attention than those in the training groups. In itself, this might have affected the results.

3.6. Summary and conclusions

In this chapter, a range of issues related to MS fatigue and physical training has been investigated and a number of oft-cited empirical studies have been examined. On the whole, there is a general agreement among writers that MS patients are at risk of developing physiological and psychological problems as a result of inactivity. Writers also agree that MS patients can benefit from training, provided that it is performed under the supervision of a professional physiotherapist. However, in almost all the clinical experiments reviewed above, emphasis is on patients with mild to moderate impairment with EDSS score ranging between 1 and 6.5. Moreover, there appears to be a tendency to exclude relatively old patients from participating in the trials. This can imply that old MS patients with severe disabilities may not benefit from exercise. Given the fact that there is no concrete evidence to support this claim, it can be still argued that training can be tailored to meet the abilities of those patients. After all, we need to remember that they are more susceptible than others to health and inactivity related problems.

The studies reviewed above also appear to have other failings. One is that in some of those studies, the results are not fully explained and exercise intensity is not clear. More important is that researchers tend to treat participants as a homogeneous group and pay little, if any attention, to their mixed abilities and individual differences. Furthermore, although it is widely accepted that fatigue is a multidimensional symptom, the majority of the reviewed studies still regard it as a unidimensional symptom and measure it accordingly. In fact, there is no consensus among writers on a core set of outcome measures to be employed in physical training interventions. Added to this, in almost all the studies above (with the exception of only one study on attitude towards exercise), researchers rely on self-report questionnaires and quantitative analysis and pay no heed to qualitative data which can be a source of rich information. It is also possible that some recruits to some trials may not be fatigued, in the first place. Obviously, this would lead to biased results. Furthermore, rather than taking into account the patients' preferences, perceptions of exercise and what they feel about it, researchers often tend to impose the type of exercise and training activities on those patients. There is the possibility that patients recruited to some clinical trials in previous studies already participate in exercise in one way or the other. Hence, it is possible that any additional benefit gained through exercise in those research studies is likely to be minimal. In fact, it would be difficult to attribute any gains or adverse effects to the training programme, itself.

Despite the failings of some previous studies on exercise, they can still provide us with general guidelines we need to consider when designing our training programme. Beginning with training modality, although endurance exercises are popular among researchers, no type of training appears to be superior to the other, and participants can benefit from resistance, endurance or combined training activities. However, regardless of its type, the literature in our hands shows that participants can tolerate it, provided it is initially performed at low to moderate intensity. For resistance training, 2 to 3 sets of 8-15 RM given in 3 or 4 weekly sessions each lasting between 30 and 45 minutes are initially recommended. This can be increased by 1 set and up to 10 reps but only after a few weeks. The same applies to endurance training in terms of training frequency and session duration, and initial training using 50-70% of VO2 is recommended. After a few weeks, training sessions can be increased by one. In regards to combined training, it advisable that endurance and resistance exercises is provided on alternate days. It is also suggested that the training intervention should last for a minimum of 9 weeks. Lessons learned from the experimental studies outlined above should enable the present researcher to design his training programme. More about this point is mentioned in Chapters 5 and 6.

Chapter 4: Perceptions of MS patients towards exercise: a pilot study

4.1. Background

At an early stage of the present study, it was seen necessary to obtain the baseline information required to design individualised exercise interventions and investigate their effect on fatigue in MS patients. To say the least, it was rather important that the present researcher establishes whether or not fatigue was a problem in the local MS population in the first place. Also important were the questions of MS patients' perception of fatigue, attitude towards exercise, willingness to participate in an exercise trial and the type of exercise they preferred. To answer these questions, a questionnaire survey was drafted and ethical approval, Ref. 12/NW/0107, (Appendix 3), dated, 13th March 2012) was obtained to administer the survey on a sample of MS patients. Evidently, because the intention had been to draw recruits for the subsequent exercise trial from eligible respondents in the Staffordshire area, the survey was initially administered on a sample of patients drawn from the MS patient database at the Department of Neurology, University Hospital of North Staffordshire.

Soon after the data collection process was completed in September 2012, news of unexpected research findings on MS in the present writer's home country, Kuwait, was brought to his attention. Until then, MS research in the small Persian Gulf state was almost an uncharted territory, and the country was classified as located in a low risk zone for the disease. However, contrary to that understanding, Roughani et al., (2011 and 2013) found an MS prevalence rate of 85 per 100,000 Kuwaiti nationals. They also reported a three-fold increase in the MS incidence in the country during the past decade. Added to this, they found that the majority of patients were diagnosed with the illness at a young age and that approximately 70% of those patients have been diagnosed with the illness for only a few years. Nevertheless, when these findings were reported by the researcher to his supervisory team, they were of the view that more information about Kuwaiti MS patients and their perceptions of the illness and exercise would probably add to our knowledge about the illness. Consequently, contact was established with Kuwaiti authorities to discuss the possibility and feasibility of carrying out a questionnaire survey on a sample of MS patients in Kuwait. The outcome of the discussion was positive and arrangements were immediately made to obtain approval from Kuwaiti authorities to carry out the survey. Approval was granted in late 2012, and the same questionnaire survey that was carried out in the United Kingdom was translated and administered on a sample of 100 Kuwaiti MS patients registered at the Dasman Hospital.

In light of the questionnaire survey findings, it was seen more feasible to implement the training programme in Kuwait rather than in the United Kingdom, and it was implemented in that country later in 2013 (see 4.8 below). Although this would mean that findings of the British survey do not serve the real purpose of the present research, it is to be noted that the British and Kuwaiti samples exhibited different characteristics and perceptions as to MS fatigue and exercise. In fact, there is good reason to suggest that some perceptions towards the MS disease and physical activity are culturally determined and based. This being so, it may still be useful to allude to the distinct perceptions exhibited by the two samples. It is hoped that the findings trigger more interest in comparative studies on the role culture plays in determining MS patients' attitude towards the disease and exercise as a health promoting activity, and even the course of the disease, itself. Nevertheless, it should be emphasised that the survey questionnaire was not initially designed for or intended to serve any comparative purposes. Rather, it was mainly aimed at finding out the proportion of MS patients who were willing to take part in an exercise trial, their clinical characteristics, the type of help and support they receive and also, their individual preferences with respect to exercise type.

4.2. Participants and Method

The questionnaire survey was administered on a British sample and a Kuwaiti sample of MS patients. Each sample consisted of 100 adults (34 males and 66 females). The male-female ratio is in line with research findings about women being twice more likely to develop the disease than men (Mohr and Cox, 2001). Patients were included in the survey if they were able to complete the questionnaire by themselves or with the help of others, were aged between 18 and 65 years, and had a confirmed diagnosis of MS as diagnosed by McDonald’s diagnostic criteria 2010 (Polman et al., 2011). Patients included in the survey were from both early and late stages of the disease, and some from different treatment groups as some were on disease modification treatment and others only on symptomatic treatment. Their level of disability was also variable. This was done to make sure that the patients included were representative of the group attending routine MS clinics and minimise any selection bias. Those who were incapable of giving informed consent (i.e. those who were known to have cognitive impairment) as well as those who were experiencing an exacerbation were not approached. Although completing the questionnaire can be considered as implicit consent, it is to be noted that many participants were contacted at a later date. Hence, consent was formally recorded by asking patients to provide a complete signature at the end of the covering letter (Appendix 4). A copy of that letter was given to the participants.

For the UK sample, participants were identified from the MS patient database at the Department of Neurology, University Hospital of North Staffordshire. Similarly, Kuwaiti participants were identified from MS patients registered at the Neurological Department, Dasman Hospital. Eligible participants in both groups were approached in one of two ways. For a start, only those arriving in the outpatient clinic for their routine appointment were presented with copies of the questionnaire (Appendix 5) and the information sheet (Appendix 6). It was explained to them beforehand that participation was voluntary. Those who were willing to take part in the survey were given two choices: either fill in the questionnaire while they wait to be seen by their doctor then hand it back to the receptionist, or fill it in when they go back home. In the former case, they could use a room in the clinic equipped with the necessary facilities for the purpose. In the latter case, they were asked to return completed questionnaires by post. No matter what their choice was, a stamped and addressed envelope was included with the questionnaire. Through this method, it was possible to approach the entire Kuwaiti sample and 40 patients from the British sample over a four-week period. After the fourth week, postal questionnaires were sent to the remaining (n=60) British candidates. It is worth mentioning that in Arab culture, a disabling disease can be humiliating in that it usually generates pity, sorrow and even pain, particularly in members of the patients' family. This explains why the majority of Kuwaiti respondents insisted on filling out the questionnaire in the clinic, as this would enable them to keep the secret of their illness to themselves.

4.3. The questionnaire

The questionnaire consists of four parts. In part 1, general information is sought about the participant, including age, gender and date of diagnosis. Part 2 is concerned with the participants' MS condition, their disease severity levels, relapse frequency and perceived causes, the kind of support they receive, and the symptoms they experience as a result of the disease. Part 3 seeks to establish whether respondents' attitudes towards physical exercise have changed since diagnosis with the disease, and also, whether or not they currently engage in regular physical activities and the kind of help and support they receive. In part 4, respondents are asked whether or not they are willing to take part in an exercise trial and the type of exercise they wish to take.

4.4. Data analysis

Table 4.1 shows that of the 100 questionnaires distributed to the British sample, 65 were completed and returned. By contrast, of the same number of questionnaires distributed to the Kuwaiti sample, only 55 were completed and returned. Eight returned questionnaires (3 from the British sample and 5 from the Kuwaiti sample) were invalid, hence were excluded from analysis. This brings valid response rates to 62% (British sample) and 50% (Kuwaiti sample). Valid questionnaires were coded then analysed using the Statistical Package for Social Sciences (SPSS Version 15) which is often described as an ideal choice for analysing quantitative data. Descriptive statistics, including frequencies and percentages were utilised to summarise data and compare and describe the distribution of responses.

Table 4.1: Distributed questionnaires and valid responses (M= male, F= female).

Sample	Distributed		Total	Returned		Total	Valid		Total Valid	Valid %
	M	F		M	F		M	F		
United Kingdom	34	66	100	21	44	65	20	42	62	62%
Kuwait	34	66	100	24	31	55	22	28	50	50%

It is to be assumed that patients who chose not to take part in the survey were either unwilling or unable to participate in the intended exercise trial. Those individuals represent 35% and 45% of approached British and Kuwaiti patients respectively.

4.5. Results

Findings of the two surveys are presented below. The demographic and clinical characteristics of the participants are considered first. The participants' levels of engagement in physical activities before and after diagnosis with the MS disease are considered next. The survey concludes with answers to the question as to whether individual participants are willing to take part in the planned exercise intervention and, if so, the type of exercise they wish to take. Throughout the presentation, results obtained from the male group and the female group in each sample are contrasted (i.e. British males are contrasted with British females, and Kuwaiti males are contrasted with Kuwaiti females). Where appropriate, results obtained from the same gender group in the two samples (i.e. British and Kuwaiti males, and British and Kuwaiti females) are also compared. Accordingly, focus throughout the presentation is on the percentage values pertaining to the gender of the participant. Percentage values for the entire British as well as the entire Kuwaiti samples also appear in the tables. However, reference to these is only made where necessary.

4.5.1. Demographic and clinical characteristics of the participants

4.5.1.1. Age and gender

As seen in Table 4.2, the British sample (n=62) consisted of 20 males and 42 females (32.3% and 67.7% of the sample respectively). The overwhelming majority of those participants (85% of the male group and 83.3% of the female group) were 41 years old or over. Next came participants who fell within the age group 26-40 (15% and 14.3% of the male and female groups respectively). None of the participating British males was aged between 18 and 25, and only one female participant (2.4% of the female sample) fell within that age group. In general, the proportion of participating British males and females was almost in similar in each of the three age groups. On the other hand, Kuwaiti participants (n=50) were 22 males and 28 females (44% and 56% of the sample respectively). Whereas 50% of males in this sample (n=11) were aged between 18 and 25, only 17.9% of their female counterparts (n=5) fell within this age group. In sharp contrast, the proportion of male participants aged between26 and 40 was much lower than that of the females in this same age group (27.3% and 64.2% respectively). Those who were 41 years or over represented 27.3% and 17.9% of the Kuwaiti male and female groups respectively.

On the whole, unlike British participants who were relatively old (84% being 41 years or over), Kuwaiti participants were relatively younger in that a total of 80% were below 40 years of age. In this latter group, males were also relatively younger than females.

Table 4.2: Participant age and gender (M= male, F= female, N= number).

	United Kingdom N= 62 (M=20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
Age (Years)	M	%	F	%	All	%	M	%	F	%	All	%
18-25	0	0%	1	2.4%	1	1.5%	11	50%	5	17.9%	16	32%
26-40	3	15%	6	14.3%	9	14.5%	6	27.3%	18	64.2%	24	48%
41+	17	85%	35	83.3%	52	84%	5	22.7%	5	17.9%	10	20%
Total	20	100%	42	100%	62	100%	22	100%	28	100%	50	100%

4.5.1.2. Duration of the disease

Table 4.3 shows that the proportion of participating British males who had been diagnosed with MS over the ten year period before the survey was lower than that of their female counterparts (30% and 50% respectively). Conversely, the proportion of British participants who had been with the disease for 10 to 20 years was higher for males than females (40% and 23.8% respectively). The same thing goes for those who had been with the disease for 20 to 30 years (20% of males and 9.5% for females). In this same sample, similar proportions of males and females (10% and 9.5%) reported being diagnosed with MS for 30 to 40 years. None of the British male participants reported being with MS for over 40 years but 7.2% of the female group said they had been with the disease for that considerably long period of time.

As regards the Kuwaiti sample, almost similar proportions of males and females (77.3% and 78.6% respectively) reported they had been diagnosed with MS during the past ten years of their lives. Similar proportions of the two sexes (18.2% of males and 17.9% of females) also reported being diagnosed with MS for 10 to 20 years. Only two participants, a male (4.5% of the male group) and a female (3.5% of the female group) stated they had been with the disease for 20 to 30 years. None of the Kuwaiti male or female respondents reported being with MS for over 30 years.

Table 4.3: Duration of the disease (M= male, F= female, N= number).

	United Kingdom N= 62 (M=20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
Duration (Years)	M	%	F	%	All	%	M	%	F	%	All	%
1-10	6	30%	21	50%	27	43.4%	17	77.3%	22	78.6%	39	78%
10-20	8	40%	10	23.8%	18	29.1%	4	18.2%	5	17.9%	9	18%
20-30	4	20%	4	9.5%	8	13%	1	4.5%	1	3.5%	2	4%
30-40	2	10%	4	9.5%	6	9.7%	0	0%	0	0%	0	0%
40+	0	0%	3	7.2%	3	4.8%	0	0%	0	0%	0	0%
Total	20	100%	42	100%	62	100%	22	100%	28	100%	50	100%

Overall, the majority of respondents in both the British and the Kuwaiti samples have had the MS disease for 1-10 years. However, the proportion of Kuwaiti patients who have had the disease for this relatively short period of time is considerably higher than that of their British counterparts (78% of the former sample and 43.4% of the latter). Also, compared to 29.1% of the British sample who had been with the disease for 10 to 20 years, only 18% of the Kuwaiti sample reported being with the MS condition for that length of time. Moreover, 13% of the British sample and only 4% of the Kuwaiti sample stated they have been with the disease for 20-30 years. Also, whereas no Kuwaiti participant reported being with MS for over 30 years, 14.5% of British participants said they had been with the disease for 30 years or more.

4.5.1.3. Severity of the disease

Just over 40% of the British sample (55% of the male group and 33.3% of the female group) described their MS condition as mild (Table 4.4). A further 56.5% of this sample mentioned a moderate condition. However, it is to be noted that the proportion of women with this level of severity is nearly twice than that of men (66.7% of the former group and 35% of the latter). Only two British males (10% of the male group) but no British females described their condition as severe. By contrast, 68% of Kuwaiti participants (59% of the men group and 75% of the women group) thought that their condition was of the mild type. Although the rate of this level of severity is somewhat similar in both the British and Kuwaiti male groups, it was reported by three fourths of Kuwaiti female respondents and by only one third of the corresponding British group. On the other hand, moderate MS appears to be more prevalent in the British female sample than in the Kuwaiti female sample (affecting two thirds of respondents in the former sample and only just over one fifth of respondents in the latter). As is the case with mild MS, almost similar proportions of British and Kuwaiti males reported having the moderate type of the disease. The rate of severe MS is also similar in both male and female groups.

Table 4.4: Severity of the disease (M= male, F= female, N= number).

	United Kingdom N= 62 (M=20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
Severity	M	%	F	%	All	%	M	%	F	%	All	%
Mild	11	55%	14	33.3%	25	40.3%	13	59%	21	75%	34	68%
Moderate	7	35%	28	66.7%	35	56.5%	7	31.9%	6	21.5%	13	26%
Severe	2	10%	0	0%	2	3.2%	2	9.1%	1	3.5%	3	6%
Total	20	100%	42	100%	62	100%	22	100%	28	100%	50	100%

4.5.1.4. Relapse frequency

Nearly two thirds of the British sample (representing 40% of women and 76.2% of men in the sample) reported having a relapse once per year. Also in this sample, 50% of males and 21.4% of females reported having two relapses per year. The remaining 10% of the male group and 2.4% of the female group stated they had three relapses a year. Put differently, relapses appear to be more frequent in British males than in their female counterparts.

With reference to the Kuwaiti sample, the overwhelming majority of respondents (81.8% and 82.1% of the male and female groups respectively) stated they had a relapse once per year. The rest of the sample (18.2% of males and 17.9% of females) reported having two attacks per annum. None of the Kuwaiti respondents reported having more than two relapses per year.

On the whole, 64.5% and 82% of participants in the British and Kuwaiti samples respectively reported having a relapse once per year. However, relapses at this rate appear to be more common in Kuwaiti males than in their British counterparts (reported by 81.1% of participants in the former group and 40% of participants in the latter). On the other hand, the overwhelming majority, and at the same time, nearly similar proportions of participants in the two female groups reported having a relapse once a year (76.4% of British females and 82.1% of Kuwaiti females). Two relapses per year were reported by 30.6% and 18% of the British and the Kuwaiti samples respectively. Relapses at this rate appear to be more common in the British male group than all other groups.

Table 4.5: Relapse frequency (M= male, F= female, N= number).

	United Kingdom N= 62 (M=20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
Per year	M	%	F	%	All	%	M	%	F	%	All	%
Once	8	40%	32	76.2%	40	64.5%	18	81.8%	23	82.1%	41	82%
Twice	10	50%	9	21.4%	19	30.6%	4	18.2%	5	17.9%	9	18%
Thrice	2	10%	1	2.4%	3	4.8%	0	0%	0	0%	0	0%
Total	20	100%	42	100%	62	100%	22	100%	28	100%	50	100%

4.5.1.5. Relapse causes

When asked what in their opinion caused relapses, almost similar proportions of British and Kuwaiti respondents (40.3% and 40% of the two samples respectively) gave “do not know” as an answer (Table 4.6). In the British sample, the proportion of men who failed to identify the possible causes of relapses was higher than that of women (50% and 35.7% respectively). In the Kuwaiti sample, this pattern is reversed (36.4% of males and 42.9% of males). Back to the British sample, 30% of male respondents thought that fatigue was the first major cause of relapses, and the other three factors (infection, depression and heat) came second in ranking (each factor being cited by 25% of those respondents). On the other hand, fatigue was seen as the first major cause of relapses in British females (reported by 40.5% of those respondents). Next came infection and heat (each being reported by 35.7% of the group). Depression as a cause of relapses in this group came third in ranking (cited by 21.4% of those women). In other words, three elements appear to have a more negative effect on British females than on British males: fatigue, infection, and heat. On the other hand, depression appears to have a more negative impact on males than on females.

As regards the Kuwaiti sample, 54% of male participants thought that heat was the main cause of relapses, 40.1% reported depression as the second major cause, third and fourth in ranking were fatigue and infection, reported by 36.4% and 27.3% of that group of participants. By contrast, heat was reported as the first major cause of relapses by 46.2% of Kuwaiti female participants, depression and fatigue were identified as the second major cause (each being reported by 42.9% of those females), and infection was described as the third major cause (reported by 35.7% of the group). Put differently, whereas Kuwaiti females more than Kuwaiti males appear to be affected by fatigue, depression and infection, heat appears to have a more negative impact on Kuwaiti males than on their female counterparts.

Table 4.6 shows that identical proportions of the two female groups reported infection as one of the major causes of relapses (35.7% of respondents in each group).The same can be said about the two male groups where infection was reported by almost equal proportions of respondents (25% and 27.3% of British and Kuwaiti males respectively). Nevertheless, this does not necessarily suggest that one universal pattern is peculiar to males and another to females. In fact, as noted in the discussion above, not only those differences exist between the two sexes of the same sample, but also, they can be seen in different groups of the same sex. At least, this appears to be the case when those groups of MS patients belong to distinct ethnicities or cultures and are geographically dispersed. For example, whereas fatigue was rated as the first major cause of relapses by British males, it was rated third by their Kuwaiti counterparts. At the same time, it was reported by 30% of the former group and 36.4% of the latter. Also, the proportion of Kuwaiti males who perceived fatigue as the first major cause of relapses is more than double that of the British males. Similarly, whereas depression was considered as an area for concern by only one in four males in the British group, it was viewed as such by two in five Kuwaiti males. In this respect, it is worth noting that unlike the British sample where females appear to be less troubled by depression than males, the pattern in the Kuwaiti sample is reversed. The proportion of Kuwaiti females who described depressions as a causal factor of relapses is also double than that of British females (42.9% compared to 21.4%). With reference to fatigue, although this appears to affect higher proportions of females than males, it was associated with relapses by almost equal proportions of the two female groups (40.5% and 42.9% of British and Kuwaiti females respectively). On the other hand, whereas heat is perceived as a cause of relapses by a higher proportion of Kuwaiti females than British females, this same factor is reported to result in a higher rate of relapses in British females than British males but a lower rate in Kuwaiti females than their male counterparts.

Table 4.6: Relapse causes (M= male, F= female, N= number).

	United Kingdom N= 62 (M=20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
Cause	M	%	F	%	All	%	M	%	F	%	All	%
Don't know	10	50%	15	35.7%	25	40.3%	8	36.4%	12	42.9%	20	40%
Fatigue	6	30%	17	40.5%	23	37%	8	36.4%	12	42.9%	20	40%
Infection	5	25%	15	35.7%	20	32.2%	6	27.3%	10	35.7%	16	32%
Depression	5	25%	9	21.4%	14	22.6%	9	40.1%	12	42.9%	21	42%
Heat	5	25%	15	37.5%	20	32.2%	12	54.5%	13	46.2%	25	50%

4.5.1.6. MS symptoms

MS affects different patients in different ways. At the same time, some symptoms of the disease are often described by most patients as more common and/or more worrying than others. Participants in this survey were presented with a list of symptoms which are often associated with MS and asked to identify the symptoms they experience. They were also requested to report whether or not they were worried or troubled by each of the symptoms they identified (Table 4.7a).

Beginning with the British sample, the most common symptoms reported by the male group were balance (95%), fatigue (75%), and loss of sensation (70%). Slurred speech, spasticity, spasms, tremor and weakness were also reported by nearly two thirds (60% - 65%) of the group. Less common symptoms were: poor concentration ability and depression (50% each), swallowing (45%), and stress and pain (40% each). The least reported symptoms were: blurred vision, lethargy, dizziness and bladder and bowels disorders. Each of these symptoms appears to affect nearly one third (30%-35%) of the group. In terms of the impact of reported symptoms on the patients' quality of life and behaviour, the overwhelming majority of British males rated balance and fatigue as the two most annoying symptoms (reported by 95% and 75% of the group respectively). Two other symptoms, tremor and loss of sensation, were also described as worrying by 50% of the group, and between 35% and 45% reported that they were troubled by problems related to concentration, stress, swallowing, vision, weakness, speech, spasms, spasticity and pain. Less worrying symptoms were dizziness, lethargy and bladder and bowels disorders (reported by 10% to 30% of the group).

The most common symptoms reported by the British female group were weakness (76.1%), fatigue (73.8%), balance (66.6%), pain (61.9%), and loss of sensation (54.7%). Depression, stress and bladder problems were reported by every other member of the group, followed by poor concentration (45.2%), bowels disorders (42.8%), speech difficulties (38%), lethargy (35.7%), and dizziness (30.9%). Swallowing difficulties, blurred vision, spasticity, spasms and tremor were reported by 11.9% to 28.5% of those females. Two thirds of the group described fatigue and balance as the two most worrying symptoms. These were followed by stress (47.6%), weakness (40.4%), poor concentration, loss of speech and pain (35.7% each), and depression (30.9%). All other symptoms were described as worrying by 7.1% to 26.1% of the females. These were: slurred speech, bowels and bladder disorders, lethargy, swallowing difficulties, spasticity, tremor, and blurred vision.

In regards to the Kuwaiti sample, the most common symptoms reported by the male group were: fatigue (90.9%), depression (81.8%), pain and stress (68.1% each), and balance and weakness (63.6% each). Another seven symptoms were reported by much lower proportions of those males: lethargy (45%), poor concentration (36.3%), blurred vision and dizziness (31.8% each), bladder problems (27.2%) and tremor and bowel disorders (13.6% each). Five symptoms (reported by all British participants) were not reported by any Kuwaiti male respondent. These were: spasticity, spasms, speech difficulties, swallowing problems, and loss of sensation. Worrying symptoms reported by that group of participants were as follows in terms of ranking: fatigue (86.3%), stress (68.1%), depression (59%), pain (45.4%), poor concentration (36.3%), weakness (31.8%), balance and lethargy (22.7% each), tremor (13.6%), dizziness and bladder problems (9% each), and bowels disorders (4.5%). Although blurred vision was rated as a common symptom by nearly one third of those respondents, none of them described it as annoying.

The most common symptoms reported by the last group of participants, the Kuwaiti female group, were: balance (85.7%), fatigue (82.1%), weakness, stress and depression (67.8% each), pain (60.7%), and lethargy (57.1%). Less reported symptoms were: swallowing and bowels problems (42.8% each), bladder disorders (39.5%), poor concentration ability (35.7%), dizziness (32.1%), and blurred vision (25%). Spasms, slurred vision and tremor were respectively reported by only 17.8%, 14.2% and 3.5% of the group. Two symptoms spasticity and loss of sensation were not reported. Most worrying symptoms reported by the group were: fatigue (75%), stress (64.3%), depression (57.1%), and weakness (42.8%). Nearly one third of the group described swallowing as a worrying problem, and one in four females said they were troubled by problems related to balance, lethargy, concentration and bladder and bowels function. Four females (14.1% of the group) said they were annoyed by dizziness, two (7.1%) by blurred vision, and only one (3.5%) by tremor. Although 60.7% of the group noted that pain was a common symptom, they all stated that it was not worrying. Similarly, all females who said that they experienced problems with speech stated that they were not alarmed by such problems.

Table 4.7a: This table identifies problems of patients and also shows proportion of patients who were worried about these problems with MS.

	United Kingdom M= 20 F=42								Kuwait M= 22 F=28							
Symptoms	M	%M	L95% CI	U95% CI	F	%F	L95% CI	U95% CI	M	%M	L95% CI	U95% CI	F	%F	L95% CI	U95% CI
Tremor	12	60	38.53	81.47	5	11.9	2.11	21.7	3	13.64	-0.7	27.98	1	3.57	-3.3	10.45
worrying	10	83.33			5	100			3	100			1	100		
Concentration	10	50	28.09	71.91	19	45.24	30.19	60.29	8	36.36	16.26	56.47	10	35.71	17.97	53.46
worrying	7	70			15	78.95			8	100			7	70		
Depression	10	50	28.09	71.91	21	50	34.88	65.12	18	81.82	65.7	97.94	19	67.86	50.56	85.16
worrying	5	50			13	61.9			13	72.22			16	84.21		
Stress	8	40	18.53	61.47	21	50	34.88	65.12	15	68.18	48.72	87.65	19	67.86	50.56	85.16
worrying	7	87.5			20	95.24			15	100			18	94.74		
Fatigue	15	75	56.02	93.98	31	73.81	60.51	87.11	20	90.91	78.9	102.92	23	82.14	67.96	96.33
worrying	15	100			28	90.32			19	95			21	91.3		
Speech	13	65	44.1	85.9	16	38.1	23.41	52.78	0	0	0	0	4	14.29	1.32	27.25

worrying	8	61.54			11	68.75			0	0			0	0		
Swallowing	9	45	23.2	66.8	9	21.43	9.02	33.84	0	0	0	0	12	42.86	24.53	61.19
worrying	7	77.78			6	66.67			0	0			9	75		
Vision	7	35	14.1	55.9	8	19.05	7.17	30.92	7	31.82	12.35	51.28	7	25	8.96	41.04
worrying	7	100			3	37.5			0	0			2	28.57		
Dizziness	6	30	9.92	50.08	13	30.95	16.97	44.93	7	31.82	12.35	51.28	9	32.14	14.84	49.44
worrying	5	83.33			6	46.15			2	28.57			4	44.44		
Sensation	14	70	49.92	90.08	23	54.76	39.71	69.81	0	0	0	0	0	0	0	0
worrying	10	71.43			15	65.22			0	0			0	0		
Pain	8	40	18.53	61.47	26	61.9	47.22	76.59	15	68.18	48.72	87.65	17	60.71	42.62	78.8
worrying	8	100			15	57.69			10	66.67			0	0		
Balance	19	95	85.45	104.55	28	66.67	52.41	80.92	14	63.64	43.53	83.74	24	85.71	72.75	98.68
worrying	19	100			28	100			5	35.71			7	29.17		
Spasticity	13	65	44.1	85.9	11	26.19	12.89	39.49	0	0	0	0	0	0	0	0
worrying	8	61.54			6	54.55			0	0			0	0		
Spasms	13	65	44.1	85.9	12	28.57	14.91	42.23	0	0	0	0	5	17.86	3.67	32.04
worrying	9	69.23			7	58.33			0	0			2	40		
Bladder	7	35	14.1	55.9	21	50	34.88	65.12	6	27.27	8.66	45.88	11	39.29	21.2	57.38

worrying	3	42.86			10	47.62			2	33.33			7	63.64		
Bowels	6	30	9.92	50.08	18	42.86	27.89	57.82	3	13.64	-0.7	27.98	12	42.86	24.53	61.19
worrying	2	33.33			11	61.11			1	33.33			7	58.33		
Weakness	12	60	38.53	81.47	32	76.19	63.31	89.07	14	63.64	43.53	83.74	19	67.86	50.56	85.16
worrying	7	58.33			17	53.13			7	50			12	63.16		
Lethargy	7	35	14.1	55.9	15	35.71	21.22	50.21	10	45.45	24.65	66.26	16	57.14	38.81	75.47
worrying	6	85.71			10	66.67			5	50			7	43.75		

In the table above, it can be seen that certain MS symptoms affect equal proportions of males and females within the same sample of respondents (e.g. depression and fatigue in the British sample and concentration and dizziness in their Kuwaiti counterparts). Other symptoms are also present in equal or almost equal proportions of the same sex groups (e.g. dizziness and weakness in the male groups and pain and bowels disorders in the female groups). However, the majority of MS symptoms appear to affect the four participating groups in completely different ways. For example, in the British sample, tremor and balance problems are more common in males than females, but pain and bladder and bowels disorders are more common in the female group. The same can be said about other symptoms in the Kuwaiti sample. Moreover, whereas certain symptoms are common in one particular group, they are less common, rare or even absent in others (e.g. compare symptoms related to speech, swallowing and spasticity in the four groups). Added to this, regardless of how common the symptoms are, they also appear to have a different impact on the quality of life in different groups of respondents. For example, not all tremor cases reported by nearly two thirds of British males are described as worrying. On the other hand, although only a few tremor cases were reported by the other three groups, all such cases were described as annoying. Also, whereas balance was reported by a sizeable majority of Kuwaiti respondents, only a small minority of those individuals appear to be troubled by this symptom. By contrast, all balance cases reported by British respondents are found to be annoying. In fact, this applies to almost every symptom in the list in Table 4.7a. However, for the sake of brevity and also as a point of reference, the four groups (British males versus British females, Kuwaiti males versus Kuwaiti females, British males versus Kuwaiti males, and British females versus Kuwaiti females) are separately compared in Table 4.7b in terms of the level of concern over MS symptoms. For example, in the first two columns, British males (BM) find tremor more worrying than do British females (BF), and equal or almost equal proportions of BM and BF describe concentration as a worrying symptom. In the last two columns, Kuwaiti females (KF) are less troubled by tremor than are BF, and whereas the former group is troubled by pain, the latter is not. The marks (+), (-), (=) and (0) indicate the level of concern over the symptom between the two parties in each of the four groups.

Table 4.7b: Worrying symptoms: levels of concern (BM/F= British males/females, KM/F= Kuwaiti males/females).

	BM	BF	KM	KF	BM	KM	BF	KF
Tremor	+	-	+	-	+	-	+	-
Concentration	=	=	+	-	=	=	+	-
Depression	-	+	+	-	-	+	-	+
Stress	-	+	+	-	-	+	-	+
Fatigue	+	-	+	-	-	+	-	+
Speech	+	-	0	0	+	0	+	0
Swallowing	+	-	0	+	+	0	-	+
Vision	+	-	0	+	+	0	=	=
Dizziness	+	-	-	+	+	-	=	=
Sensation	+	-	0	0	+	0	+	0
Pain	+	-	+	0	-	+	+	0
Balance	+	-	-	+	+	-	+	-
Spasticity	+	-	0	0	+	0	+	0
Spasms	+	-	0	+	+	0	+	-
Bladder	-	+	-	+	+	-	=	=
Bowels	-	+	-	+	+	-	=	=
Weakness	-	+	-	+	+	-	-	+
Lethargy	+	-	-	+	+	-	=	=

4.5.1.7. Help and support with MS

Participants in the survey were asked whether or not they sought or received help and support from different groups of professionals as a result of their health condition (Table 4.8). In answer to this question, Kuwaiti respondents reported an extremely limited number of sources. For example, none of those respondents reported seeking or receiving help from a counsellor, optician, psychologist occupational therapist or social worker.

Assistance from a physiotherapist was reported by only two females (7% of the female group), one female cited her GP, and another mentioned her dietician. No male mentioned receiving help from a GP, physiotherapist or dietician. Even the two females who reported help from a physiotherapist mentioned that that form of treatment was received in the United Kingdom. However, all members of the sample (males and females) mentioned they were dependent on their neurologist for assistance.

Compared to their Kuwaiti counterparts, British respondents, particularly females, reported they received help and support from a wide range of professional groups with a wealth of knowledge, experience and skills. Beginning with the male group in this sample, neurologists were identified as the first major source of assistance (reported by 55% of the group), followed by GPs (40%), and occupational therapists (30%). Practice nurses and physiotherapists were mentioned by one in four respondents, social workers by one in five, and counsellors by nearly one in seven. Only one member of the group (representing 5% of the group) mentioned his optician, and no reference was made to dieticians or psychologists. On the other hand, 52% of the British female group said they sought help from their neurologists, 31% from GPs, and nearly 24% from physiotherapists. Smaller proportions of those females reported other sources: practice nurses (19%), counsellors (16.7%), social workers (12%), occupational (9.5%), opticians and dieticians (7% each), and psychologists (Table 4.8).

Table 4.8: Help and support (M= male, F= female, N= number).

	United Kingdom N= 62 (M=20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
Who helps	M	%	F	%	All	%	M	%	F	%	All	%
Neurologist	11	55%	22	52%	33	53%	22	100%	28	100%	50	100%
GP	8	40%	13	31%	21	34%	0	0.0%	1	3.5%	1	2%
Dietician	0	0.0%	3	7%	3	5%	0	0.0%	1	3.5%	1	2%
Psychologist	0	0.0%	2	4.8%	2	3%	0	0.0%	0	0.0%	0	0%
Occupational therapist	6	30%	4	9.5%	10	16%	0	0.0%	0	0.0%	0	0%
Optician	1	5%	3	7%	4	6.5%	0	0.0%	0	0.0%	0	0%
Counsellor	3	15%	7	16.7%	10	16%	0	0.0%	0	0.0%	0	0%
Practice nurse	5	25%	8	19%	13	21%	0	0.0%	0	0.0%	0	0%
Physiotherapist	5	25%	10	23.8%	15	24%	0	0.0%	2	7%	2	4%
Social worker	4	20%	5	12%	9	14.5 %	0	0.0%	0	0.0%	0	0%

4.5.2. Physical activity before and after diagnosis

To gauge patients' attitude towards exercise as a health promoting activity, participants were asked whether or not they used to exercise before diagnosis, whether they still exercise, and if so, the kind of activities they perform and the support they receive. Reasons for not exercising after diagnosis were also investigated.

4.5.2.1. Physical activity before diagnosis

The first question on physical activity put to participants was whether or not they were regularly engaged in physical training activities before they had been diagnosed with the MS disease. In answer to this question, 70% of British male respondents and 78.5% of their female counterparts stated they were involved in such activities. On the other hand, only 31.8% and 17.8% of Kuwaiti male and female respondents respectively gave a positive answer. Put differently, this would mean that in healthy British and Kuwaiti populations, three in four and one in four adults respectively appear to be appreciative of exercise as a health promoting activity (Table 4.9).

Table 4.9: Physical activity before diagnosis (M= male, F= female, N= number).

	United Kingdom N= 62 (M=20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
	M	%	F	%	All	%	M	%	F	%	All	%
Yes	14	70%	33	78.5%	47	75.8%	7	31.8 %	5	17.8%	12	24%
No	6	30%	9	21.5%	15	24.2%	15	68.2%	23	82.2%	38	76%

Next question put to participants pertains to the type of physical activity they used to perform before they had been diagnosed with the MS. In the British male group, 60% noted they had been involved in aerobic exercises, 35% strengthening, 30% stretching, and 25% aquatics as well as racket sports. Three other types of activities were mentioned by lower proportions of those male respondents: martial arts 15%, dancing 10% and yoga 5%. By contrast, British female respondents indicated that aerobics were the most popular type of activity in the health female population (reported by nearly 55% of the group), followed by stretching (28.5%), racket sports (nearly 24%), and dancing921.4%). Strengthening exercises were also reported by 16.6% of those females, aquatic exercises by 14.3%, yoga by nearly 12%, and martial arts, the least popular type of training, by only one respondent (2.4% of the group).

In the Kuwaiti male group, 22.7% said they had been involved in aquatic exercises, and the same proportion of 13.6% mentioned aerobic, stretching and strengthening exercises. Racket sports and martial arts were (each) cited by 9% of the group, but no reference was made to yoga or dancing. In the corresponding female group, three participants (10.7% of the group) mentioned stretching, and equal proportions of 7.1% said they used to have aerobic and aquatic training. All other types of exercise activities (namely strengthening, martial arts, dancing, yoga and racket sports) were not reported by that group.

In all, whereas the majority of British respondents of the two sexes appear to have been involved in a wide range of pre-diagnosis training activities, only a small minority of Kuwaiti respondents, particularly females, appear to have been left with a limited number of choices (Table 4.10).

Table 4.10: Type of physical activity before diagnosis (M= male, F= female, N= number).

	United Kingdom N=62 (M= 20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
Activity	M	%	F	%	All	%	M	%	F	%	All	%
Aerobics/Walking	12	60%	23	54.8%	35	56.4%	3	13.6%	2	7.1%	5	10%
Stretching	6	30%	12	28.5%	18	29%	3	13.6%	3	10.7%	6	12%
Strengthening	7	35%	7	16.6%	14	22.4%	3	13.6%	0	0%	3	6%
Aquatic exercise	5	25%	6	14.3%	11	17.7%	5	22.7%	2	7.1%	7	14%
Martial arts	3	15%	1	2.4%	4	6.4%	2	9%	0	0%	2	4%
Dancing	2	10%	9	21.4%	11	17.7%	0	0%	0	0%	0	0%
Yoga	1	5%	5	11.9%	6	9.6%	0	0%	0	0%	0	0%
Racket sports	5	25%	10	23.8%	15	24%	2	9%	0	0%	2	4%

Moreover, even when the same type of activity is reported to have been undertaken by all participants, it is often the case that males and females (particularly those in the Kuwaiti sample) show different levels of interest in that activity. For example, although racket sports and stretching were reported by almost equal proportions of the British male and female groups, males more than females appear to prefer aerobics, aquatics, strengthening and martial arts. On the other hand, dancing and yoga appear to be more appealing to females than males. Also, compared to their male counterparts, Kuwaiti females showed much lower levels of interest and involvement in aerobic, stretching and aquatic exercises.

4.5.2.2. Physical activity after diagnosis

In 4.5.2.1, it was noted that participants' responses to the question on involvement in pre-diagnosis physical training activities are reflective of the healthy population's attitude towards and/or perceptions of exercising. The conclusion drawn from those responses was that unlike the British healthy population where a sizeable majority (70% males and 78% females) appear to be involved in exercising, only a small minority of the Kuwaiti healthy population (31.8% males and 17.8% females - Table 4.9) appear to have a pro-training culture.

Given the negative impact of MS and its symptoms, it is not surprising that MS patients become less physically active than healthy individuals. Even then, the patients' rate of involvement in physical activity appears to be determined by a number of variables, most notably levels of disability, age, gender, geographic location and culture. For, when patients were asked whether or not they were engaged in physical activity after diagnosis, 60% and 71.5% in the British male and female groups (a decline of 10% and 7%) gave a positive answer. On the other hand, the rate went down from 31.8% to 18.2% (i.e. by 13.5%) in the Kuwaiti male group of patients, and from 17.8% to 10.7% (a drop of 7%) in the female group (Table 4.11). However, as will be seen in the discussion below, more important than the rate of involvement in training are the extent and level of that involvement.

Table 4.11: Physical Activity (exercising) after diagnosis (M= male, F= female, N= number).

	United Kingdom N= 62 (M= 20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
	M	%	F	%	All	%	M	%	F	%	All	%
Yes	12	60%	30	71.5%	42	67.7%	4	18.2%	3	10.7%	7	14%
No	8	40%	12	28.5%	20	32.3%	18	81.8%	25	89.3%	43	86%

Participants who remained physically active after diagnosis were asked to identify the type of activities, in which they were involved, and also, the frequency and duration of their training sessions. In the British male group (n=12), seven participants (58.3%) mentioned strengthening exercises at the rate of 2 - 5 sessions per week. Five (41.6%) said they performed aerobic exercises, also at the rate of 2 - 5 sessions a week. Four (33.3%) mentioned 3 - 6 weekly training sessions of stretching exercises. Another four reported up to four weekly sessions of aquatic training, and two respondents said they had 2 - 5 weekly sessions of posture exercises.

In terms of session duration, each session of aerobic and strengthening exercises was reported to take up to 30 minutes, a stretching or posture session between 10 - 15 minutes, and aquatic training sessions were reported to last for a longer period of time between 30 - 60 minutes.

In the female group of the British sample (n=30), aerobic exercises were reported by 53.3% of the group, strengthening 50%, stretching 33.3%, and posture and aquatic exercises 23.3% each. Compared to their male counterparts, British females reported shorter but more weekly sessions of aerobic and stretching exercises (3 - 7 sessions x 10 – 15 minutes, and 4 - 7 sessions x 5 - 10 minutes consecutively). They also reported less frequent and shorter sessions of strengthening and aquatic exercises (1 - 3 sessions of either type, each lasting 5 - 10 minutes in the former and between 30 - 45 minutes in the latter). The number of weekly posture training sessions reported by those females was equal to that of the males but each lasted for a relatively short period of time (5 - 10 minutes). One or more than one type of exercise was reported by both British male and female active exercisers.

In the active Kuwaiti male group (n=4), up to three weekly sessions of aerobic exercises were reported by all four members of the group. Two of those respondents also mentioned 2 - 4 weekly sessions of stretching exercises, and only one reported up to 4 sessions of strengthening exercises. Each aerobic and stretching session lasted for 10 - 15 minutes, and each strengthening session was of short duration of between 5 - 10 minutes. In the active Kuwaiti female group (n=3), two females reported 1 - 4 weekly sessions of aerobics and 2 - 5 sessions of stretching, and only one female mentioned a maximum of 2 weekly strengthening sessions. Each session of the two former types of training took between 5 and 10 minutes, and sessions of the latter type lasted for only 3 to 5 minutes.

Overall, compared to their Kuwaiti counterparts, all active British males trained more frequently and performed different types of activities for longer periods of time. Similarly, compared to the Kuwaiti female group, British females reported larger numbers of weekly training sessions of longer periods of time. Unlike Kuwaiti females, they also reported engaging in a large number of exercise types. In short, compared to British respondents of the two sexes , we can hardly claim that Kuwaiti respondents are active exercisers.

Table 4.12: Type of exercise after diagnosis

Exercise type		United Kingdom		Kuwait	
		Male	Female	Male	Female
Aerobics	Number %	5 41.6%	16 53.3%	4 100%	2 66.6%
	Session/w	min. 2 max. 5	min. 3 max. 7	min. 1 max 3	min. 1 max.4
	Duration/m	min. 15 max. 30	min. 10 max. 15	min. 10 max. 15	min. 5 max. 10
Stretching	Number %	4 33.3%	10 33.3%	2 50%	2 66.6%
	Session/w	min. 3 max. 6	min. 4 max. 7	min. 2 max. 4	min. 2 max. 3
	Duration/m	min. 10 max. 15	min. 5 max. 10	min. 10 max. 15	min. 5 max. 10
Strengthening	Number %	7 58.3%	15 50%	1 25%	1 33.3%
	Session/w	min. 2 max. 5	min. 1 max. 3	min. 1 max. 4	min.1 max. 2
	Duration/m	min. 15 max. 30	min. 5 max. 10	min. 5 max. 10	min.3 max. 5
Posture	Number %	2 16.6%	7 23.3%	0 0%	0 0%
	Session/w	min. 2 max. 5	min.2 max. 5	min. 0 max. 0	min. 0 max. 0
	Duration/m	min. 10 max. 15	min. 5 max. 10	min. 0 max. 0	min. 0 max. 0
Aquatic	Number %	4 33.3%	7 23.3%	0 0%	0 0%
	Session/w	min. 1 max. 4	min. 1 max. 3	min. 0 max. 0	min. 0 max. 0
	Duration/m	min. 30 max. 60	min. 30 max. 45	min. 0 max. 0	min. 0 max. 0

Percentage based on the numbers of those who remained physically active after they had been diagnosed with MS (British sample: M=12, F=30, Kuwaiti sample: M= 4, F= 3).

4.5.2.3. Current advice and guidance

Table 4.13 shows that different professional groups provide British patients with assistance and guidance on physical training. In the male group of this sample, 35% reported receiving help from neurologists and gym instructors, 30% from GPs and physiotherapists, and 10% from practice nurses and counsellors. On the other hand, 38% of the British female group reported relying on their neurologists, 33.3% on physiotherapists, 28.5% gym instructors, 26.2% GPs, and 4.7% on practice nurses and counsellors. By contrast, Kuwaiti respondents, particularly females appear to have an extremely limited number of choices. In the male group, two respondents (9%) said they sought or received help from neurologists, and only one respondent (4.5% of the group) mentioned a gym instructor. In the female group, three respondents (10.7%) said they received help from their neurologist and another two mentioned receiving advice from (British) physiotherapists.

Table 4.13: Current advice or help with physical activity (M= male, F= female, N= number).

	United Kingdom N= 62 (M= 20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
Who helps	M	%	F	%	All	%	M	%	F	%	All	%
Neurologist	7	35%	16	38%	23	37%	2	9%	3	10.7%	5	10%
GP	6	30%	11	26.2%	17	27.5%	0	0%	0	0%	0	0%
Gym instructor	7	35%	12	28.5%	19	30.6%	1	4.5%	0	0%	1	2%
Physiotherapist	6	30%	14	33.3%	20	32.2%	0	0%	2	7.1%	2	4%
Practice nurse	2	10%	2	4.7%	4	6.5%	0	0%	0	0%	0	0%
Counsellor	2	10%	2	4.7%	4	6.5%	0	0%	0	0%	0	0%

4.6. Barriers to exercise

It was noted above that 20 British (8 males and 12 females) and 43 Kuwaiti (18 males and 23 females) participants have stated that they have chosen not to engage in physical training after they had been diagnosed with MS (see Table 4.11). Those participants gave different explanations as to why they remain physically inactive (Table 4.14). In the British sample, 50% of the male group cited fatigue as the main reason, next came transport and family or work commitments (each being reported by 25% of the group), and in third place were problems related to facilities or lack of faith in physical training (each reported by 12.5% of those males). In the British female group, fatigue was perceived as an inhibiting factor by 41% of physically inactive women, family or work commitments 33.3%, lack of encouragement 25%, transport 20%, facilities and transport 16.6% each, and only one female (5% of the group) thought that exercise was not useful. On the opposite side, 77.7% of inactive Kuwaiti males thought that lack of encouragement was the main obstacle, 61% were of the view that training was not rewarding, 55.5% mentioned fatigue, 44.4% problems related to training facilities, and 27.7% family and work responsibilities. On the other hand, almost all inactive Kuwaiti females (96% of the group) gave lack of encouragement as the main reason for not exercising, 92% mentioned problems related to training facilities, 62.7% failed to see the benefits of training, 52% cited fatigue, and 32.2% reported commitments towards family and work as another cause. Unlike some of their British counterparts, all physically inactive Kuwaiti respondents do not find a link between transport and lack of training.

Table 4.14: Reasons for not exercising (M= male, F= female, N= number).

	United Kingdom N= 20 (M=8, F= 12)						Kuwait N= 43 (M= 18, F= 25)					
	M	%	F	%	All	%	M	%	F	%	All	%
Fatigue	4	50%	5	41%	7	45%	10	55.5%	13	52%	23	53.5%
Family/Work	2	25%	4	33.3%	6	30%	5	27.7%	8	32%	13	30.2%
Not useful	1	12.5%	0	0%	1	5%	11	61%	16	64%	27	62.7%
Facilities	1	12.5%	2	16.6%	3	15%	8	44.4%	23	92%	31	72%
Transport	2	25%	2	16.6%	4	20%	0	0%	0	0%	0	0%
Encouragement	0	0.0%	3	25%	3	15%	14	77.7%	24	96%	38	88.4%

Percentages based on the numbers of those who have not been physically active after they had been diagnosed with MS (See Table 4.11).

4.7. Willingness to participate in the trial

In answer to the question whether or not participants were willing to take part in a supervised physical training programme, 87% of the British sample with almost equal proportions of the two sexes (85% and 88% of the male and female groups respectively) said they were willing to participate (Table 4.15). This is despite the fact that the majority of those respondents were already involved in physical training activities (see Table 4.11). By contrast, 70% of the Kuwait sample (50% of the male group and 85.7% of the female group) agreed to take part in the proposed trial. In all, whereas the overwhelming majority of British male and British and Kuwaiti female respondents appeared to be keen on taking part in the training programme, only one in two in the Kuwaiti male group appeared to be interested (Table 4.15).

Table 4.15: Willingness to participate in the exercise trial (M= male, F= female, N= number).

	United Kingdom N= 62 (M=20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
	M	%	F	%	All	%	M	%	F	%	All	%
Yes	17	85%	37	88%	54	87 %	11	50%	24	85.7%	35	70%
No	3	15%	5	11.9%	8	13%	11	50%	4	14.3%	15	30%
Total	20	100%	42	100%	62	100%	22	100%	28	100%	50	100%

Table 4.16 shows respondents’ perceptions of different types of training activities. In the British male group, the majority (75%) said they would opt for aerobic exercises if they

were given a choice, 60% preferred stretching exercises, 50% agreed on strengthening activities, and 45% chose aquatic exercises. Yoga and posture exercises were the least preferred types of activity in this group. Aerobics were also the first preferred type of training in the British female group (chosen by 81% of those respondents), strengthening exercises came second (66.6%), stretching exercises third (54.7%), and aquatics fourth (40.5%). Smaller proportions of the group said they would engage in yoga and posture training (19% and 14.3% respectively). By contrast, none of the Kuwaiti male or female respondents showed interest in three types of training: aquatic, yoga and posture. On the other hand, the overwhelming majority of the female group stated they would choose aerobic exercises (89.2%), strengthening (78.5%), and stretching (71.4%). In the male group, aerobic training was the most preferred type of activity, though it was selected by only 45.5% of respondents, a slightly smaller proportion of 41% mentioned strengthening activities, and 27.2% opted for stretching exercises.

Table 4.16: Preferred type of exercise (M= male, F= female, N= number).

	United Kingdom N= 62 (M= 20, F= 42)						Kuwait N= 50 (M= 22, F= 28)					
Activity	M	%	F	%	All	%	M	%	F	%	All	%
Aerobic exercises	15	75%	34	81%	49	79%	10	45.5%	25	89.2%	35	70%
Stretching exercise	12	60%	23	54.7%	35	56.5%	6	27.2%	21	71.4%	27	54%
Strengthening exercise	10	50%	28	66.6%	38	61.3%	9	41%	22	78.5%	31	62%
Aquatic exercise	9	45%	17	40.5%	26	42%	0	0%	0	0%	0	0%
Yoga	2	10%	8	19%	10	16.1%	0	0%	0	0%	0	0%
Posture exercise	2	10%	6	14.3%	8	13%	0	0%	0	0%	0	0%

4.8. Summary and conclusions

In the opening section of this chapter, it was noted that although the present survey was administered on two samples of British and Kuwaiti MS patients, it was never intended to serve any comparative purposes. Rather, the survey was carried out on British subjects only because the original plan was to implement the exercise intervention in the United Kingdom, and the decision of implementing it in Kuwait was taken soon after the survey had been conducted in that country (see 4.1 and also below). In other words, it is only the findings of the Kuwaiti, not the British, survey that have a direct bearing on the present research and the training intervention. Those findings, their implications and the lessons learnt from them are considered at a later stage in this paper. Nevertheless, because the two surveys unveiled marked group differences within and across the two samples, it is felt that their results need to be highlighted and the questions they raised to be brought to the attention of interested researchers.

In general, compared to their British counterparts, Kuwaiti respondents are younger, have been diagnosed with the disease for a shorter period of time, their disability is less severe, and they are less likely to have more than one relapse per year. In relation to relapse causes, whereas depression is the least reported cause by British respondents, it is the most reported causal factor by Kuwaitis. Some MS symptoms also appear to be more common in one sample than the other. For example, higher proportions of British respondents reported balance, tremor, loss of sensation, blurred vision, concentration, slurred speech, spasticity, spasms, dizziness, swallowing and bladder and bowls problems. On the other hand, higher proportions of Kuwaiti respondents reported depression, stress, fatigue, pain, weakness and lethargy. In this respect, it is worth noting that Kuwaiti participants find depression, stress and fatigue more worrying than do British respondents. However, unlike their British counterparts, they appear to be less worried or not worried at all about symptoms such as balance, tremor, slurred speech, loss of sensation and spasticity. Other major differences exist between the two samples in terms of the support they receive and perception of and attitude towards exercise. For, whereas British respondents reported receiving advice and guidance from a wide range of sources, Kuwaiti respondents appear to rely entirely on their neurologist. Also, whereas the majority of British respondents reported active involvement in physical activity before and after diagnosis, only a small minority of Kuwaiti respondents mentioned they used to engage in physical activity when they were healthy, and even a smaller minority said they continued to exercise after they had been diagnosed with the disease. Nearly two thirds of

Kuwaiti respondents were also of the view that not much would be gained from training. This compares to only 5% of British respondents.

The study also revealed marked difference between the two sex groups within each sample as well as differences between the same sex groups across the two samples. What is mentioned below is only a simple illustration (for more details, the reader is referred to the tables in the study:

Age: Nearly no difference in terms of age groups between British males and females, but Kuwaiti males appear to be relatively younger than their female counterparts.

Disease duration: Length of time respondents have been with the disease varies between British males and females, but is almost constant in the Kuwaiti sample.

Disease severity: In the British sample, mild MS is more common in males than in females, and moderate MS is more common in females than in males. In the Kuwaiti sample, the case is the opposite. Moreover, the proportion of British females with moderate MS is much higher than that of the Kuwaiti females.

Relapse causes: In both samples, females appear to be affected by fatigue and infection more than are males. In the British sample, females are more sensitive to heat than males, but in the Kuwaiti sample, the picture is reversed. The proportion of Kuwaiti females who reported depression as a possible cause of relapses is double than that of the British females.

MS symptoms: Tremor is reported by a high proportion of British males but by only small numbers of participants in all other groups. In booth samples, fatigue is reported by higher proportions of males than females. Two symptoms are absent in the Kuwaiti females but absent in their male counterparts (slurred speech and swallowing. Some symptoms are present in both British males and females, but are absent or almost absent in the Kuwaiti sample (e.g. spasms, spasticity, loss of sensation).

Attitude towards training: In the British sample, higher proportions of females than males remain physically active after diagnosis. Compared to their Kuwait counterparts, British females are more active and engage in a much wider range of activities.

When results obtained from the Kuwaiti sample and the UK sample were contrasted, it was decided that it would be more feasible to implement the intended exercise intervention on a group of recruits to be drawn from Kuwaiti respondents who stated that they were willing to participate in supervised training activities. The rationale behind implementing the trial in that country is simple. For, as we have seen from the questionnaire above, unlike British respondents who appear to be actively involved in the management of their condition and also in supervised or unsupervised physical training activities, Kuwaiti respondents haven’t been engaged in physical exercise since they were diagnosed with the illness. In fact, the notion of exercise as a health promoting activity appears to be somewhat alien to Arab culture. Put differently, had the trial been conducted on British subjects, any gains obtained during the experiment would have been minimal. It would also been difficult to establish whether such gains (or adverse effects) were the results of the supervised programme or other training activities. On the other hand, because Kuwaiti MS patients had not been involved in exercising before the trial, the benefits they may gain would, in the main, be attributed to the training programme, itself.

Chapter 5: Methodology

5.1. Introduction

The objectives of the present study were stated in the opening sections of this paper. To recapitulate, the primary objective is to investigate the effect of customised, individualised, self-selected and different exercise modalities on fatigue in MS patients. The secondary objectives are to assess the impact of exercise on the strength, walking ability, and activities of daily living in MS patients, and also, the psychosocial impact of MS and fatigue on patients and their attitude towards physical training. To achieve these objectives, quantitative and qualitative data were obtained through the application of self-report questionnaires, functional tests and interviews. In this chapter, methodological issues pertaining to the exercise trial are discussed.

5.2. Primary arrangements

In Chapter 4, it was noted that recruits for the exercise intervention were drawn from the Kuwaiti group of patients who took part in the pilot study on patients' perceptions towards physical exercise. Initially, 35 patients from that group stated that they were willing to take part in the exercise trial (Table 3.15). They, all, were registered at the Dasman Institute (DI) in the state of Kuwait. Late in 2012, the researcher's supervisory team at Keele University formally approached Kuwaiti authorities with a request to implement the exercise intervention in that country. Positive response was received from the Kuwaitis and, in accordance with their regulations a "Statement of Compliance", (Appendix 7), was signed by the researcher and his supervisory team in April 2013. In May 2013, ethical approval to conduct the trial (RA/069/2013, Appendix 8) was granted by the Kuwaiti Ethical Review Committee. Soon afterwards, arrangements were made to hire a training venue and appoint a Kuwaiti team of professionals to assist the researcher. The team consisted of a consultant physiatrist, a consultant neurologist and a professional exercise therapist. A gym at the Fawzia Sultan Rehabilitation Institute (FSRI) was chosen as the training venue. This institute is one of the leading healthcare organisations in the Gulf region and is renowned for its modern facilities and quality of service. At that early stage of the experiment, the researcher's chief supervisor paid his first visit to Kuwait to inspect the training facilities, meet the Kuwaiti team of assistants, consider the action plan and give permission for the experiment to be kick-started.

5.3. Participants

As noted above, potential participants (n=35) in the exercise experiment were already identified long before the researcher arrived in Kuwait to conduct the trial. However, because the majority of those patients were not willing to disclose the secret of their illness to others (sometimes not even to their friends and family members), it was not possible to contact them by post or pay them home visits. Hence, they were approached only when they arrived for their routine visits at the outpatient clinic at the Dasman Institute. Of the 35 patients who initially stated that they were willing to participate in the trial, 9 stated that they were unable or unwilling to attend. Even without asking them for an explanation, 2 mentioned work commitment as a reason; 3 said they would be outside the country at the time of the trial, and 4 hinted that they were not in need of exercising. The remaining 26 patients (8 males and 18 females) agreed to participate in the trial. They, all, met the selection criteria and were presented with an information sheet. They also, gave written informed consent to take part in the training programme (Appendix 9), and letters of their eligibility to participate in the trial were also obtained from their doctors.

All those participants were drawn from the register of the Dasman Institute (DI), a government sponsored healthcare and research establishment that provides services exclusively to Kuwaiti citizens. With the exception of only one Arab expatriate (who was registered at DI due to special circumstances), all participants were Kuwaiti nationals who shared a common culture. (As will be seen in the course of our discussion, the culture factor is rather important as it appears to shape patients' attitude towards MS and health promoting activities). Demographic information (age, gender, marital status, number of children, employment, year of diagnosis, MS type and the EDSS score) were obtained from the participants and/or their medical records.

After baseline 1 and baseline 2 tests had been performed (see below), and just before the trial was started early October, 2014, four recruits (two males and two females) decided to withdraw from the trial. One of those had renal failure, one had a relapse, and the other two gave work and family commitment as a reason for withdrawal. Five of the remaining 22 participants withdrew during the training programme for personal reasons, and another participant dropped out because she developed hernia and shoulder problems. This brings down the number of those who completed the trial to 16 (Figure 5.1).

5.4. Inclusion criteria

Patients were accepted in the study if they were between 18 and 65 years old, had a confirmed diagnosis of clinical MS. They were also accepted if they are able to stand upright, walk a 100 metres distance, and pedal on a freestanding ergometer bicycle with or without aid. In order to be included, patients also needed a clearance letter from their doctor stating that it is safe for them to take part in the training programme.

5.5. Exclusion Criteria

Patients were excluded from the study if they had a relapse within 30 days of the inclusion date, were engaged in a physical training programme and/or had any medical condition that would preclude them from training, including liver or kidney failure, uncontrolled hypertension, insulin dependent diabetes and heart diseases. Patients were also excluded if they were reliant on motorised or personal assistance to ambulate, were receiving or had recently received steroid therapy or were unable to understand or follow instructions (more about participants and dropouts will be said in Chapter). End of trial measures were performed and Interview 2 (see below) was administered when the 12-week training programme was terminated in late December, 2014, and follow-up measures were taken four weeks later (Figure 4.1).

5.6. Measures and instruments

For the purpose of the present study, a battery of tests were utilised to collect both quantitative and qualitative data on subjective fatigue, functional performance and the impact of psychosocial factors on fatigue. These are considered below. Before that, it is to be noted that participants were assessed twice before the training experiment. These are henceforth referred to as baseline 1 (B1) and baseline 2 (B2). B1 tests were performed nearly six weeks before the actual exercise trial, and B2 measures were taken over a two week period before that trial. At B1, only four measures were employed, EDSS, MFIS, Barthel Index (BI), and Hospital Anxiety and Depression Scale (HADS). In B2, these four tests were repeated in addition to the full range of tests considered below (i.e. balance tests, upper and lower extremities tests, and muscle tests). The full range of tests was also applied at weak 12 at the end of the trial, and at weak 16, four weeks after the trial had been terminated (Table 5.1).

Table 5.1. Assessment Tools

Tool	Properties	B1	B2	W12	W16
Expanded Disability Status Scale (EDSS)	Assesses aspects of functional system deficits	x	x	x	x
Modified Fatigue Impact Scale (MFIS)	Assesses physical, cognitive and psychosocial aspects of fatigue	x	x	x	x
Hospital Anxiety and Depression Scale (HADS)	Assesses anxiety and depression	x	x	x	x
The Barthel Index (BI)	Assesses the basic personal and instrumental activities of daily living	x	x	x	x
The Berg Balance Scale (BBS)	To measure static and dynamic balance impairments and assess fear of falls	-	x	x	x
Timed Up and Go (TUG)		-	x	x	x
10-metre walk test	To measure walking velocity and endurance	-	x	x	x
6-Minjute Walk (6MW)		-	x	x	x
9-Peg-hole	Assesses dexterity of upper extremity	+	x	x	x
JAMAR	To assess handgrip strength	-	x	x	x
Nicholas MMT hand-held dynamometer	To assess knee, elbow and hip flexion and extension and shoulder flexion and adduction	-	x	x	x
Interview 1	To evaluate impact and nature of fatigue	Before the training programme			
Interview 2	To rate the training programme	At the end of the training programme			

The idea behind applying B1 tests is simple: there was good reason to presume that radical changes might take place in participants' behaviour and daily routine activities over the one month period that preceded the training programme. In turn, those changes might have an impact on those patients' mobility disability, fatigue levels, mood and basic bodily functions. The changes in question pertain to the holy month of Ramadan. During this month, Muslims (and all participants were) are supposed to abstain from eating, drinking, smoking and sexual relations from early dawn hours to sunset and engage heavily in prayer and meditation throughout meditation throughout the night. Indeed, dietary change aside, Islamic prayer (alone) involves considerate physical effort (e.g. ablution and repeated bowing and prostration). Unless we establish whether or not behavioural changes precipitated by Ramadan had an impact on the study participants, it can be argued that any possible changes in post-training measurements might have been influenced by un-investigated behaviours rather than by the training alone.

5.6.1. Modified Fatigue Impact Scale (MFIS)

For the purpose of this study, the Modified Fatigue Impact Scale (MFIS) was used to assess fatigue. Rationale for employing this instrument was provided in 3.3. On the whole, the MFIS is described as one of the most reliable tools to assess MS fatigue and is now widely used in MS research. One of the main advantages of this tool is that it not only measures physical and cognitive fatigue, but also, addresses the psychosocial experience of the symptom (Tellez et al., 2005; Flachenecker et al., 2002).

5.6.2. Balance

To asses balance and fear of falls, the present study employed two instruments: the ‘Timed Up and Go’ test, TUG, (Appendix 10) and the Berg Balance Scale, BBS, (Appendix 11). In the TUG test, the subject is requested to stand up from a chair, walk a distance of three meters, turn around, walk back to the chair and be seated again. Time is recorded from the moment the subject makes the first move until he/she sits back on the chair. Scores over 13.5 seconds indicate a risk for falls (Cattaneo et al., 2006). TUG is widely used with MS patients and it has shown acceptable concurrent validity (Cattaneo et al., 2006, McConvey and Bennett, 2005). The other instrument, BBS, is also widely used in clinical research, easy to administer, and safe to use with elderly patients. It is designed to assess the person’s ability to maintain balance as he/she performs a range of dynamic and static activities. Tasks include sitting unsupported, to rising from seated position, to standing on one leg. The scale consists of 14 items, and each item is scored on a 5-poit (0-4) scale, with 0 indicating inability to attempt or perform the activity, and 4 indicating perfect execution. The BBS is reported to have high levels of internal consistency (Cronbach Alpha, 0.83-0.98) (Berg and Norman, 1996).

5.6.3. Function of upper and lower extremities

Upper and lower extremity function is usually affected in MS patients. Hence, tests of motor function are now increasingly applied in MS research and clinical trials (Motl et al., 2012; Bethoux and Bennett, 2011). For the purpose of this study, the 10 metre walk has been employed to test walking velocity, the 6-minute walk to assess ambulation endurance performance, and the 9 peg-hole to assess speed and dexterity of upper extremity.

For the 25-foot walk, participants are directed to a clearly marked 25-foot flat tiled surface and instructed to walk the distance as fast as they can. Time is calculated from the initiation of the instruction until the participant reaches the end of the 25-foot mark. The task is then administered again by asking the participant to walk back to the starting point. In performing the task, patients are allowed to use assistive devices.

The 6-minute walk is administered on a 150-foot straight course marked in 10-foot intervals. Patients are instructed to walk at their own pace with or without assistive devices. The distance they cover in the allotted time of six minutes is recorded to the nearest foot. Compared to other tests, the 6-minute walk provides more sensitive and reliable information about walking performance in MS patients (Motl et al., 2012). T also correlates strongly with overall disability measures, including the EDSS (($r = 0.73$, $P < .0001$) (Goodman et al., 20007.

The 9 peg-hole test ((Mathiowetz et al., 1985) is increasingly used in MS research and clinical trials (Fischer et al., 2001). It consists of 9 small wooden or plastic pegs, a square board with 9 holes arranged in a three by three design and spaced 3.2 cm apart, a container and a stopwatch. The patient is instructed to use his dominant hand to place the pegs in the holes and remove them immediately as fast as he/she can. Time to execute the task is recorded to the nearest one-hundredth of a second. The participant then uses the other hand to repeat the process.

5.6.4. Muscle function

In the present study, ability to generate maximal strength during exercise was assessed in different muscle groups. Maximal grip strength was assessed using JAMAR, a standard hand-held dynamometer, and Nicholas MMT was carried out using the dynamometer provided isometrically against a static load in the following manner: seated: shoulder flexion/abduction, elbow flexion/extension, knee flexion/extension (all mid range), supine lying: hip flexion (mid range), prone lying: hip extension (end muscle range). Each muscle was tested three times with 30 seconds rest provided between each test. Data was immediately recorded from the dynamometer screen by the tester during the 30 second breaks between each muscle test.

5.6.5. Daily living activities

In MS patients with moderate to severe disability, the ability to perform personal and instrumental daily living activities is often adversely affected (Mansson and Lexell, 2004). To assess limitations to daily living activities in those patients, a number of scales have been developed. One such scale, which has been utilised for the purpose of the present study, is the Barthel Index, BI, (Appendix 12) of activities of daily living. The BI was originally developed by Mahoney and Barthel (1965), but it was later modified by Granger et al., (1979) to assess the ability of patients with neuromuscular disorders to care for themselves. Hobart et al., (2001) observe that the BI has an edge over other newer and more extensive rating scales in that it is more practical and economical, has excellent reliability and validity, and is sensitive to change and easy to use. The BI quantifies patients' performance in ten daily life activities: feeding, grooming, bathing, dressing, bowel and bladder care, toilet use, ambulation, transfers, and stair climbing. Each activity on the scale is rated with a number of given points assigned to different levels of performance or needs. The lowest score, 0, indicates a totally dependent individual, and the highest score, 100, indicates a fully independent person. Too complete the form, information can be obtained from the patient, through observation, or from those who are familiar with the patient's abilities.

5.6.6. Anxiety and depression

To assess anxiety and depression in participants, the 'Hospital Anxiety and Depression Scale (HADS) has been utilised. This tool seeks to achieve "*the maximum possible separation between the concept of anxiety and depression*" (Zigmond and Snaith, 1983) and is also short an easy to administer. *HADS* contains 14 items which are divided evenly between the two constructs, and each item is rated on a four-point (ranging from 0 to 3) on the Likert scale representing level of distress experienced during the past week (0=none, 1=a little, 2= a lot, and 3= unbearable) . Total scores range from 0-21, with higher scores indicating higher levels of anxiety or depression To be more precise, scores of 7 or below are considered normal or no case, 8-11 indicate mild anxiety/depression, 11-14 reflect a moderate case and 15-21 point to a severe condition (Cresswell and Chalder, 2002). Unlike other scales used to measure anxiety and depression, HADS does not include somatic symptoms of depression, which means that it cannot be confounded by symptoms of physical illness (Moss-Morris & Petrie, 2003) and, as such, it is recommended for use with clinical patient groups rather than physically well individuals (Zigmond and Snaith, 1983).This scale is described as a valid tool for use with MS patients and is also known to be sensitive enough to detect significant changes following intervention Feinstein et al., 1999). HADS is also reported to have good internal consistency with Cronbach alpha ranging from 0.80-0.90 for both anxiety and depression subscales (Moorey et al., 1991). A copy of the scale is provided in (Appendix 13).

5.6.7. Interviews

In 3.3, it was argued that self report questionnaires may not fully capture a wide range of factors that can shape or influence MS fatigue including, depression, stress, pain, motivation, self-efficacy, sleep disturbances, patient's behaviour and the psychosocial consequences of the symptom. Because information about these factors is better obtained through qualitative data collection methods, it was suggested that our understanding of fatigue would be improved if we supplemented quantitative data obtained through self-report questionnaires with qualitative information (Braley et al., 2009; Dodd et al., 2006; Dittner et al., 2004; Comi et al., 2001; Mohr et al., 1999). With this in mind, two sets of short and semi-structured interviews serving different purposes were employed in the present study. The former was employed just before the actual raining programme was started and it aimed at establishing whether fatigue was chronic or transient, how it progresses during the day, what makes better or worse, and its impact on the patients' mood, behaviour and daily living activities. The second interview was employed after the training programme, and it was meant to identify the positive and negative outcomes of the trial and the factors that hinder or facilitate participation in physical training.

5.6.7.1. Interview sample

All patients who were originally recruited for the purpose of the study (n=26) were invited to take part in both interviews. 8 participants (3 males and 5 females) agreed to take part in the first interview and 6 participants (2 males and 4 females) in the second. Although the interview samples are relatively small, they are still reflective of the entire study sample.

5.6.7.2. Interview arrangements

Participants in the pre-training interview were approached during their routine visits to their neurologist at Dasman Institute (DI), and those who took part in the pos-training interview were approached at the training gymnasium when post-training measures were taken. The purpose of the interview was explained to participants and they, all, were assured of anonymity and confidentiality. Questions raised during the semi-structured interviews were informed by suggestions made by the MS Council (1998) and Dodd et al., (2006). More about interview participants and schedule is mentioned in Chapter 7.

The time and venue of the interview were also negotiated with every participant. The researcher made sure that no participant was under the pressure of time and that all interviews were conducted in a quiet secluded room, safe environment and without interruption. All interviews were performed either at Dasman Hospital or the training gymnasium. Each interview took 30-45minutes, and at the time of interviewing, only the researcher and the interviewee were present. With the permission of participants all interviews were tape-recorded.

5.6.7.3. Qualitative data analysis

Following the interviews, recorded conversations were transcribed verbatim by the researcher. To ensure validity and reliability, transcripts were verified against recordings and/or with the interviewee (Patton, 2002). Transcripts were then thoroughly read and coded. In an ideal situation, better results would be achieved if more than one researcher were involved in the process of coding, interpreting and analysing information. For example, Dodd et al., (2006) employed three researchers who first worked independently using different coding methods (manual and computer assisted) and then met to refine the coding and agree on the main themes. In this study, this process was not possible due to limitations of time and resources. Hence, the present researcher worked on his own and employed a simple manual method that required him to code every passage in the interview transcript with a descriptive word. Response codes were related to the main issues and questions raised during the interview. These were then arranged into key concepts and themes based on the interview objectives as well as themes brought up by the interviewees (Rubin and Rubin, 1995). During this process, attention was paid to points of agreement and disagreement, as well as repetitive information which were common among the interviewees.

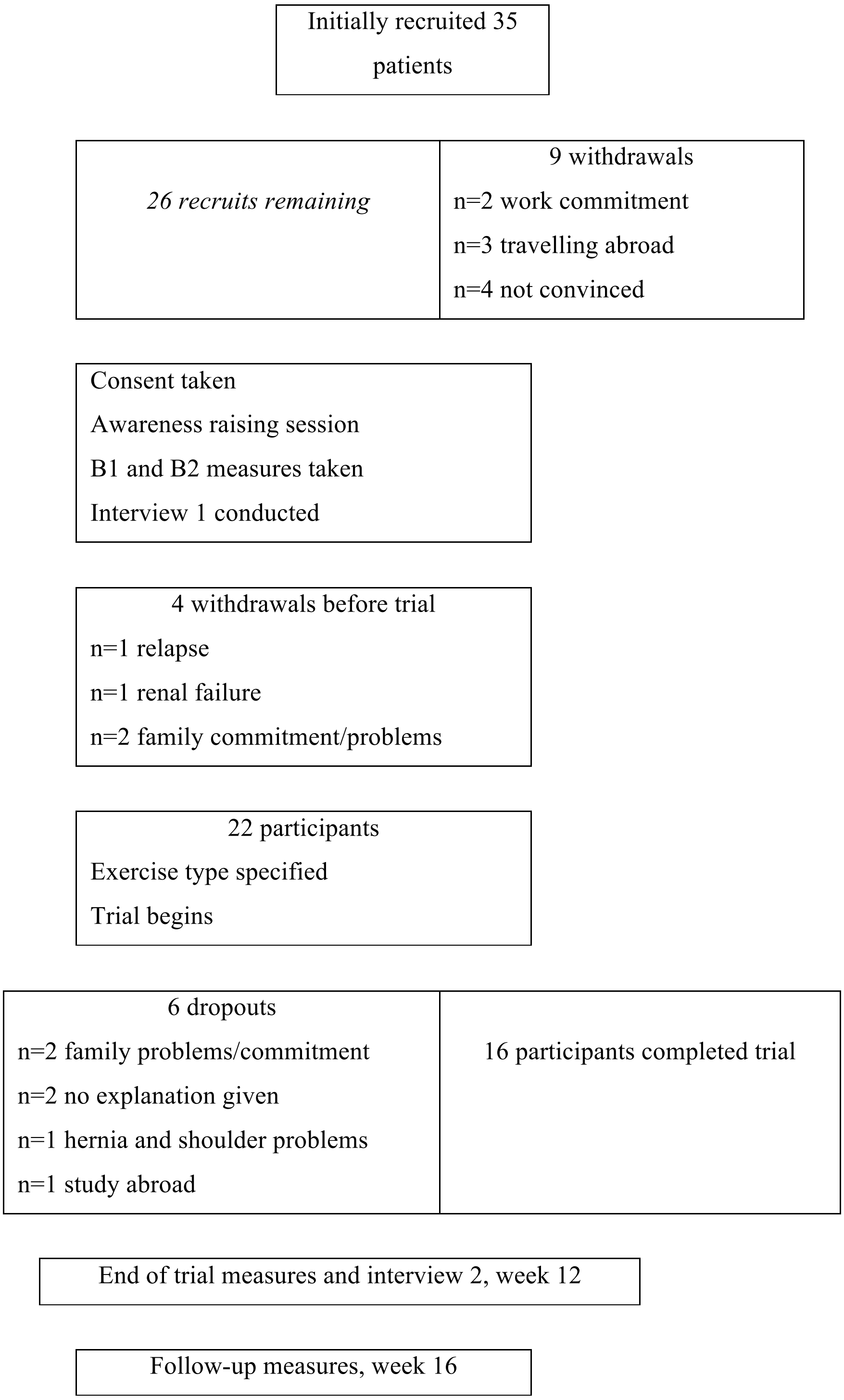
5.7. Statistical Methods

The SPSS was used to analyse the data from this quasi-controlled study. Because this is a repeated measure study design the Wilcoxon's matched pair rank test was used. The data were anaysed by the principal investigator under the supervision of his supervisor.

5.8. Data Management

All the data were collected and stored securely. The data from the forms were transferred, in an anonymous form, to an excel spread sheet which was then used to inform the analysis. Data collected were also randomly cross checked by the researcher's supervisors to assess the validity of the data transferred from the form to the spread sheet independently.

Figure 5.1: Study procedure



Chapter 6: Study findings

6.1. Introduction

In this chapter, results of the functional tests and other measures employed for the purpose of the study are presented. Before that, demographic and clinical characteristics of the participants are described. Reference is also made to the training intervention.

6.2. Subjects and measures

In Chapter 5, reference was made to study participants and methods. To recapitulate in our discussion, 26 patients (8 males and 18 females) were originally recruited for the purpose of the trial. Table 6.1 shows the demographic characteristics of those participants.

Table 6.1. Summary of demographic characteristics of participants (n=26)

Age (in years)	Mean: 37.54	S.D:8.18
Months since diagnosis	Mean: 55.23	S.D: 60.45
Gender	Male (n=8) 31%	Female (n=18) 69%
MS type	B (n=2) 7.7% SP (n=3) 11.5%	RR (n=7) 27% PP (n=14) 53.8%
EDSS	Mild 0-4 (n=2) 7.7% Moderate 4.5-6 (n=19) 73% Advanced 6.5+ (n=5) 19.3%	
Marital Status	Single (n=11) 42.3%	Married (n=15) 57.7%
Employment	Full time (n=15) 57.7% Unemployed (n=5) 19.2%	Part time (n=5) 19.2% Student (n=1) 3.8%

(Benign), PP (Primary Progressive, RR (Relapsing Remitting), SP (Secondary Progressive)

Participants’ age ranged between 23 and 51 years (Mean37.54, SD 8.18), and time since diagnosis ranged between 2 months and 15 years (Mean55.23, SD 60.45). Fourteen of those participants had MS of the primary progressive type; seven had relapsing remitting MS, three secondary progressive MS, and two benign MS. Nineteen participants scored 4.5-6 on the EDSS, two scored 4 or below, and the remaining five scored 6.5 or above. Fifteen participants were married with dependent children, and eleven were single. Finally, the majority of participants were in full-time employment (n=15), 6 were part-time employees, 2 unemployed and 1 was a student.

It was also noted earlier that measures were taken twice before the trial (referred to as baseline 1 and baseline 2, B1 and B2), at week 12 (W12) at the end of the trial, and four weeks after the programme had been terminated (W16). Only four measures were applied at B1 (EDSS, MFIS, HADS, and Barthel Index). At B1, B2, W12, and W16, the same measures were repeated in addition to BBS, TUG, 10-metre walk, 6-min walk, 9-Peg-hole, as well as assessments for hand grip strength, knee, elbow and hip flexion and extension, and shoulder flexion and adduction. Rationale for performing B1 tests was given in 4.4. Measures at B1 and B2 were performed on all recruits (n=26). Only a few days before the training programme was due to be started, four participants withdrew out of the trial. One had a relapse; another was diagnosed with renal and cardiovascular problems, and two due to work and family commitment. The remaining 22 participants selected the type of exercise of their choice and they underwent training.5 chose resistance exercise, and 17 chose combined exercise. During the first two weeks of the training programme, four participants pulled out of the trial; one had to travel abroad to pursue his studies; one developed hernia and shoulder problems and was referred to hospital for treatment, one gave no explanation, and one mentioned family duties and time pressure as a reason. In week three, one patient stopped attending training without giving a reason, and in week four another female participant thought she was not gaining much from training. Those who completed the training programme were 16 participants. W12 and W16 measures were administered on those participants Table 6.2 show subjects, assessment stages and exercise types. It is to be noted that 8 participants took part in the pre-training interview. One of those participants withdrew from the trial before it was started, another pulled out at weak 3, and the remaining 16 (4 males and 12 females) completed the programme. All participants in the post-training interview completed the trial. One participant took part in both interviews. The interview findings will be presented in Chapter 7 (also, see Chapter 5). In the remainder of this chapter, analysis will be focused only on those who completed the trial.

Table 6.2. Subjects, method and exercise type

Participant	B1	B2	W12	W16	Inter1	Inter2	Type of Exercise
C1	X	X	X	X		X	Combined
C2	X	X	X	X	X		Resistance
C3	X	X	X	X		X	Combined
C6	X	X	X	X	X		Combined
C7	X	X	X	X	X		Combined
C10	X	X	X	X			Combined
C11	X	X	X	X		X	Combined
C13	X	X	X	X	X		Resistance
C14	X	X	X	X	X	X	Combined
C15	X	X	X	X			Combined
C16	X	X	X	X		X	Combined
C18	X	X	X	X		X	Combined
C19	X	X	X	X			Combined
C20	X	X	X	X			Combined
C23	X	X	X	X	X		Combined
C24	X	X	X	X			Combined
P5(w1)	X	X					Combined
P8(w2)	X	X					Resistance
P12(w2)	X	X					Resistance
P17(w4)	X	X					Combined
P22(w3)	X	X			X		Combined
P(26w2)	X	X					Resistance
WT4	X	X			X		--
WT9	X	X					--
WT21	X	X					--

C, completed trial, P, pulled out, W, withdrew.

6.3. The training intervention

Following basic functional assessment and consultation with each participant, the exercise type was determined according to his/her wishes, abilities and needs. Of the 16 participants who completed the 12-week training programme, two chose resistance training and 14 opted for exercises of the combined type (i.e. resistance and endurance exercises). Initially, the plan was to provide 4 training sessions a week, each session lasting 45 minutes. However, given the fact that all participants had not exercised since diagnosis with the illness, it was decided that 3x30-minute sessions a week on alternate days would be sufficient for a start and that exercise intensity would be increased in due course. .

For participants who opted for combined training exercise, time was initially divided evenly between endurance training and resistance training and endurance training (15 minutes each) separated by a 4-minute rest period. Endurance training consisted of 15 minutes of treadmill walking, and resistance training consisted of 2 sets of 9 stretching and strengthening exercises, 15-20 repetitions. Those who opted for resistance training were asked to perform 3 sets 15-20 reps as a circuit (using the appropriate weights as indicated by the participant’s reports of exertion on those exercises marked with a W) on the Borg Scale. The exercises were: Upper extremities: Bicep Curl W, French Press W, Row (Theraband) Bench Press W, Shoulder front raise and lateral raise (reciprocal) W. Lower extremities: Hamstring curl W, Calf raise W, Squat W and against the wall using a gym ball where required due to poor balance, Glute Bridge (Progressed to using weight over the low abdominal area), Dead bug, Alternating superman (Progressed to bird-dog exercise). Exercise days were alternated throughout the program in accordance with the date and not the last area exercised by the patient (i.e. if a patient attended for Upper exercise and missed Lower exercise on the next scheduled day, they would return to Upper exercise if they returned on the next scheduled exercise day). Resistance was progressed using patient's reports of exertion at a certain weight as indicated using the Borg RPE. Patients were instructed on how to stretch the muscles exercised on that day and performed their own exercises at the start and end of each resistance session. Aerobic exercises were performed in a semi-supervised manner with the patients instructed to maintain their exertion at a Borg level of 13-15 as long as no adverse symptoms were experienced. There was a minimum of one person and a maximum of six people exercising in the gym at any one time, with one-two supervisors for females. For males, there was a minimum of one person and a maximum of two exercising at one time with one supervisor. In week 7 onward, intensity was increased. For combined training, participants were given the choice between increasing the treadmill walking speed or to increase the walking time by 5 minutes. They were then required to perform 3 sets of stretching and strengthening exercises. For those who opted for only resistance training, sets were increased by 1 from 3 to 4. The participant's heart rate and temperature were taken at the beginning and end of each training session and rate of exertion and speed were recorded using the RPE and CR10 scales. It is also to be noted that training was provided in air- conditioned environment. (Appendix 14 shows the results of all measures and tests administered on each participant as well as his/her demographic details. It also shows the participant's daily monitoring record).

6.4. Early measures

It was stated above that four measures (EDSS, MFIS, HADS and BI) were applied at baseline 1 to determine whether or not any changes have taken place during the month of fasting (see Chapter 5).When the results of those tests were compared to those of B2, they showed no significant changes between baseline 1 and baseline 2 (p-value 70.05) in the scores of MFIS, HADS, B1 and EDSS (Table 6.3). One possible explanation for this result is that participants' behaviour and daily routine might not have changed much during Ramadan. This is because Islam gives the ill the right to carry on with their lives as usual and not observe the month of fasting if they wish. This being said, we now turn to the results for those who completed the trial (n=16).

Table 6.3. Early measurements

	N	Mean	Std. Deviation	Z	Asymp. Sig. (2-tailed)
MFIS-bl1	26	45.08	19.179	-.496-[b]	.620
MFIS-bl2	26	43.31	16.984		
HADS-bl1	26	19.12	16.234	-1.342-[b]	.180
HADS-bl2	26	19.23	16.187		
Barthel-bl1	26	18.00	2.191	-1.342-[b]	.180
Barthel-bl2	26	17.54	2.929		
EDSS-bl1	26	5.73	.874	.000[b]	1.000
EDSS-bl2	26	5.73	.874		

6.5. Results

Demographic information

As seen in Table 6.4, four males and twelve females completed the training programme. With the exception of two participants who were over 50 years old and another four who were in their early 40s, all other participants were 40 years or younger. Three participants had been diagnosed with the disease for less than one year before the trial, seven between

2-5 years, four between 5-10 years, and only 2 over 10 years. Two participants had benign MS, five relapsing remitting MS, and another 5 primary progressive MS. Three individuals scored 4 or below on the EDSS, twelve scored 4.5-6, and only one scored 6.5. Nine participants were married and seven were single. Four were in part-time employment, nine full-time employment, two unemployed, and one a student.

Table 6.4. Demographic characteristics of participants

Participant	Age (years)	Gender (M/F)	MS duration (months)	MS type	Disability (EDSS)	Marital status	Employ-ment
C1	40	F	7	B	5	M	FT
C2	36	F	15	PP	5.5	S	FT
C3	23	F	2	RR	4	S	St
C6	27	F	16	PP	5.5	S	FT
C7	40	M	4	B	3.5	M	FT
C10	30	F	52	RR	5	S	FT
C11	41	M	30	PP	5	M	FT
C13	30	F	99	RR	6.5	S	FT
C14	26	M	66	RR	6	S	PT
C15	27	F	38	PP	5	S	FT
C16	32	F	26	RR	6	M	PT
C18	45	F	44	PP	6	M	U
C19	41	F	88	PP	5.5	M	PT
C20	52	F	176	PP	5	M	FT
C23	54	M	258	PP	6	M	U
C24	44	F	98	PP	5	M	PT

B(benign), C (completed training programme), D (dropped out), , F (female), M (male), FT (full-time), Ma (married), N (no), NT (no training), PT (part-time), PP (primary progressive), RR (relapsing remitting), S (single), SP (secondary progressive), St (student), U(unemployed),W (week), Y (yes).

Statistical analysis (Table 6.5) shows that significant beneficial effects on fatigue were obtained as a result of training at the end of the programme in week 12 (p-value < 0.05 and mean value going down from 38.00 at baseline 2 to 29.94 at week 12).

There were no significant differences between the MFIS follow-up scores at week 16 and the end of the training programme scores at week 12 (p-value > 0.05). This indicates that the fatigue benefits gained as a result of training were still maintained over the four week period that followed the trial. With reference to anxiety and depression, there were no significant differences between HADS-B2 and HADS-12w (p-value > 0.05). The same can be said about HADS-12 and HADS-16w. There were also no significant differences between the B1 scores at baseline 2 and week 12, or between week 12 and week 16 scores (p-value > 0.05). The EDSS scores remained unchanged throughout the entire period.

Table 6.5. Results of MFIS, HADS, EDSS and BI measurements (n=16)

Var	Measurement	Mean±Std Deviation	z	Asymp. Sig (2-tailed)
MFIS	Bl2 12w	38.00±15.297 29.94±13.791	-2.200-[d]	.028
	12w 16W	28.88±14.301	-.701-[d]	.483
HADS	bl2 12W	14.63±8.007 13.94±5.483	-.126-[c]	.900
	12w 16W	12.94±6.486	-1.162-[d]	.245
EDSS	bl2 12W	5.38±.719 5.38±.719	.000[b]	1.000

	12w 16W	5.38±.719	.000[b]	1.000
Barthel	bl2 12W	18.56±1.788 19.31±1.778	-1.706-[d]	.088
	12w 16W	19.47±1.060	-.816-[d]	.414

Table 6.6 shows significant differences between TUG tests carried out at week 12 and baseline 2 (p-value < 0.05) but no significant differences between the follow-up and the end of training test (p-value > 0.05). This indicates improvement in mobility and static and dynamic balance asa result of training. These gains were carried over four weeks after training. Results similar to these were obtained when the BBS tests were applied. Significant improvements were also recorded as a result of training in short walk duration speed (the 10 meter walk) and exercise tolerance (6-minute walk). These benefits were still maintained when the 10-meter walk and the 6-minute walk tests were performed four weeks after the training programme had been terminated. No significant differences were recorded in the 9-Hole-Peg test in both hands neither between week 12and and baseline 2, nor between week 16 and week 12 (p-value > 0.05).

Table 6.6. Results of TUG, 10-m Walk, 6-min Walk, BBS and 9-hole peg.

Var	Measurement	Mean±Std Deviation	z	Asymp. Sig (2-tailed)
TUG	bl2 12W	8.00±2.280 6.81±1.109	-2.549-[c]	.011
	12w 16W	7.13±1.455	-1.508-[d]	.132

10m	bl2 12W	4.13±.806 3.56±.629	-2.714-[c]	.007
	12w 16W	3.63±.719	-.378-[d]	.705
6m	bl2 12W	387.56±73.117 426.06±68.418	-3.259-[c]	.001
	12w 16W	411.69±81.302	-1.837-[d]	.066
BBS	bl2 12W	51.50±4.290 53.00±3.864	-2.135-[c]	.033
	12w 16W	53.63±3.686	-.593-[c b]	.553
Nhpt R	bl2 12W	17.00±4.274 16.19±3.902	-1.691-[c]	.091
	12w 16W	15.00±4.274	-.839-[c]	.402
Nhpt L	bl2 12W	20.75±7.767 19.25±5.916	-.860-[c]	.390
	12w 16W	17.75±5.360	-1.020-[c]	.308

As seen in Table 6.7, there were no significant differences between all hand grip tests for both hands over the entire period under investigation. By contrast, gains were made as a result of training in right and left shoulder flexion and adduction (with significant differences being recorded between week 12 and baseline 2 tests, p-value < 0.05). All these gains were still felt four weeks after training with only right shoulder flexion being the exception.

Table 6.7.Results of hand-grip, shoulder flexion and shoulder adduction tests.

Var	Measurement	Mean±Std Deviation	z	Asymp. Sig (2-tailed)
Max_grip R	bl2 12W	18.63±5.795 20.56±7.694	-1.545-[c]	.122
	12w 16W	21.25±7.514	-.884-[c]	.377
Max_grip L	bl2 12W	18.63±7.848 19.69±8.920	-1.512-[c]	.130
	12w 16W	20.69±8.072	-.985-[c]	.324
Max_shld flx R	bl2 12W	62.19±6.210 65.13±4.965	-2.540-[c]	.011
	12w 16W	67.06±5.555	-2.369-[c]	.018
Max_shld flx L	bl2 12W	61.63±7.915 66.69±6.954	-3.191-[c]	.001
	12w 16W	67.94±6.846	-1.055-[c]	.291
Max_shld add R	bl2 12W	61.06±4.404 65.50±5.099	-3.245-[c]	.001
	12w 16W	65.94±4.597	-.288-[c]	.774
Max_shld add L	bl2 12W	61.44±5.549 66.06±4.864	-3.429-[c]	.001
	12w 16W	65.69±5.400	-.314-[d]	.754

Table 6.8 shows results of elbow flexion and extension tests. These are as follows: There were significant differences between all elbow flexion and extension tests performed at week 12 and all elbow flexion and extension tests conducted at baseline 2 (p-value < 0.05). There were no significant differences between R elbow flexion-16w and R elbow flexion-12w. There were significant differences between L elbow flexion-16w and L elbow flexion-12w. There were no significant differences between L elbow extension-16w and L elbow extension-12w.

Table 6.8. Results of elbow flexion and elbow extension tests

Var	Measurement	Mean±Std Deviation	z	Asymp. Sig (2-tailed)
Max_elbflxR	bl2 12W	63.50±7.385 67.44±7.891	-3.142-[c]	.002
	12w 16W	68.75±6.414	-1.297-[c]	.195
Max_elbflxL	bl2 12W	63.38±8.016 67.50±8.230	-2.802-[c]	.005
	12w 16W	68.75±10.829	-2.107-[c]	.035
Max_elb ext R	bl2 12W	62.81±5.319 65.38±5.175	-2.273-[c]	.023
	12w 16W	66.50±6.099	-1.515-[c]	.130
Max_elb ext L	bl2 12W	62.94±6.465 67.94±9.609	-2.358-[c]	.018
	12w 16W	66.75±5.106	-.444-[c]	.657

Results of knee and hip flexion and extension (Tables 6.9a and 6.9b) were as follows: There were significant differences between all right and left knee and hip flexion and extension tests performed at week 12 and those performed at baseline 2 (p-value > 0.05 between all tests). This indicates that there was a positive effect of training on knee and hip flexion and extension. This positive effect was still felt four weeks after the training programme in left knee extension and right and left hip flexion and extension.

Table 6.9a. Results of knee flexion and extension

Var	Measurement	Mean±Std Deviation	z	Asymp. Sig (2-tailed)
Max_kf R	bl2 12W	64.38±5.328 68.88±5.290	-2.702-^{c}	.007
	12w 16W	71.38±6.469	-2.494-^{c}	.013
Max_kf L	bl2 12W	64.00±5.046 67.88±5.560	-2.642-^{c}	.008
	12w 16W	71.00±7.211	-2.259-^{c}	.024
Max_kext R	bl2 12W	64.25±6.476 74.88±10.776	-3.417-^{b}	.001
	12w 16W	80.13±7.588	-1.892-^{b}	.058
Max_kext L	bl2 12W	63.13±5.608 73.50±9.805	-3.301-^{b}	.001
	12W 16W	78.31±8.187	-1.822-^{b}	.069

Table 6.9b. Results of hip flexion and extension

Var	Measurement	Mean±Std Deviation	z	Asymp. Sig (2-tailed)
Max_hipflx R	bl2 12W	63.75±5.285 68.56±5.573	-3.168-^{c}	.002
	12W 16W	68.19±4.875	-.429-^{d}	.668
Max_hipflx L	bl2 12W	63.81±5.394 68.31±5.677	-2.929-^{c}	.003
	12W 16W	68.81±5.845	-.892-^{c}	.372
Max_hipext R	bl2 12W	60.88±5.632 65.75±5.615	-3.413-^{c}	.001
	12w 16W	68.00±4.226	-1.775-^{c}	.076
Max_hipext L	bl2 12W	60.81±5.718 65.38±4.897	-2.826-^{c}	.005
	12w 16W	67.53±3.871	-1.291-^{c}	.197

6.6. Summary

Study results can be summed up in the following points:

1. There were no significant differences between the four measures (MFIS, HADS, B1 and EDSS) taken at baseline 1 and baseline 2.

2. The 12-week combined and resistance training programme resulted in significant reductions in fatigue levels. This positive effect was still maintained 4 weeks after the training programme had been terminated.

3. There were significant improvements as a result of the training programme in: fine mobility and static and dynamic balance (TUG); short duration walking speed (10m test); exercise tolerance (6-minute walk); balance and fear of fall (BBS). Follow up tests at week 16 show that all those gains were still maintained.

4. As a result of the training programme, significant improvements were also made in left and right shoulder flexion and adduction, and left and right elbow, knee and hip flexion and extension. Four weeks after the training programme had been terminated, improvements were still felt in: left shoulder flexion and left and right shoulder adduction, right elbow flexion and left and right elbow extension, left knee extension, and left and right hip flexion and extension.

5. There was no significant effect of training on anxiety and depression (HADS); personal basic functional activities (B1); fine motor coordination and finger dexterity (9-HolePeg) and hand grip (JAMAR).

6. It is also to be noted that training in an air conditioned environment resulted in no change in body temperature, that there was increase in heart rate within each session in many participants, which is an indicator of increased fitness, and also an increase in weight lifted and/or a reduction in effort.

Chapter 7: Interview findings

7.1. Introduction

In Chapter 3, argument has been made in favour of employing both quantitative and qualitative analysis to better our understanding of fatigue. In realisation of this principle, two sets of semi-structured interviews have been employed for the purpose of the present study. The former aims to establish what MS fatigue is, the course it takes during the day, how it is alleviated or aggravated, and the impact it has on the patient's mood and behaviour. The latter is aimed at identifying the outcomes of the training programme from the viewpoint of the participants, their motive for attending training, and the factor that hinder or facilitate participation in physical training activities. The first interview was conducted before the training experiment, and the second was administered soon after the trial had been terminated. Rationale for both interviews was provided in Chapter 5, and the interview procedure and qualitative data analysis were also described. In this chapter, the findings of the interviews are presented.

7.2. The pre-training interview

7.2.1. Interview schedule

Questions raised during the first interview polarised around the nature of MS fatigue (see Appendix 16). On the whole, the main issues under consideration were:

1. The difference between fatigue experienced before diagnosis with MS and fatigue after diagnosis.
2. How fatigue progresses during the day.
3. Factors that make fatigue better or worse.

4. The impact of fatigue on the patient's mood, behaviour and daily living activities.

7.2.2. Participants

All participants recruited for the purpose of the trial were invited to take part in the interview, but only 8 (3 males and 5 females) accepted the invitation. One of those participants withdrew out of the trial before it was started, another pulled out of the trial in week 3, and six completed the training programme. As seen in Table 7.1, the mean age for participants is 37.25, SD: 10.10. Months since diagnosis, Mean78.5, SD:90.73. Four interviewees had primary progressive MS, three relapsing remitting MS and 1 benign MS. Only one participant scored 6.5 on EDSS, and the rest had a score of 6 or below. Five were single, three married, four in full-time employment, two partly employed, and two unemployed.

Table 7.1. Pre-training interview sample demographics

Age in years	Interview 1 (n=8)	Mean: 37.25	S.D:10..10
Months since diagnosis	Interview 1 (n=8)	Mean: 78.5	S.D:90.73
Gender	Interview 1	Male (n=3) 37.5%	Female (n=5) 62.5%
MS type	Interview 1	B (n=1) 12.5% SP (n=0) 0%	RR (n=3) 37.5% PP (n=4) 50%
EDSS	Interview 1	Mild 0-4 (n=1) 12.5% Moderate 4.5-6 (n=5) 62.5% Advanced 6.5+ (n=2) 25%	
Marital Status	Interview 1	Single (n=5) 62.5%	Married (n=3) 37.5%
Employment	Interview 1	FT (n=5) 62.5% Un (n=2) 25%	PT (n=1) 12.5% St (n=0) 0.0%

7.2.3. Interview findings

Themes arising from the interview are considered under the headings: the nature of MS fatigue causes of fatigue, alleviating fatigue, and its psychosocial impact on the patient.

7.2.3.1 The nature of fatigue

All participants reported experiencing fatigue on a daily basis, though at varying levels of severity. Time of onset of the symptom during the day, its features and the way it develops also appears to vary from one participant to the other. In general, although fatigue appears to be related to the quality and amount of sleep as well as the time (during the day) of physical or mental activities and their demands, this is not always the case. On the issue of sleep, all participants stated that their night sleep is usually disrupted for one or more than one of three main reasons: pain, fatigue and nightmares. One participant said she hardly has any sleep at night because of what she described as "dark thoughts". In her words:

> *Those thoughts come to me when I am left alone at night. I do also feel sorry for myself and often cry. When my parents wake up in the morning, they ask me if I had been crying but I deny it.*

In fact, as will be seen in our discussion, sorrow and grief have become part of the participants' daily lives, particularly females. Three other participants said they often wake up for no obvious reason. For the majority of the participants, uninterrupted sleep is a rarity. One participant said she "would be lucky" if she had two or three nights of good and uninterrupted sleep per month, 4 said "one or two nights a week", 2 said "almost every other night", and one said he sleeps well "almost all days of the week, 5 or 6 nights".

When asked how they felt in the morning after a "good" night sleep, two said they "usually do not feel tired", four said they "sometimes feel tired, sometimes not", and two stated that they "always feel tired" when they wake up in the morning, regardless of the quality and amount of might sleep. When the participants' night sleep is disrupted, which is often the case; all participants said they felt fatigued in the morning. According to one male participant, morning fatigue was "not unusual" because he used to "experience it long before he had been diagnosed with the illness". However, the majority of participants agreed that morning fatigue was mild and mainly physical and that normal daily activities were tolerated. Seven participants stated that fatigue starts building up gradually and steadily as the day progresses and reaches climax during the early hours of the afternoon. This is regardless whether or not they were fatigued in the morning. Only one male participant said that his fatigue levels remained "almost constant" throughout the day and that he "occasionally" experiences "hours of discomfort and unusual tiredness".

In general, participants appeared to agree that there is a point in time when fatigue becomes "annoying" or "intolerable" according to one participant. This type of fatigue sometimes occurs during or after strenuous physical or mental activities, sometimes it is provoked by the slightest activity, and at other times it happens even in the absence of any form of activity. It can also take place any time of the day. On the whole, this type of fatigue has both physical and cognitive features, the former being more dominant. No participant mentioned cognitive fatigue in isolation from physical fatigue.

As to the physical aspects of fatigue, whereas some features appear to be common, others are not. Beginning with common features, all participants described in detail what they called "total loss of strength" or "total loss of energy" and "weakness". The following quotes are an illustration of what they reported.

One participant said:

> *I just feel that my muscles have lost strength altogether. They become dead, just like a piece of material. Even when I am feeling thirsty, I hesitate before trying to handle a glass of water because I know I would drop it or put in the wrong place. I become a sort of weak, clumsy and coward altogether.*

Elaborating on weakness, another participant said:

> *Not only that my hands become weak. I also feel that my legs cannot support me. Unless I sit down, I know that they will give way and that I will collapse.*

Another participant noted that even when she manages to move, the best she can hope for is to "drag her feet". According to her, "*even this type of activity requires a lot of thinking and planning".*

As to the uncommon features of excessive physical fatigue experienced by the interviewees, one participant mentioned "slurred speech", and another mentioned "tremor". Four mentioned "total loss of balance" and a similar number mentioned “excessive yawning". Another uncommon feature is "sweating" mentioned by only two participants. In this respect, it is worth alluding to the case of one male patient who participated in the exercise programme but did not take part in the interview about fatigue. That patient denied that he had MS and insisted that he was wrongly diagnosed with the illness. When asked why he attended training, he said he only wanted to prove his point to others and to himself.

With reference to cognitive impairment, this was a clear feature of fatigue. On the whole, this is manifested in the participants' inability to carry on with activities that require concentration or intensive mental effort. For example, the majority mentioned that they find it difficult to read or grasp the meaning of written texts. In the words of one participant:

> *I read the same sentence slowly and more than once. Yet, I seem to forget what it is about. I feel my attention and memory are not normal.*

In this connection, all female participants said they found it difficult to concentrate and be focused even when they try to prepare a simple meal. As for the males, they do not have problems with cooking because they never do it and rarely enter the kitchen (a hallmark of Arab culture). However, they reported having problems with concentration when filling in forms, playing computer games or sending and receiving mobile phone texts.

7.2.3.2 Causes of fatigue

When the interviewees were asked what they thought the causes of fatigue were and how it was aggravated, they all agreed on two major factors: physical and/or mental activity, stress and heat. More precisely, they noted that fatigue would be easily provoked when both strenuous physical and mental activities are present but that it is induced more by physical than by the mental effort. With this in mind, they all find an urgent need to take regular breaks when they are engaged in any activity. Otherwise, there is the possibility of fatigue increasing or having a relapse. According to female participants, they feel safer at home because they can take short breaks when they are doing the cleaning, or the cooking. However, for reasons to be discussed later (see post-interview), most women in full employment find it difficult to have any breaks at work. With reference to heat, this appears to be more of a problem for males than for females. This is possibly because unlike women, who are either at home or work, males spend longer time outdoors. On their part, although female participants did mention heat as a factor that can aggravate fatigue, they noted that humidity is more disturbing. Three participants mentioned "disrupted night sleep" as a source of fatigue, and another four (all females) thought that "depression" can easily induce the symptom.

7.2.3.3 Alleviating fatigue

All participants agreed that the best strategy to alleviate fatigue is to rest and/or have some sleep. What is interesting to note here is that the "sleep strategy" appears to be more effective during the day than at night. In the words of one female participant:

> *When I am fatigued at night, the symptom is not relieved no matter how long I try to rest or sleep. On the other hand, when I am fatigued during the day, rest or sleep abolish fatigue, often in a manner of minutes.*

Other participants agreed with this comment, though the amount of time they said they needed for rest and sleep varied. Three said they did not actually need to sleep and that all they needed was "to sink in the chair" and stay inactive until fatigue disappears. When asked how long it usually takes fatigue to vanish, one said "about 15 minutes" and the other two mentioned "one to two hours, possibly more, depending on the level of fatigue". The other four said they needed a "couple of hours" of sleep. Again, when asked about the type of "inactivity" they required, they all answered that they stop both mental and physical activities. All also noted that in order for the rest/sleep strategy to work, the environment must be peaceful and quiet. One male participant has this to say:

> *I just want to be left alone and in peace. I do not want to hear or talk to any soul. Not even to myself. Then, the moment fatigue starts to retreat, I hear my wife shouting: "Are you okay? Is there anything you need?" God! How good that woman is at inducing fatigue. The problem is even worse when the children are around and not in school.*

When that participant was asked if his wife and children knew about his illness, he simply answered: "Why should they?". In fact, as noted earlier in this discussion, the majority of Kuwaiti (and Arab) MS patients usually regard their illness as a personal secret they should not reveal.

When participants felt that heat or humidity might precipitate fatigue, they said they usually turned on the air conditioning system. Three said that taking a shower would help. To evade fatigue, some patients took what they called "precautionary measures" or "pre-emptive technique". This strategy is employed when they plan to go out for an event, and it requires them to have some sleep (even if they did not need it) before going out. One female participant also thought that mental and physical activity at work can prevent fatigue. When this same participant was reminded of what she had said earlier in the interview about the need to have regular breaks at work, her answer was.

> *I mean reasonable activity. The activity that makes you feel cheerful, good and lively. It all depends on your mood and the people around you, of course. Sometimes I even*

> *think that I need breaks because I feel bored and troubled by the work environment, I mean work colleagues.*

7.2.3.4. Impact of fatigue

When participants were asked what impact fatigue had on their lives, some went to describe in detail the effects of the symptom and their MS experience as a whole. As they spoke, they showed clear signs of sorrow, pain, grief, frustration and even anger. The comments they made did clearly indicate that the impact of fatigue and MS was for them an issue of great importance and concern. One interviewee commented with bitterness: "*we are often directly or indirectly reminded that we are ill but are never asked about the impact of the illness on our lives or told what we can do about it*". Another interviewee said with a sad smile on his face: "*It is good to talk and take it off one's chest*!". However, from the accounts given by those participants, it is evident that MS in general and fatigue in particular can lead to behavioural changes with profound physical, social and psychological consequences.

Four interviewees noted that although mild fatigue, "which is almost always present", can affect their physical and mental performance, it remains bearable and they can still cope with it. However, the main concern for those patients is that they do not know exactly how or when excessive fatigue or relapses are evoked or what the consequences will be. One participant noted:

> *When I am at work, I try to take things easy lest fatigue or other symptoms associated with it become visible and colleagues know about my illness. But no matter how hard I try, I sometimes feel it coming and begin to feel more tired. In a sudden, I lose interest in what I am doing and stop working. Sometimes, I stay at my desk feeling sorry for*

> *myself and thinking about my colleagues who think that I am lazy and irresponsible, and at other times, I try to find excuses to run away home.*

Remarks similar to those above were made by another participant who added that she sometimes pushes herself to "get things done". In her words, "*by the end of the work day, I find myself exhausted and shaking and feel an urgent need to rush back home to go to bed". That same participant added that despite her worries, she* would "*do the impossible to keep* (her) *job*". It is worth noting that that participant is an expatriate who is not protected by Kuwaiti labour laws that apply only to locals. Another interviewee said she felt guilty because her mother gave up her job to look after her. A male participant said he opted for a part time job because he could not cope with the type of work he was doing. Two participants noted that they had been feeling stressed since the days they were waiting for diagnosis. One even angrily noted that, "h*ad the diagnosis process been speeded up, (his) condition wouldn't have deteriorated*". Four respondents also pointed to "*occasional clashes and tension"* in their families due to behavioural changes dictated by the illness. They further noted that their condition forced them to abandon plans for a better future (e.g. better employment, education) and resulted in social withdrawal, disruption to daily living activities and changes in established relations. Two of those participants said they were not happy because they "*lack independence*" and added that their "*sense of self-esteem was not as it used to or should be".* One participant was reluctant to talk about any negative effect of fatigue or of the illness, possibly because she thought others might feel sad or sorry for them, or possibly because they were more determined and optimistic. According to another interviewee, he hated to think about the illness and was used to pushing himself to remain physically and mentally active. In his words: "which is better, succeed sometimes or fail all the time?

7.2.3.5. Two unusual cases

Two participants in the trial were a male (Y) and a female (Z). Although Y and Z did not take part in the pre-training interview, they still have an interesting story that is related to MS in general and fatigue in particular. It is worth noting that Y was aged 41 years, with primary progressive MS and an EDSS score of 5. Z was 45 years old, with primary progressive MS, and EDSS score of 6.

During the fourth week of the training programme, a male participant (Y) and a female participant (Z) decided to take a few days off training to travel to Iraq in order to take part in the annual march between the two holy cities of Najaf and Karbala. The pilgrimage is performed in commemoration of the highly revered saint and martyr, Imam Hussein, who with his entire family were brutally murdered at the hands of Yazid, the dissident and Umayyad caliph at the end of the 7th century A.D. The rituals of the pilgrimage dictate that the faithful take the 50 mile journey from Najaf to Karbala on foot, stopping only for sleep and rest whilst chanting, swaying and praying all the way. Although Y and Z were advised by their doctor not to travel, they still insisted on performing what they described as their "holy duty". One week later, they were back to attend the training programme and tell their story. Both participants gave a similar account of their foot trip. Here is only a brief account of their journey and its impact on fatigue.

Y and Z stated that they made the 50-mile foot journey in just over two days and a half, without walking aids. They said they used to sleep at night and stop for about 20 minutes for rest and/or food at the end of every hour. In total, each of them walked for 25 hours, at the rate of two miles an hour. Both said that they were taking disease modifying drugs but no medication for fatigue. They also said they were aware that the long march might trigger a relapse but that they were determined "no matter what", to reach their goal. In fact, they gave the impression that they hoped for a relapse. In the words of Z, "the harder it is, the more rewarding it becomes". They also noted they slept well during the journey and did not experience the "usual" sleep disturbances. Neither of them seemed to have experienced any MS symptoms during the trip except for the very "occasional and usual dizziness and stumbles". Although both mentioned they felt physically exhausted at one stage, they still insisted that they did not experience mental fatigue and that their ability to concentrate was not affected. In terms of weather, the spell of rain and relatively warm days (25°c) did not seem to have affected them. Both said they had been performing the pilgrimage long before they had fallen ill and continued to do so every year after they had been diagnosed with the disease.

It is to be noted that the end of training measures showed a significant decrease in fatigue (by over 60%) in both Y and Z. This level was still maintained 4 weeks after the trial when follow-up measures were applied. Compared to other participants, they also displayed lower levels of anxiety and depression. (Transcript for a short interview with participant Y is seen in Appendix 15).

7.3. The post-training interview

7.3.1. Interview schedule

The post-training semi-structured interview was focused on the participants' attitude towards training (see Appendix 16). Main issues considered during the interview were:

1. The positive/negative outcomes of the training programme.

2. Motives for attending the trial?

3. Participants' thoughts about programme leaders and other participants.

4. Suggestions to improve future training programmes.

7.3.2. Participants

Participants in the post-training interview were 2 males and 4 females. Age, Mean 34.5(SD: 8.78). Months since diagnosis, Mean, 29.17 (SD: 23.74). Two participants had primary progressive MS, three relapsing remitting MS, and 1 benign MS. Mobility disability was mild in 1 and moderate in 5. Three were married and three single, one was a student, one unemployed, two in full-time employment, and two partially employed (Table 7.2).

Table 7.2. Interviews 2 (n=6): Sample demographics

Age in years	Interview 2 (n=6)	Mean: 34.5	S.D: 8.78
Months since diagnosis	Interview 2 (n=6)	Mean:29.17	S.D:23.74
Gender	Interview 2	Male (n=2) 33%	Female (n=4) 67%
MS type	Interview 2	B (n=1) 16.6% SP (n=0) 0%	RR (n=3) 50% PP (n=2) 33.4%
EDSS	Interview 2	Mild 0-4 (n=1) 16.6% Moderate 4.5-6 (n=5) 83.4% Advanced 6+ (n=0) 0.0%	
Marital Status	Interview 2	Single (n=3) 50%	Married (n=3) 50%
Employment	Interview 2	FT (n=2) 33.3% Un (n=1) 16.6%	PT (n=2) 33.3% St (n=1) 16.6%

7.3.3. Interview findings

The interview polarised around two main questions: the positive and negative outcomes of the training programme as seen by those participants, and their motive behind attending training. Given the fact that physical exercise, as a health promoting activity, is somewhat alien to Kuwaiti Arab culture, it was seen appropriate to begin the interview with a question that would enable the researcher to establish what the participants' perceptions of exercise were and whether or not those perceptions had changed as a result of training. The question was: when you first arrived for training, what did you think about exercise and what exactly did you aim to achieve?

7.3.3.1. Motive for training

In answer to the question above, one female participant stated that she reluctantly agreed to take part in the training programme only to please her father. In her words:

> *My father told me that I had nothing to lose by trying, and it was agreed that I would quit training the moment I felt it was going to trigger fatigue or a relapse.*

Another female participant stated that although she initially had "strong feelings and doubts about training", she still decided to "give it a try" only because she felt she would be “in safe hands”. When she was asked to elaborate, she had this to say:

> *A friend invited me to her fitness club last year. Although I was no match for the training ladies, I still enjoyed exercising. At one point, an old lady challenged me to copy her moves. I failed, of course. They all had a good laugh and I pretended to join them. But deep inside, I felt depressed and hurt. That same day, I had a relapse.*

At this point in her story, the interviewee was asked if her friend knew about her illness. She gave two deep sighs, one before and the other after her "NO" answer. She then asked a question and, herself, gave the answer:

> *You know why I had a relapse that day? Maybe because I was fatigued, but I do know that I was fatigued because I was stressed.*

A third female participant admitted that she was not initially interested in training per se and that she mainly wanted to meet people with MS to "exchange views and see what they do". When she was asked why she was not interested in exercising, her answer was that she never trained when she was healthy and was not expected to train and take risks when she was ill.

The fourth participant, a male, said he was aware of the benefits of training and that he was encouraged to join because trainers were "professionals who know about MS" and his abilities and needs.

The fifth and sixth participants are Y and Z of the 85 kilometre walk (described above and in Appendix 15). These are highly motivated, determined and optimistic individuals as evidenced by their extraordinary pilgrimage story. Unlike other participants, they are open about their illness and not ashamed of it. When Y and Z were asked why they joined the programme and what they aimed to achieve, the former said he wanted to do “something enjoyable”, and the latter said she would rather be with others doing something useful that staying at home thinking about her illness.

The stories of the six interviewees and the attitudes they brought with them to the first training session have been narrated in some detail for one main purpose: to enable us to better understand and interpret the results obtained through questionnaires and functional measures. This point will be qualified in our final discussion where it is argued that our understanding of fatigue will remain incomplete unless the psychosocial impact of the symptom is appreciated rather than being underestimated..

7.3.3.2. Training outcomes

The most obvious and positive outcome of the training programme was that all participants completed the training course. This is despite the fact that interviewees some participant arrived for the first training session with doubts about their abilities and negative, or at best neutral, perceptions of physical training. Factors that contributed to positive changes in those interviewees' perception of exercise pertain to the physical, psychological and social outcomes of training.

On the physical side, all six interviewees pointed to significant improvements in fatigue, endurance, mobility and flexibility. One interviewee boastingly stated:

> *At the end of the training programme, I was able to help my mother prepare meals and make my father cups and cups of tea. He often tells me that I am spoiling him.*

Another interviewee jokingly said that she was "able to climb the tallest tree ". Similar comments were made by participant another female participant who noted that training made her stronger and energetic to the extent that she was no longer dependent on her crutches. Two participants said they witnessed an increased range of motion tn their arms and legs, and one said he was, at the end of training, used to walking to work and back home and enjoy it. Participant Y commented that excessive rest or sleep can generate fatigue. This, according to him, explains why he tries to be busy and physically and mentally active. Similarly, Z said she preferred to keep busy and that rest makes her feel tired.

The psychological outcomes of the training programme are possibly as important as the physical. In fact, there is good reason to argue that the latter would have been difficult to achieve without the former. The story of one female participant is quite telling:

> *During the early days of training, I used to feel pains and really tense. This is because I was daunted by fears of having a relapse. But with encouragement, I was able to overcome my fears. Courage was what I needed. I now have it.*

One interviewee said he regained self- confidence as a result of training. Another noted that she was more confident of herself, had no doubts about her abilities and was beginning to enjoy life. Two participants said they felt improvements in their mood, mental and physical abilities and relations with other people. Y said he felt more cheerful, lively and hopeful. Z said she was enjoying social life with her relatives and friends and having more time to help her children with their school work.

No interviewee reported any negative outcomes of training, and all praised trainers for their dedication, encouragement and professionalism. However, two female interviewees thought that better results would have been achieved if all members of the training team were locals or expatriate Arabs due to cultural differences and communication problems with non-Arabic speaking trainers. Five of the six participants were of the view that the training programme should have lasted for a longer period of time. They further noted that training for MS patients should be an ongoing process and provided free of charge. In this respect, it is worth mentioning a statement made by one interviewee who thought that the majority of those who participated in training shared with him the same view:

> *Like many others, when I first agreed to join the training programme, I did have the feeling that exercises might help, but I was not sure. So, I decided to give it a try and see how it goes. The first few sessions went well with no excessive fatigue or a relapse. Together with encouragement, that gave me a push. Day by day, fears, anxiety and stress began to retreat, and I began to feel more and more confident and physically and mentally stronger. Had I been free from anxiety and fear when the programme started, I am positive I would have gained more benefits from training.*

7.4. Summary

Participants in the pre-training interview gave a vivid description of the nature and impact of MS fatigue. It is usually felt on a daily basis, comes easily and suddenly, is present and often mild in the morning even after good sleep, and it starts building up during the day to reach its peak n the afternoon. Physical fatigue is usually accompanied by mental fatigue, and both are thought to be aggravated by strenuous physical or mental activities, stress, humidity and heat. In some cases, patients feel fatigued for no obvious reason. Cold showers and short naps are often seen as an effective strategy in alleviating the symptom. As a result of fatigue, physical, mental and social activities are restricted, social relations and performance at work are negatively affected, patients are often depressed, and they experience a sense of sadness, frustration and low self-esteem.

Participants in the post-training interview clearly indicated that they were not fully aware of the benefits of exercise when they first joined the training programme. Some were even fearful of exercising and doubtful about its results. In the main, participants (particularly females) initially found in the programme an opportunity to “socialise”, break solitude, and explore new possibilities to improve their condition and mood. However, they reported a slow but gradual change in those perceptions during training, and gains in terms of improved fatigue, mobility, mood and quality of life. In their view, had they approached training with a positive attitude, they would have gained even more benefits. Commenting on the training programme, there has been the view that participants, especially females, would have felt more comfortable with Arabic speaking trainers. Some were also of the view that the training programme should have lasted for a longer period of time.

In the following chapter, the interview findings, among others, are put in the context of the research objectives outlined in the opening sections of this paper.

Chapter 8: Conclusions

8.1. Introduction

In the opening chapter, it was noted that the objective of the present study is to explore the potential of physical activity in alleviating MS fatigue. The body of research in this area of knowledge is vast and still growing. If we manage to learn lessons from that research, we can possibly contribute to it by approaching it from a different perspective. With this in mind, the present writer conducted a comprehensive literature review activity (Chapters 2 and 3) that enabled him to identify areas in research where progress can be made. The conclusion has been that if we are to establish the real effect of exercise and explore its potential, we: a) need to view MS fatigue is a multidimensional symptom, b) in order for this symptom to be properly assessed, both quantitative and qualitative date are needed, c) any training programme should be tailored to meet the abilities and needs of the participants, d) participants' attitude towards training should be gauged, and e) they should be also fatigued and with no previous training experience. These guidelines informed the present research from design to execution. The end result has been that: this study has achieved its objectives. In this final chapter, we will be reflecting on the present study and its findings.

8.2. Overall outcomes

When talking about the results of the present research project, the pilot study on patients' perceptions of exercise (Chapter 4) would be a good starting point. Although that study was not designed to serve any comparative purposes (see 4.1 and 4.8), it still revealed some important information that should not escape our attention.

Individual differences are to be expected in a given group of MS patients, even when those patients belong to the same ethnic or racial group. In fact, this is not new knowledge, and it is not uncommon that writers allude to such differences. However, when we segregate and compare the two sex groups in a given sample (say Kuwaiti males and females in the pilot study), an interesting pattern emerges. Whereas only a few similarities exist between the two sex groups in that sample, huge differences still remain, and they extend to age, disease duration, relapse rates and causal factors, disability levels, MS type, the majority of MS symptoms, the impact of those symptoms on the patient, the kind of support individuals seek or receive, and attitude towards physical exercise.

Differences and similarities also exist between the British male and female groups. However, it is very often the case that they do not follow the pattern we witnessed in the Kuwaiti sample. For example, unlike Kuwaiti participants, hardly any differences can be seen between British male and female groups in terms of age, attitude towards exercise or the type of advice and service they receive. Some symptoms are also common in equal or almost equal proportions of the two British groups. At the same time, marked differences in terms of relapse frequency and disease severity and symptoms and their impact are still seen between the same two groups of the sample.

In a nutshell, clinical, demographic and attitudinal differences between the opposite sexes are present in both the Kuwaiti and the British samples, though such differences are more prominent in the former sample. But what about differences and similarities between the same sex groups across the two samples?

The pilot study shows that huge differences exist between the two British and Kuwaiti male groups. In fact, those differences are far too many, and the reader is referred to Tables 4.1-4.16 for details. For example, compares to their Kuwait counterparts, British males are much older, have been with the illness for a longer period of time, their MS condition is more advanced and severe, are more likely to have more than one relapse per year, have a more positive attitude towards physical activity, are less sensitive to fatigue, infection, depression and heat. In terms of MS symptoms and their impact levels, rates vary (often considerably) between the two groups, and whereas a number of symptoms are totally absent in Kuwaiti males, they are very or somewhat common in British males. As is the case in the male groups, huge differences also exist between the two female groups, and both exhibit different perceptions and concerns.

To sum up, differences between the same sex groups in the two samples of the pilot study are far too many, and it would in fact be difficult to talk about real similarities. In itself, this shows how difficult it is to contemplate a unified, valid and universal set of MS gender specific characteristics or rules. In other words, what applies to (say) British females, does not necessarily apply to all other female groups. Although it is true that the type of the disease as well environmental conditions may be in part responsible for those differences, there is good reason to suggest that culture appears to shape some important symptoms of the disease and determine the course they take. At least in our study, stressors imposed by the rigid cultural norms are reported not only to trigger other symptoms, but also, to alter the patients' quality of life and determine how they think and behave. This statement will be qualified in the next section. Nevertheless, this finding leads to the question as to the possible role culture can play in shaping MS symptoms, how strong that role be, and whether it strong enough to influence the course of the disease. By bringing this question to the attention of interested researchers, it can be claimed that this study has contributed to MS research.

Back to the results of the 12-week combined and resistance training programme, these showed significant improvements in fatigue (MFIS); fine mobility and static and dynamic balance (TUG); short duration walking speed (10m walk); exercise tolerance (6-minute walk); balance and fear of falls (BBS); shoulder flexion and adduction (Nicholas MMT); and elbow, knee and hip flexion and extension (Nicholas MMT). All these improvements were still maintained four weeks after the training programme had been terminated. On the other hand, there was no significant effect of training on anxiety and depression (HADS); personal basic functional activities (B1); fine motor coordination and finger dexterity (9-HolePeg) and hand grip (JAMAR). During the training programme, no changes in body temperatures were detected because training was provided in an air-conditioned environment, no exacerbations or adverse effects as a result of training were reported, and there was noticeable increase in heart rate within each session in the majority of the participants. Adherence rate to training was very good, particularly among female patients.

Information obtained from Kuwaiti patients through the pilot study and the interviews shows that: a) their physical and social activities are extremely restricted, b) they are totally dependent on pharmacological treatment and their neurologist to manage their condition, c) they are not aware of the benefits of exercise as a health promoting therapy, and d) their mood is adversely affected as a result of the disease, lacking support and social pressures. During the interviews, participants clearly noted that when they first joined the training programme, they felt tense, were fearful of physical exertion and doubtful of any positive results of exercising. In the main, the motive of those patients (especially females) to join the programme was initially to meet fellow patients, socialise and break solitude, listen to professionals who are interested in their condition, and explore other avenues that might help them manage the disease and regain control. According to them, when they realised that no risks were involved in training, and in light of encouragement they received from programme organisers and fellow participants, their attitude towards exercise began to slowly and gradually change, and they began to feel more and more the benefits of training. More than one participant commented that had they initially approached the training programme with a more positive attitude, they would have started gaining benefits from day one and their gains would have increased. In itself, this comment indicates that fatigue is probably more related to the mood of the participant rather than to physical activity. To better understand the study results, we need to know more about the participants and put their training experience in a wider context.

8.3. Reflections

The comment made by the interviewees who noted that they had been living with anxiety since the days they were waiting to be diagnosed is quite telling. Indeed, given the fact that diagnosis is a complex process that may take a long period of time can, itself, lead to uncertainty and provoke anxiety. Moreover, when news of the chronic disease is communicated to patients, the majority are not expected to take it lightly. At least, not when they are told that the illness is incurable, unpredictable and can be disabling. Rather, the uncertainty about the course the illness will take and about the future will, no doubt, generate anxiety and fear. Added to this, as we have seen in Tables 4.2 and 4.3, the majority of Kuwaiti patients were diagnosed with MS in early adulthood when they are making important decisions about their future, such as starting a family or pursuing a particular career. As a result of their condition, it is not surprising that many of those patients begin to reconsider their priorities and plans, question the value of life, and develop a feeling of personal loss.

It can be argued that the stress and depression generated by the unpredictable, incurable and disabling MS are a universal rule. However, at least as far as Kuwaiti (and Arab) MS patients are concerned; it does appear that stressors need to be quantified in broader terms. For, as we have seen in the interviews, the majority of Kuwaiti patients choose to keep the news of their illness as a secret known only to them and their parents and partners. In two cases, even the parents did not know about the illness of their daughter and a wife was not told about the illness of her husband. There is also the case of the two female cousins, close friends and neighbours who were forced to unveil their secret to one another only because they joined the training programme. This is because in Arab tradition, disability is seen as a curse and a source of misery and shame. In that part of the world, the disabled know that not many people would be happy or willing to identify with them or take them as partners, and pity is the best thing they can hope for. Unmarried MS patients (particularly females) know that they may never be able to start a family, and those who are married know that they and other members of their families will be leading a miserable life.

Revelations made by some patients during the interviews reflect a sense of guilt because they find themselves dependent on their families for help. There is also a sense of sorrow and sadness because they had to opt for a part-time job or contemplating abandoning work altogether because they were overweighed by job demands. A sense of sadness was also evident in the statements of those who noted that they were unable to disclose their feelings to members of their families, close friends and work colleagues. Interviewees also spoke in some detail about the double life they are forced to lead in that they need to pretend that they are fit and well, especially in public places and at work. They also noted they were fearful of physical exertion lest relapses, fatigue and other symptoms are triggered and, as a result, the secret of their illness is revealed and they lose face. Indeed, given the limitations imposed on those patients by their illness and the mounting social and psychological pressure, it would be surprising if they did not feel frustrated, vulnerable, alienated, defeated and depressed

To add to the problems of Kuwaiti MS patients, except for the help they receive from their neurologist (Tables 4.8 and 4.13), not much is expected from the outside world. At the same time, all the neurologist can do is to prescribe drugs that hardly help them to manage their condition and advise them to try to be mobile and active. Yet, as we have seen in the discussion above, those patients remain fearful of exercising and are not aware of its benefits. In fact, as seen in Tables 4.9, 4.10 and 4.11, exercise as a health promoting activity is almost alien to Arab culture, and even healthy individuals are not used to physical training activities, let alone people with a disabling disease. Even if it happens that some of those patients are willing to exercise, it is likely that they will be discouraged by other members of the family lest fatigue or other symptoms are provoked. Added to this, professional trainers and rehabilitation institutions are a rarity, and their services are mainly directed to individuals with non-chronic conditions or disabilities.

Despite the account given above, the possibility that some participants were aware of the advantages of physical activity and approached the training programme with a positive attitude is not to be discounted. Participants Y and Z, who performed the 50 mile walk

(7.2.3.5 and Appendix 15) provide a good example. However, it is evident that those two individuals represent an exceptional case in that they are highly motivated, optimistic, and strongly identify with their faith. As regards other participants, this does not appear to be the case. This problem is better understood when we put it into its cultural context.

According to Arab tradition, respected men do not usually talk about their problem, at least not when those problems are related to a humiliating, chronic and disabling disease. Even when those males are offered help, it is likely that they will reject it and deny a need for it. This is unless they are extremely desperate for help and, at the same time, are certain that it is provided in secret and at the hands of people they closely know and trust. This explains why only a few males (relative to females) were persuaded to take part in the trial. In that patriarchal culture, the two sexes are strictly segregated, and at least as far as social life and leisure time is concerned, males have a relatively wide range of options. On the other hand, in order for females to be labelled virtuous, they must remain confined to their homes and serve other members of the nuclear family. Hence, when MS female patients are invited to take part in a training programme, they would be more willing than male patients to accept the invitation for at least one good reason. Needless to mention the immense social pressure as well as the pressure of MS on those patients, it is likely that they treat that programme as a rare event that would provide them with the opportunity to break away from the boring routine and stress at home, meet fellow female patients, and talk about their problems to those who appear to be willing to help and interested in their condition. In fact, this was their main objective of joining the training programme, and they did not hesitate to state it during the interviews. Their secondary objective was to explore whether exercise can actually help them manage their condition. Although they were not sure about this latter objective, they thought they would not lose much if they gave the training experience a try especially that it would be provided by professional trainers who understood their condition, abilities and needs. Again, this objective was explicitly stated during the interviews. Nevertheless, reflecting on their training experience, those same interviewees noted that they achieved more than they hoped for: improved fatigue and mobility and developing a positive attitude towards training. More than that, they made new friends and formed a "Multiple Sclerosis Group". However, according to the participants, themselves, the gains they made occurred slowly and gradually, and they took place only after patients had quelled their fears of physical activity and the anxiety and uncertainty those fears had always generated.

With the above stated, it can be safely argued that with encouragement and support, negative attitude towards training can be reversed, and patients, even those with no previous training experience, can benefit in terms of reduced fatigue, mobility, increased independence and quality of life. In fact, it is felt that participants in the present study could have reaped more benefits. However, this would have been possible if those patients had approached the training programme with a more positive attitude, not the negative mood and stress and depression on the scale just described.

In closing, there is no argument that the social and psychological pressures on Kuwaiti MS patients and their families as a result of the disease are staggering. At the same time, it is felt that they do not receive the support they deserve and need. It is about time Kuwaiti policy makers, health professionals and other service providers developed training and support programmes that can be facilitated through counselling and education.

8.4. Study limitations

Although the present study advocated the inclusion of MS adult patients regardless of their age or level of disability in training, it has not been possible to recruit relatively old patients or those with advanced disabilities. Hence, effect of training on those groups of patients remains unknown, and it needs to be investigated. It is also to be noted that some trainers were foreign expatriates with cultural and linguistic backgrounds different to those of the trainees. However, this has been necessary because of severe shortages in qualified Arabic speaking trainers, particularly females. To go about this problems, arrangements were made for participants to meet and interact with the (Arabic speaking) programme organisers before and after every training session. Furthermore, although it is true that that carers and family members of MS patients can be an important source of information, it has not been possible to include them in the interviews due to cultural sensitivities. It is also to be noted that by not having a control group, we may have over estimated treatment effect. The mains reason for this is the variety of bias (e.g. regression to the mean, time course of changes) that were not controlled for.

8.5. Suggestions for further research

Until a cure to MS fatigue is found, there remains a need to continue exploring the potential of exercise therapy in alleviating this symptom, and hence minimise or slow down deconditioning, empower patients and help them lead a fulfilling life. Hence, it is felt that more needs to be known about patients' attitude towards exercise and thus encourage them to participate in health promoting activities. It is also felt that the impact of stress and depression on fatigue requires further investigation. In particular, special attention should be paid to stressors which are shaped and determined by culture. To better understand the effect of stressors and establish their sources and how they can be alleviated, it is suggested that both qualitative and quantitative data collection methods are employed. In this respect, in order to overcome the limitations of the present study, it is suggested that Kuwaiti (and Arab) researchers consider a sequence of qualitastive studies followed by a randomised control trial to more comprehensively understand the effects of exercise on MS and the steps that are to be taken to implement this research in practice.

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Appendices

Appendix 1

Kurtzke Expanded Disability Status Scale (EDSS)

☐ 0.0 - Normal neurological exam (all grade 0 in all Functional System (FS) scores*).

☐ 1.0 - No disability, minimal signs in one FS* (i.e., grade 1).

☐ 1.5 - No disability, minimal signs in more than one FS* (more than 1 FS grade 1).

☐ 2.0 - Minimal disability in one FS (one FS grade 2, others 0 or 1).

☐ 2.5 - Minimal disability in two FS (two FS grade 2, others 0 or 1).

☐ 3.0 - Moderate disability in one FS (one FS grade 3, others 0 or 1) or mild disability in three or four FS (three or four FS grade 2, others 0 or 1) though fully ambulatory.

☐ 3.5 - Fully ambulatory but with moderate disability in one FS (one grade 3) and one or two FS grade 2; or two FS grade 3 (others 0 or 1) or five grade 2 (others 0 or 1).

☐ 4.0 - Fully ambulatory without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability consisting of one FS grade 4 (others 0 or 1), or combination of lesser grades exceeding limits of previous steps; able to walk without aid or rest some 500 meters.

☐ 4.5 - Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability usually consisting of one FS grade 4 (others or 1) or combinations of lesser grades exceeding limits of previous steps; able to walk without aid or rest some 300 meters.

☐ 5.0 - Ambulatory without aid or rest for about 200 meters; disability severe enough to impair full daily activities (e.g., to work a full day without special provisions); (Usual FS equivalents are one grade 5 alone, others 0 or 1; or combinations of lesser grades usually exceeding specifications for step 4.0).

☐ 5.5 - Ambulatory without aid for about 100 meters; disability severe enough to preclude full daily activities; (Usual FS equivalents are one grade 5 alone, others 0 or 1; or combination of lesser grades usually exceeding those for step 4.0).

☐ 6.0 - Intermittent or unilateral constant assistance (cane, crutch, brace) required to walk about 100 meters with or without resting; (Usual FS equivalents are combinations with more than two FS grade 3+).

☐ 6.5 - Constant bilateral assistance (canes, crutches, braces) required to walk about 20 meters without resting; (Usual FS equivalents are combinations with more than two FS grade 3+).

☐ 7.0 - Unable to walk beyond approximately 5 meters even with aid, essentially restricted to wheelchair; wheels self in standard wheelchair and transfers alone; up and about in wheelchair some 12 hours a day; (Usual FS equivalents are combinations with more than one FS grade 4+; very rarely pyramidal grade 5 alone).

☐ 7.5 - Unable to take more than a few steps; restricted to wheelchair; may need aid in transfer; wheels self but cannot carry on in standard wheelchair a full day; May require motorized wheelchair; (Usual FS equivalents are combinations with more than one FS grade 4+).

☐ 8.0 - Essentially restricted to bed or chair or perambulated in wheelchair, but may be out of bed itself much of the day; retains many self-care functions; generally has effective use of arms; (Usual FS equivalents are combinations, generally grade 4+ in several systems).

☐ 8.5 - Essentially restricted to bed much of day; has some effective use of arm(s); retains some self-care functions; (Usual FS equivalents are combinations, generally 4+ in several systems).

☐ 9.0 - Helpless bed patient; can communicate and eat; (Usual FS equivalents are combinations, mostly grade 4+).

☐ 9.5 - Totally helpless bed patient; unable to communicate effectively or eat/swallow; (Usual FS equivalents are combinations, almost all grade 4+).

☐ 10.0 - Death due to MS.

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*Excludes cerebral function grade 1.

Note 1: EDSS steps 1.0 to 4.5 refer to patients who are fully ambulatory and the precise step number is defined by the Functional System score(s). EDSS steps 5.0 to 9.5 are defined by the impairment to ambulation and usual equivalents in Functional Systems scores are provided.

Note 2: EDSS should not change by 1.0 step unless there is a change in the same direction of at least one step in at least one FS.

Sources: Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology. 1983 Nov;33(11):1444-52.

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Appendix 2

Modified Fatigue Impact Scale (MFIS)

المقياس المعدل لتأثيرالإرهاق

N	English	Never لا ابدا	Rarely نادرا	Sometimes أحيانا	Often أحيانا كثيرا	Almost always تقريبا بشكل دائم
1	I have been less alert لدي مستوى متدني من اليقظة	0	1	2	3	4
2	I have had difficulty paying attention for long periods of time. أجد صعوبة في التركيز لفترات طويلة	0	1	2	3	4
3	I have been unable to think clearly. أجد صعوبة في التفكير بذهن صافي	0	1	2	3	4
4	I have been clumsy and uncoordinated. ألاحظ لدي سلوك متعثر وغير منسق	0	1	2	3	4
5	I have been forgetful. كثير النسيان	0	1	2	3	4
6	I have had to pace myself in my physical activities. يتوجب علي مراقبة حركتي وأنشطتي الجسدية والبدنية	0	1	2	3	4
7	I have been less motivated to do anything that requires physical effort. لدي حافز متدني لأداء المهمات التي تتطلب جهدا جسديا	0	1	2	3	4
8	I have been less motivated to participate in social activities. لذي حافز متدني للمشاركة بالأنشطة الإجتماعية	0	1	2	3	4

9	I have been limited in my ability to do things away from home. مقدرتي على الأداء المنزلي او العمل محدودة	0	1	2	3	4
10	I have had trouble maintaining physical effort for long periods أجد صعوبة في الحفاظ على لياقتي البدنية لفترات طويلة	0	1	2	3	4
11	I have had difficulty making decisions. أجد صعوبة بالاتخاذ القرارات	0	1	2	3	4
12	I have been less motivated to do anything that requires thinking. لدي حافز متدني للقيام بأعمال تتطلب الجهد الذهني	0	1	2	3	4
13	My muscles have felt weak أشعر بضعف في العضلات	0	1	2	3	4
14	I have been physically uncomfortable. أشعر بعدم الإرتياح البدني	0	1	2	3	4
15	I have had trouble finishing tasks that require thinking أجد صعوبة لإنجاز المهام التي تتطلب جهد ذهني	0	1	2	3	4
16	I have had difficulty organizing my thoughts when doing things at home or at work. أجد صعوبة في ترتيب أفكاري حين القيام بمهام في العمل او المنزل	0	1	2	3	4

17	I have been less able to complete tasks that require physical effort. أجد صعوبة لإنجاز المهام التي تتطلب جهدا بدنيا	0	1	2	3	4
18	My thinking has been slowed down. مقدرتي على التفكير تنحدر بشكل تدريجي	0	1	2	3	4
19	I have had trouble concentrating. أجد صعوبة في التركيز	0	1	2	3	4
20	I have limited my physical activities. قمت بتقليص أنشطتي البدنية	0	1	2	3	4
21	I have needed to rest more often or for longer periods. كثيرا ما أحتاج إلى الراحة لأوقات طويلة	0	1	2	3	4
Score						

Appendix 3

Health Research Authority

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13 March 2012

Mr Ali Ashour
PhD Student
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Institute for Science & Technology in Medicine
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Mackay Building, Room No. 002
ST5 5BG

Dear Mr Ashour

Study title:	**A pilot study to investigate the perceptions of Multiple Sclerosis patients towards exercise for reducing fatigue**
REC reference:	**12/NW/0107**

Thank you for your email of 12 March 2012, responding to the Proportionate Review Sub-Committee's request for further clarification and changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Confirmation should also be provided to host organisations together with relevant documentation.

Approved documents

The documents reviewed and approved by the Committee are:

Document	*Version*	*Date*
Covering Letter		18 January 2012
Covering Letter		12 March 2012
Evidence of insurance or indemnity	Keele University	21 July 2011
GP/Consultant Information Sheets	004	20 January 2012
Investigator CV	Mr Ali Ashour	
Letter from Sponsor	Keele University	18 January 2012
Letter of invitation to participant	003	20 January 2012
Other: Professor Clive Hawkins		
Other: Professor Anand Pandyan		
Participant Consent Form	005	22 January 2012
Participant Information Sheet	1.1	12 March 2012
Protocol	001	20 January 2012
Questionnaire: Non validated	1.1	12 March 2012
REC application	3.4	23 January 2012
Referees or other scientific critique report	Peer Review	08 December 2011
Response to Request for Further Information		12 March 2012
Summary/Synopsis	006	22 January 2012

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

12/NW/0107 Please quote this number on all correspondence

With the Committee's best wishes for the success of this project

Yours sincerely

pp **Dr Lorraine Lighton**
Chair

Email: Shehnaz.ishaq@northwest.nhs.uk

Enclosures: "After ethical review – guidance for researchers"

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Appendix 4

Institute for Science & Technology in Medicine
and Department of Neurology

University Hospital of North Staffordshire NHS Trust NHS

Keele University And the University Hospital Of North Staffordshire

Keele University

Title: A pilot study to investigate the preferences of Multiple Sclerosis patients towards exercise for reducing fatigue.

My name is Ali Ashour, and I am a PhD research student at the Institute for Science & Technology in Medicine, Keele University. My research project is supervised by Professors Clive Hawkins and Anand Pandyan. My PhD research is focused on the impact of exercise on multiple sclerosis (MS) patients and its ability to help them cope with fatigue. It is possible that exercise may be beneficial in patients with MS and details related to research carried out on the effects of exercise can be found at the following websites:

Website	Link	Tel. Helpline
MS Trust	http://www.mstrust.org.uk/	0800032 3839
Webpage related to Exercises	http://www.mstrust.org.uk/information/exercises/	*Free Phone Information
Webpage related to Fatigue	http://www.mstrust.org.uk/atoz/fatigue.jsp	
MS Society	http://www.mssociety.org.uk/	02084380700
Webpage related to Exercises	http://www.mssociety.org.uk/what-is-ms/treatments-and-therapies/exercise	
Webpage related to Fatigue	http://www.mssociety.org.uk/ms-events/ms-life/workshops-and-talks	

My study is specifically looking at the whether exercise reduces fatigue or the feelings of fatigue. In order to design an appropriate exercise protocol for the clinical trial I need some additional information. I am interested in establishing whether patients are already participating in any form of physical activity (or exercise) and also whether patients would consider participating in a clinical trial involving exercise. If patients are interested in participating in a clinical trial involving exercise then I would also like to get some information related to their exercise preference. This short questionnaire will help me collect this information in a structured way. I do hope that you can spare ten to fifteen minutes of your time to complete the enclosed questionnaire and (a) return this in the clinic or (b) send it back to me in the self addressed and stamped envelope provided. If you are unable to fill this questionnaire in by yourself you may ask someone else to complete this on your behalf.

Although the information you provide can be useful to my research there is no direct benefit to you. You are under no obligation to fill and return this questionnaire and your quality of care will not be affected in any way if you do not complete this questionnaire. Also, note you are not being asked to sign a separate consent form as returning a completed questionnaire is considered equivalent to giving valid consent in this particular instance.

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study you can speak to my supervisors (address at the end of this document), and if you are not satisfied with this response you can send a formal complaint to Ms N Leighton (address at the end of this document)

If you still have any questions or need help to fill in the survey, please contact me on (address at the end of this document) (Monday to Friday, 9 p.m. to 5 a.m.). Your support for this research is very greatly appreciated.

I do thank for your time and help.

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بسمه تعالى

هذا الاستبيان هو جزء من بحث اجريه حاليا في كلية الطب والعلوم الصحية في جامعة كيل بالمملكة المتحدة. الهدف من هذا البحث الى القيام بدراسة مسحية لمعرفة ما يفضله مريض التصلب المتعدد (MS) من التدريب والتمرينات الرياضية ، كما يهدف هذا البحث على وجه التحديد إلى الكشف عن ما اذا التمرينات الرياضية تقلل من الشعور بالتعب والارهاق ام لا. من أجل تصميم برتوكول لوضع دراسة مناسبة احتاج بعض المعلومات الاضافية والتى هي عباره عن:

١» الحصول على بعض المعلومات المتعلقة بما يفضله المريض اتجاه التمرينات.

٢» تحديد ما اذا كان المريض يرغب بالمشاركة في الدراسة في أي شكل من أشكال النشاط البدني.

لذلك سيفيدني هذا الاستبان القصير على جمع المعلومات بطريقة منظمة، وآمل ان تتمكن من تعبئته خلال ١٠ دقائق من وقتك وإعادته للمختص، كما اود ان اشير إلى انه من الممكن ان يقوم اي شخص اخر بتعبئة الاستبيان للاشخاص الغير قادرين على القيام بذلك.

بعض المواقع المفيدة المتعلقة بالتمرينات لمرضى التصلب المتعدد (MS):

الموقع	الرابط	Website
منظمة التصلب المتعدد	http://www.mstrust.org.uk/	**MS Trust**
بعض التمرينات	http://www.mstrust.org.uk/information/exercises/	Webpage related to Exercises
شرح مفصل للتعب	http://www.mstrust.org.uk/atoz/fatigue.jsp	Webpage related to Fatigue
منظمة التصلب المتعدد	http://www.mssociety.org.uk/	**MS Society**
بعض التمرينات	http://www.mssociety.org.uk/what-is-ms/treatments-and-therapies/exercise	Webpage related to Exercises
شرح مفصل للتعب	http://www.mssociety.org.uk/ms-events/ms-life/workshops-and-talks	Webpage related to Fatigue

أتقدم لكم بالشكر الجزيل لإستكمال هذا الاستبيان الذي يشمل على١٧ سؤال، وللتنبيه اتعامل في هذا الاستبيان بسرية تامة لمعلومات المريض والخصوصية في التحليل.

إذا كان لديك أي سؤال او استفسار رجاءا مراسلتي على البريد الاكتروني الأتي:

a.ashour@keele.ac.uk

Appendix 5

العنوان: دراسه مسحية لمعرفة ما يفضله مريض التصلب المتعدد (MS) نحو التمرينات الرياضية

Title: A pilot study to investigate the preferences of Multiple Sclerosis patients towards exercise for reducing fatigue.

Date of birth: ....:تاريخ الميلاد

Gender: Female/ انثى ☐ Male/ ذكر ☐ :الجنس

Date of MS diagnosis:...:تاريخ تشخيص المرض

١- كيف يمكنك وصف مدى حدة حالتك الصحية؟

1. How would you describe the severity of your condition?

Advanced/ مرحلة متقدمة ☐ Moderate/ متوسطة ☐ Mild /خفيفة ومعتدلة ☐

٢- ماهي الأعراض التي تعاني منها نتيجة لحالتك المرضية؟ { يمكنك وضع إشارة "صح" أمام ما تراه مناسبا لحالتك}.

2. What are the symptoms that you experience as a result of the illness? (You may tick (/) more than one box if that is applicable).

إرتعاش Tremor		فقدان المقدرة الحسية Loss of sensation	
عدم المقرة على التركيز Inability to concentrate		الألم Pain	
الإكتئاب Depression		إختلال في التوازن Balance problem	
الضغوط النفسية Stress		تشنجات Spasticity	
الإرهاق Fatigue		شد عضلي Muscle spasms	

مشاكل في النطق Speech difficulties	☐	مشاكل في المثانه Bladder problems	☐
صعوبات في الإبتلاع Swallowing difficulties	☐	مشاكل في الأمعاء Bowel problems	☐
إزدواجية وعدم وضوح الرؤيا Double or blurred vision	☐	ضعف Weakness	☐
شعور بالدوخان Dizziness	☐	الخمول الشديد Lethargy	☐

Other(s)... .... اشياء اخرى
....
....
....
. ...

٣- أي من الحالات المذكورة اعلاه يثيرعندك القلق؟

3. What of the above mentioned symptoms that worries/worry you mostt?

Other(s)... .... اشياء اخرى
....
....
....
. ...

٤- نتيجة لحالتك المرضية، هل تتلق الدعم أو العلاج من جهات الرعاية الأجتماعية او الصحية؟

4. Do you receive any support or treatment for your MS condition from social care or health professionals?

☐ No /لا ☐ Yes / نعم

اذا كانت الاجابة "لا" اذهب للسؤال رقم ٦

If the answer is "No", please go to Question (6)

٥- إذا كانت إجابتك ب"نعم" على السؤال السابق، فمن من الجهات التالية يقدم لك الدعم؟ {يمكنك وضع إشارة "صح" امام اكثر من خيار اذا كان مناسبا}

5. If the answer to Question 4 is "Yes", who of the following specialists provide/provides care? (You may tick more than one box if applicable):

أخصائي امراض عصبية Neurologist		أخصائي مهني Occupational therapist		مدرب رياضي Gym instructor	
خبير تغذية Dietician		أخصائي عيون Optician		العلاج الطبيعي Physiotherapist	
طبيب نفسي Psychologist		مستشار Counsellor		موظف الخدمة الأجتماعية Social worker	
طبيب الخاص GP		ممرضة المركز الصحي practice nurse			

Other(s)... .... اشياء اخرى
....
....
....
. ...

٦- متى على الأغلب تواجه الإنتكاسة الصحية؟

6. How often do you have a relapse?

Other(s)... .... اشياء اخرى
....
. ...

٧-متى كانت آخر مرة وقعت فيها بإنتكاسة صحية؟

7. When was the last time you had a relapse?

Other(s)... .... اشياء اخرى
....
. ...

٨- في رأيك، ماهي أسباب الإنتكاسة؟

8. In your opinion, what causes the relapse?

لا أعرف I do not know	
الإرهاق Fatigue	
العدوى والإلتهابات Infection	
إرتفاع حرارة الجسم Increased body temperature	

Other(s)... .... اشياء اخرى
....
....
. ...

٩- هل سبق وأن مارست أي نوع من الرياضة أو الأنشطة الجسدية قبل تشخيص حالتك المرضية؟

9. Did you do exercise or any form of physical activity (…) before being diagnosed with MS?

No /لا ☐ Yes /نعم ☐

{إذا كانت الأجابة بنعم، يرجى وضع علامة "صح" لتلك الأنشطة الجسدية قبل تشخيص حالتك المرضية}

(If your answer is “yes” you may tick more than one box if applicable)

يوجا Yoga		الرقص Dancing		المشي Walking	
أنشطة في الهواء الطلق Outdoor activities		الألعاب القتالية Martial Arts		الألعاب الهوائية {جهاز المشي} Aerobic exercise	
التدريب في الماء Aquatic exercise		تدريبات التقوية الجسدية Strengthening exercise		تدريبات الإطالة Stretching exercise	

١٠- هل تتلقى مشورة أو توجيه بشأن الرياضة؟

10. Do you get any advice on exercise?

No/ لا ☐ Yes/ نعم ☐

{إذا كانت الأجابة بنعم، فمن تلك الجهة التي تقدم المشورة}؟

(If your answer is “Yes” who gives you that advice)?

أخصائي امراض عصبية Neurologist	☐	أخصائي مهني Occupational therapist	☐	مدرب رياضي Gym instructor	☐
خبير تغذية Dietician	☐	أخصائي عيون Optician	☐	العلاج الطبيعي Physiotherapist	☐
طبيب نفسي Psychologist	☐	مستشار Counsellor	☐	موظف الخدمة الأجتماعية Social worker	☐
طبيب الخاص GP	☐	ممرضة المركز الصحي practice nurse	☐		

Other(s)... .... اشياء اخرى

....

....

....

....

....

. ...

١١- هل تمارس أي أنشطة أو تدريب رياضي في الوقت الحاضر؟

11. Do you currently take exercise or engage in any form of physical activity? If

Yes (please go to Question 12) نعم {الرجاء الذهاب للسؤال رقم ١٢}

No (please go to Question 13 لا {الرجاء الذهاب للسؤال رقم ١٣}

١٢- إذا كانت الإجابة على السؤال رقم ١١ ب" نعم" ، يرجى تحديد نوعية النشاط أو التدريب الذي تقوم به مع ذكر المدة التي تقضيها في التدريب.

12. If your answer to Question 11 is "Yes", please tick the type of exercise you currently do and state the length of time you to spend in training?

مدة كل جلسة تدريبية Time per Session	عدد جلسات التدريب أسبوعيا Number of session per Week	نوع النشاط الرياضي Type of exercise
		الأنشطة الهوائية {الأيروبيك}: بين أمور أخرى ، تتضمن هذه الأنشطة على استخدام الدراجات الهوائية والمشي على الأجهزة المتحركة وهي تستهدف تنشيط القلب والرئتين. Aerobic exercises: Among others, these include cycling and treadmill training and they work the heart and lungs.
		تمارين التقوية: الهدف منها تقوية العضلات وتتضمن رفع وتحريك الأثقال وشد الكتل المطاطية. Strengthening exercises: These are aimed at strengthening muscles, and they involve lifting and moving weights or pulling against an exercise elastic band.
		تمارين التمدد: هذه التمارين تكسب العضلات والمفاصل نوعا من المرونة. Stretching exercises: These can be helpful in maintaining supple muscles and flexible joints.
		تمارين حركية: تهدف لحفظ التوازن وتنسيق الأداء بين أطراف الجسم. Posture exercises: These can help in maintaining balance through keeping different parts of the body properly aligned.
		تمارين مائية: وتؤدى في الماء أو فوقه. Aquatic exercises: These take place in or upon water.
		تمارين أخرى: مثل اليوجا والرقص والمشي وأنشطة الهواء الطلق والألعاب القتالية. Other (e.g. yoga, dance, walking, outdoor activities, dancing, martial arts).

١٣- ماهي الأسباب التي تردعك عن القيام بأي تدريب أو نشاط رياضي ؟

13. Why do you not exercise?

Other(s)... يرجى تحديدها

....

....

....

. ...

١٤- هل لديك إستعداد للمساهمة في تجربة تتضمن أنشطة رياضية؟

14 Would you be prepared to take part in a trial that involves exercise?

Yes (please go to Question 15) نعم {الرجاء الذهاب للسؤال رقم ١٥}

No (please state why if you are able to) لا { يرجى تحديد الأسباب التي تمنعك عن القيام بذلك}

Other(s)... يرجى تحديدها

....

....

....

....

....

....

. ...

١٥- ماهي نوعية الأنشطة التي تود القيام بها في تلك التجربة؟

15. What exercise would you like to see (take) in this clinical trial? List the exercise?

Other(s)... يرجى تحديدها

....

....

....

....

. ...

١٦- أذا كنت ترغبين بالمشاركة في التجربة، هل توافقين على ان يكون المعالج رجل؟

16- If you take part in research will you be happy to be treated by a male researcher?

No /لا ☐ Yes /نعم ☐

١٧- أذا كانت الموافقة بنعم:هل توافقين على ان يقون الباحث بالقيام بالقياسات الخاصة بالدراسة ؟

17-If you take part in research will you be happy for a male researcher to take measurements need for the research project?

No /لا ☐ Yes /نعم ☐

شكرا جزيلا

Thank You

Appendix 6

University Hospital of North Staffordshire
NHS Trust NHS

Keele University

Institute for Science & Technology in Medicine and Department of Neurology

Keele University And the University Hospital Of North Staffordshire

Title: A pilot study to investigate the preferences of Multiple Sclerosis patients towards exercise for reducing fatigue.

My name is Ali Ashour, and I am a PhD research student at the Institute for Science & Technology in Medicine, Keele University. My research project is supervised by Professors Clive Hawkins and Anand Pandyan. My PhD research is focused on the impact of exercise on multiple sclerosis (MS) patients and its ability to help them cope with fatigue. It is possible that exercise may be beneficial in patients with MS and details related to research carried out on the effects of exercise can be found at the following websites:

Website	Link	Tel. Helpline
MS Trust	http://www.mstrust.org.uk/	0800032 3839
Webpage related to Exercises	http://www.mstrust.org.uk/information/exercises/	*Free Phone Information
Webpage related to Fatigue	http://www.mstrust.org.uk/atoz/fatigue.jsp	
MS Society	http://www.mssociety.org.uk/	02084380700
Webpage related to Exercises	http://www.mssociety.org.uk/what-is-ms/treatments-and-therapies/exercise	
Webpage related to Fatigue	http://www.mssociety.org.uk/ms-events/ms-life/workshops-and-talks	

My study is specifically looking at the whether exercise reduces fatigue or the feelings of fatigue. In order to design an appropriate exercise protocol for the clinical trial I need some additional information. I am interested in establishing whether patients are already participating in any form of physical activity (or exercise) and also whether patients would consider participating in a clinical trial involving exercise. If patients are interested in participating in a clinical trial involving exercise then I would also like to get some information related to their exercise preference. This short questionnaire will help me collect this information in a structured way. I do hope that you can spare ten to fifteen minutes of your time to complete the enclosed questionnaire and (a) return this in the clinic or (b) send it back to me in the self addressed and stamped envelope provided. If you are unable to fill this questionnaire in by yourself you may ask someone else to complete this on your behalf.

Although the information you provide can be useful to my research there is no direct benefit to you. You are under no obligation to fill and return this questionnaire and your quality of care will not be affected in any way if you do not complete this questionnaire.

Also, note you are not being asked to sign a separate consent form as returning a completed questionnaire is considered equivalent to giving valid consent in this particular instance.

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study you can speak to my supervisors (address at the end of this document), and if you are not satisfied with this response you can send a formal complaint to Ms N Leighton (address at the end of this document)

If you still have any questions or need help to fill in the survey, please contact me on (address at the end of this document) (Monday to Friday, 9 p.m. to 5 a.m.). Your support for this research is very greatly appreciated.

I do thank for your time and help.

Contact details of researcher:

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Appendix 7

معهـد دسمـان للسكـري Dasman Diabetes Institute	**GUIDELINES FOR CONDUCTING APPROVED RESEARCH PROJECTS**

Research Protocol No.	RA 2013-010
Principal Investigators/Co-Investigators	Dr. Aziz Al Feeli and Mr. Ali Ashour
Study Title	An investigation into the effects of a customized patient selected exercise intervention on fatigue in patients with MS.

1 The Investigators are required to abide by the laws of the State of Kuwait, rules and regulations of the Ministry of Health and Policies and Guidelines of the Dasman Diabetes Institute.

2 The study should be conducted in accordance with the International Conference on Harmonization (ICH) guidelines for Good Clinical Practice (GCP), ethical principles of Belmont Report and Declaration of Helsinki.

3 Only the Ethical Review Committee (ERC) approved version of the Consent Form (copy attached) should be used for the enrollment of research participants. The Consent document should be adequately completed, signed, and dated. A copy of the signed Consent should be given to the participant and the original should be retained in the research records of the Principal Investigator.

4 The rights and welfare of research participants should be protected at all times.

5 Research data should be secured so that only authorized users have access to the study records and databases. Personally identifiable information and data should only be collected when necessary; secondary disclosure of personally identifiable data is not permitted.

6 It is the Principal Investigator's responsibility to ensure the compliance of investigating team to applicable regulations, policies and guidelines.

7 The Principal Investigators also need to notify as soon as possible, the ERC in the case of:

  i. Their departure from the Institute.
  ii. Any amendments to the study protocol.
  iii. Termination of the study for whatever reason.
  iv. Any serious and/ or unexpected adverse events (SUAE) that research participants may experience, using the Adverse Events Reporting Form.
  v. Any other information that may affect the benefit to risk ratio of the proposed study.

Appendix 8

معهد دسمان للسكري
Dasman Diabetes Institute

INTERNAL MEMORANDUM

TO: **Dr. Aziz Al Feeli**
Principal Investigator

DATE: 27 May 2013
REF: RA/069/2013

FROM: **Ms. Rashmi Shiju**
Research Compliance Officer
Ethical Review Committee

CC: **Dr. Abdulla Bennakhi**
Chairman
Ethical Review Committee

SUBJECT: **DDI Protocol No: RA-2013-010**
Protocol Title: An investigation into the effects of a customized patient selected exercise intervention on fatigue in patients with MS.

This is in reference to your reply, dated 22 May 2013, to the concerns of the Ethical Review Committee (ERC) on the above referenced proposal.

The reply was reviewed on 27 May 2013 through expedited review process. It is my pleasure to inform you that the reply was accepted and the revised informed consent form and revised research proposal have been approved; attached please find copy of the approved consent form and necessary guidelines for conducting this study.

The study investigators are required to submit a Progress Report by 26 May 2014. The approval of this study will automatically be suspended on the stated date, pending the submission and acceptance of a Progress Report.

Wish you success in your research undertakings.

Encl: As stated
CC: Dr. Kazem Behbehani, Director General
Mr. Michael Ferbuyt, CEO

Appendix 9

معهد دسمان للسكري **Dasman Diabetes Institute**	**Participant's Record No:** رقم المشارك
INFORMED WRITTEN CONSENT FOR PARTICIPATION IN RESEARCH	**وثيقة موافقة للمشاركة في بحث علمي**

PART-A Research Participants' Information Sheet	**الجزء الأول- معلومات للمشارك في البحث**
THE STUDY TITLE: An investigation into the effects of a customised patient selected exercise intervention on fatigue in patients with MS	**عنوان البحث: (كما في البرتوكول)** التحقق من اثر التعب من خلال التدريب الموجه لمرضى التصلب اللويحي المتعدد (MS) .
PURPOSE OF THE STUDY: You are being asked to voluntarily participate in a research study undertaken by PhD researcher (Mr Ali Ashour). The main purpose of this study is to investigate the impact of a 12-week exercise-trainingprogramme on fatigue in MS patients.	**الغرض من البحث:** يطلب منك التطوع بالمشاركة في البحث الذي يجريه باحث الدكتوراه علي فؤاد عاشور الهدف الأساسي من عمل هذه الدراسة التحقق من تأثير برنامج التدريبات لمدة ١٢ أسبوع على التعب عند مرضى التصلب اللويحي المتعدد.
STUDY DESCRIPTION: Once you have given us consent for study participation we will do the following.Dr Al-Roughani will also check if you are safe to participate in the exercise study. 1. We will take a series of measurements to check your status. We will then repeat these measurements a week later to confirm that your condition is stable. 2. We will then ask you to identify the exercises you are interested in and over the next week customize the level of the exercise to your ability. 3. We will then supervise you carrying out the exercise for a further period of 11-weeks. During this time we will monitor your heart rare and body temperature. 4. At this point we will repeat all the measurements to check if the exercise has been of use to you. 5. We will then ask you to return in four weeks time for a final measurement. This is to check if you have been able to carry	**وصف البحث:** بعد اخذ موافقتك على المشاركة سيقوم الدكتور عزيز الفيلي بالتحقق من مقدرتك من المشاركة في برنامج التدريب وضمان ملائمة البرنامج لمقدرتك: **١-سنقوم باخذ عدد من القياسات المتعلقة بحالتك. سيتم إعادة تلك المقاييس بعد اسبوع بعدما تستقر حالتك.** **٢- سيكون لك بعد ذلك حرية اختيار نوعية التدريب الذي سيتم اعداده ليتلائم مع قدراتك الشخصية.** **٣ ستقوم بعد ذلك بالقيام بالتدريبات لمدة ١١ أسبوع يتم خلالها مراقبة نبضات القلب ودرجة حرارة الجسم بشكل دوري.** **٤- بعد نهاية التدريب سنقوم باخذ القياسات مرة اخرى للتحقق من مدى فاعلية البرنامج .** **٥- بعد ٤ أسابيع من انتهاء البرنامج سنقوم بإجراء القياسات مرة اخرى للوقوف على فاعلية التدريب على مدى الطويل .**

FORTHE RESEARCH AFFAIRS OFFICIAL USE ONLY

This Consent Document is approved by the Ethical Review Committee of "DASMAN DIABETES INSTITUTE". It is only valid for use if the validity dates are indicated and initialed by an authorized official.

STUDY NO :	R	A	2	0	1	3	0	1	0

From 27/ 05 / 2013 **To:** 26 / 05 /2014

(DD / MM/YY)

Ethical Review Committee
Dasman Diabetes Institute

Authorized Official's Initials

out exercises on your own and also test if there has been any further changes in your condition.	
POTENTIAL RISKS AND DISCOMFORTS: There are some risks reported as a result of taking exercise. 1. You might experience some discomfort after training, but this feeling disappears in a short period of time. 2. We will be asking you to exercise in a temperature-controlled room to avoid sweating and fatigue. We will also monitor your temperature to reduce this risk further. 3. We will ensure we monitor your heart rate during exercise to ensure that you are not over exercising.	المخاطر المحتملة وعدم الراحة: هناك بعض الصعوبات التي قد تواجه المتدرب. ١- قد تواجه الشعور بعدم الارتياح بعد اداء التمرين، ولكن هذا الشعور سيتوقف خلال فترة التدريب تدريجيا. ٢ سيكون التدريب في صالة يتم التحكم بدرجة حرارتها حتى لا يكون هناك تعب. ٣- سيتم القيام بمراقبة نبضات القلب بشكل دوري كضمان للسلامة.
POTENTIAL BENEFITS: At this stage we are unable to tell you the exact benefits you will get from this study. Exercise may reduce fatigue and improve mobility and quality of life. In this study we are testing if this will be a true effect.	الفوائد المحتملة: الفوائد المحتملة لهذه الدراسة هي : في هذه المرحلة ليس هناك من ضمان للاستفادة من التدريب، ولكن احتمالات واردة لتخفيف وتيسير الحركة نتيجة للبرنامج التدريبي .
ALTERNATIVE TO PARTICIPATION: You have the right to decline the invitation for participation in the trial. You may also withdraw from the trial at any point in time	البدائل عن المشاركة (إن وجدت): البديل للمشاركة في الدراسة هي عدم المشاركة و لك الحرية المطلقة لإختيار المشاركة او عدم المشاركة في هذه الدراسة.
COST(S) & REIMBURSEMENTS: The participation is free of cost to you and you will not receive reimbursement for any expenses that you may incur because of your participation in this study.	التكاليف / التعويضات المالية: مشاركتك في هذه الدراسة مجانية و سوف (لن يتم) تعويضك عن التكاليف المالية المترتبة على مشاركتك في الدراسة.

TERMINATION OF PARTICIPATION: Your participation in this study will be terminated if you decide to withdraw from the study or if the investigator found that you are no more eligible to participate in this study.	**إنهاء المشاركة (إذا أمكن):** سيتم إنهاء مشاركتك في الدراسة إذا قررت الإنسحاب من الدراسة او إذا قرر الباحث بأنك غير مستوفي للشروط المشاركة في البحث.
COMPENSATION AND TREATMENT: In the event of injury resulting from your participation in the research study, hospitalization and professional attention, if required, will be provided by DDI at no cost to you. Financial compensation is not available.	**التعويضات و المعالجات:** في حالة حدوث أي ضرر – لا قدر الل..– من جراء المشاركة في هذه الدراسة سيتكفل معهد دسمان بتقديم الرعاية الطبية اللازمة إذا لزم الأمر ولكنه لا يلتزم بمنح أي تعويضات مالية بديلة.
VOLUNTARY PARTICIPATION: Participation in this study is voluntary. Your decision not to participate or withdraw from the study, will not affect your medical care and you will not lose any of the benefits to which you are otherwise entitled.	**المشاركة التطوعية:** المشاركة في هذه الدراسة تطوعيه وإذا قررت عدم المشاركة فانك لن تتعرض لأي مضايقات أو لفقدان حقك المشروع في المعالجة ، كما أن قرارك بالانسحاب من الدراسة لن يؤثر علي تلقيك لخدمة علاجية بديلة متوفرة.
MAINTAINING CONFIDENTIALITY: As a participant in this research study, your personal identifying information including your medical record will remain confidential with respect to any publications of the results of this study. Your medical record in connection with this study will be kept confidential to the extent permitted by the law. However, your medical record may be reviewed by the investigators of this study, the Ethical Review Committee, and/or other relevant regulatory.bodies in accordance with applicable laws and regulations.	**السرية:** كمشارك في هذه الدراسة ستكون هويتك ومحتويات ملفك الطبّي سرية في جميع التقارير المتعلقة بنتائج الدراسة كما سيبقي رقم سجلك الطبي سري في الحدود التي يسمح بها القانون ويمكن الاطلاع عليه من قبل الباحثين واللجنة المراقبة لمعاير للأبحاث أو الوكيل الداعم للدراسة في حدود النظم والقوانين المطبقة بهذا الخصوص.

معهد دسمان للسكري
Dasman Diabetes Institute

Participant's Record No: رقم المشارك

INFORMED WRITTEN CONSENT FOR PARTICIPATION IN RESEARCH

وثيقة موافقة للمشاركة في بحث علمي

CONTACT PERSONS:

You may call the Research Affairs at Telephone # 00965 22242 999, extension 2303 for general questions concerning research at DasmanDiabetes Institute or the rights of research participants. If you have any specific questions or concerns with regard to this study, you may contact Dr. Raed Al Roughani telephone # + 965 22242 999 Extension 1034.

It is of note that working hours at the DasmanDiabetes Institute during the week extend from 8:00 am to 05:00 pm

A signed copy of the Consent Document will be given to you.

الأشخاص الذين يمكن الاتصال بهم:

للاستفسار عن الأبحاث بمعهد دسمان للأبحاث و التدريب والوقاية أوحقوق المشاركين يمكنك الإتصال بشئون الأبحاث على هاتف رقم: 0096522242999 تحويلة رقم 2303. وفي حالة وجود أسئلة محدّدة تتعلّق بهذا البحث نرجو الاتصال على الدكتور ____________ على هاتف رقم 0096522242999 تحويلة رقم ____1034

علماً بأن وقت الدوام في المركز خلال ايام الأ سبوع من الساعة الثامنة صباحاً و حتى الخامسة مساءً.

سيتم تزويدك بنسخة موقعة من هذا الإقرار.

FORTHE RESEARCH AFFAIRS OFFICIAL USE ONLY

This Consent Document is approved by the Ethical Review Committee of "DASMAN DIABETES INSTITUTE". It is only valid for use if the validity dates are indicated and initialed by an authorized official.

STUDY NO :	R	A	2	0	1	3	0	1	0

From 27/ 05 / 2013 **To:** 26 / 05 /2014
(DD / MM/YY)

Ethical Review Committee
Dasman Diabetes Institute

Authorized Official's Initials

PART-B INFORMED WRITTEN CONSENT

I, ______________________________,

the undersigned, give my Informed Consent for participation in a research study, after Investigator (PhD student Ali Ashour) has fully explained to me the study and all of my inquiries about this study have been answered.

By signing this document, I testify to have read the information in this consent form and all my questions about the research study have been answered to my satisfaction.

1. The purpose of this research is to assess the impact of exercise on fatigue

2. My participation in the study requires, a medical examination a few physical tests and participation in the exercise protocol.

3. The potential risks and benefits of participation in the study, as indicated in the participant information sheet (part A of this document), have been explained to me.

4. I understand that although there is no direct benefit to me, the information gained from this research may help scientists and doctors to learn more about the effects of exercise on MS fatigue.

5. I further testify that my participation is completely voluntary and I have the right to withdraw from this study whenever I wish. I can request disposing of any information or samples taken from me. My decision to withdraw from the study at any time will not affect the medical care that I receive. I can refuse participating to start with without prejudice from my treating physician.

الجزء الثاني: موافقة خطية على بينة للمشاركة في الدراسة

أنا ______________________________

أوقع على هذه الموافقة بَعد أن شَرح لي الباحث/ علي فؤاد عاشور, أنني سِأشارك في بَحث علمي و أجاب عن كُل تساؤلاتي بِخصوص هَذا البَحث.

و بتوقيعي هذا أُقر بأنني أحطت عِلماً بما يلي:

,أن عنوان البحث : التحقق من الاثار المترتبة للتدريب الموجه على درجة التعب عند مرضى التصلباللويحي المتعدد.

1. الهدف من هذا البحث :التحقق من تأثير برنامج التدريبات لمدة ١٢ أسبوع على التعب عند مرضى التصلب اللويحي المتعدد.

2. المشاركة في الدراسة يتطلب مني:
يتطلب مني المشاركة في الاجابة على بعض الاستفسارات والمشاركة في بعض القياسات المتعلقة بالاداء.

3. قد شَرح لي المخاطر والفوائد المتوقعة لهذه المُشاركَة كما هو مفصل في الجزء الأول من هذه الوثيقة (معلومات للمشارك في البحث)

4. بالرغم إن لا توجد فوائد مباشرة من هذه الدراسة ، لكن المعلومات المكتسبة من هذه البحوث قد تساعد العلماء و الأطباء على اكتشاف مسببات هذا المرض بشكل أفضل.

(وينطبق هذا البيان للدراسات بدون فائدة مباشرة للمشاركين)

5. إن مشاركتي هَذه هي تطَوع مِني بمَحض إرادتي. كما أن بإمكاني سَحب مشارَكتي في الدِراسة متى شئت و أن أطلب إتلاف أي عينات أو مَعلومات مُتَعلِقة بي دون أن يؤثر انسحابي على تلقي الرّعاية الطّبيّة اللازمة و لا علاقة لها بالعناية الطبية المقدمة لي. أن باستطاعتي رَفض المُشاركَة ابتداء دون أن يجرح موقفي مع القائمين على برنامج التدريب.

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6. If I do not enroll in this study the alternative option is not to participate.

7. I will bear any extra cost as a result of my participation in this project. In case of any injury resulting from my participation, the DDI will arrange for me the necessary medical care.

8. I understand that the information resulting from my participation in this study will be kept confidential to the extent allowed by law and no unauthorized person or entity will have access to it, unless I give a separate different consent. No reference will be made to my identity or family/my tribe in any published article about this study.

9. I understand that I am not entitled for the compensation of any expenses incurred as a result of my participation in this study.

Research Participantor
Legal Representative:

Print Name ____________________

Signature: ____________________

Date: ____________________

Relationship: ____________________

(if signed by person other than the research subject)

Address ____________________

____

Telephone No.

6. وفي حال رَفضي المشاركة يكون البَديل هوعدم المشاركة.

7. سوف(**أحتمل**) أي تكاليف مالية مترتبة على مشاركتي في هذا البحث. وفي في حالة حدوث أي ضرر علي من مُشاركتي – لا قدر الل.. سوفَ يُوفر لي معهد دسمان العناية الطبية اللازمة.

8. أفهم إن المَعلومات الناتجَة عَن مُشاركتي في البَحث سوف تُعامَل بسرية تامَة ولَن يَطلِع عَليها أي شَخص أو جِهة عَدا المسؤولَين عن إجراء الدِراسة إلا بموافقتي و لن تكون هناك إشارة إلى شخصي أو عشيرتي في أي بَحث مَنشور عَن هذه الدِراسة.

9. أفهم بأنني (**لا استحق**) استرداد المصروفات التي نتجت عن مشاركتي في هذه الدراسة.

المشارك في الدراسة أو من يوقّع عنه:

الاسم : ____________________

التوقيع ____________________

التاريخ

____

صلة القرابة: --------------------
(إذا كان الموقع غير المشارك)

العنوان : ....

....
......

الهاتف :

....

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وثيقة موافقة للمشاركة في بحث علمي

Witness/Translator (If required)

I confirm that the information in this consent has been accurately translated and/ or read to the participant:

Print Name: ______________________

ID #: ______________________

Signature: ______________________

Date: ______________________

الشاهد/المترجم:

أقر بأنني قد قرأت/ أو ترجمت للمشارك هذه المعلومات بشكل صحيح.

الاسم:--

رقم البطاقة :--

التوقيع:--

التاريخ :--

Investigator or his/her Delegate

I have fully explained to the above participant/ legal representative the nature and purpose of the above-mentioned research project.

Signature: ______________________

Date: ______________________

Print Name: ______________________

I.D. Number: ______________________

الباحث أو من ينوب عنه/عنها

أقر بأنني قد شرحت للمشارك أو ولي أمره المذكور أعلاه بصورة كاملة طبيعة وأهداف الدراسة المذكورة.

التوقيع:--

التاريخ:--

الاسم:--

رقم بطاقة :--

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STUDY NO :	R	A	2	0	1	3	0	1	0

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Appendix 10

Timed Up and Go (TUG) Test

Name:____________________________ MR: _______________________ Date:________

1. Equipment: arm chair, tape measure, tape, stop watch.
2. Begin the test with the subject sitting correctly (hips all of the way to the back of the seat) in a chair with arm rests. The chair should be stable and positioned such that it will not move when the subject moves from sit to stand. The subject is allowed to use the arm rests during the sit – stand and stand – sit movements.
3. Place a piece of tape or other marker on the floor 3 meters away from the chair so that it is easily seen by the subject.
4. Instructions: "On the word GO you will stand up, walk to the line on the floor, turn around and walk back to the chair and sit down. Walk at your regular pace.
5. Start timing on the word "GO" and stop timing when the subject is seated again correctly in the chair with their back resting on the back of the chair.
6. The subject wears their regular footwear, may use any gait aid that they normally use during ambulation, but may not be assisted by another person. There is no time limit. They may stop and rest (but not sit down) if they need to.
7. Normal healthy elderly usually complete the task in ten seconds or less. Very frail or weak elderly with poor mobility may take 2 minutes or more.
8. The subject should be given a practice trial that is not timed before testing.
9. Results correlate with gait speed, balance, functional level, the ability to go out, and can follow change over time.

Normative Reference Values by Age

Age Group	Time in Seconds (95% Confidence Interval)	
60 – 69 years	8.1	(7.1 – 9.0)
70 – 79 years	9.2	(8.2 – 10.2)
80 – 99 years	11.3	(10.0 – 12.7)

Cut-off Values Predictive of Falls by

Group	Time in Seconds
Community Dwelling Frail Older Adults	> 14 associated with high fall risk
Post-op hip fracture patients at time of discharge[3]	> 24 predictive of falls within 6 months after hip fracture
Frail older adults	≥ 30 predictive of requiring assistive device for ambulation and being dependent in ADLs

Date	Time	Date	Time	Date	Time	Date	Time

References

1. Bohannon RW. Reference values for the Timed Up and Go Test: A Descriptive Meta-Analysis. Journal of Geriatric Physical Therapy, 2006;29(2):64-8.
2. Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the timed up & go test. Phys Ther. 2000;80:896-903.
3. Kristensen MT, Foss NB, Kehlet H. Timed "Up and Go" Test as a predictor of falls within 6 months after hip fracture surgery. Phys Ther. 2007.87(1):24-30.

Additional References

Bischoff HA, Stahelin HB, et al. Identifying a cut-off point for normal mobility: A comparison study of the timed "up and go" test in community-dwelling and institutionalized elderly women. Age and Ageing. 2003;32:315-320.

Boulgarides LK, McGinty SM, et al. Use of clinical and impairment-based tests to predict falls by community-dwelling older adults. Phys Ther. 2003;83:328-339.

Podsiadlo D, Richardson S. The timed “up & go": A test of basic functional mobility for frail elderly persons. JAGS. 1991;39:142-148.

Appendix 11

BERG BALANCE SCALE

1. Purpose

The Berg's utility includes grading different patients' balance abilities, monitor functional balance over time and to evaluate patients' responses to treatment.

2. Content

The Berg is a test of 14 items; it is performance based and has a scale of 0-4 for each item (higher score for independent performance) with a maximum score of 56.
The Berg is considered the gold standard assessment of balance with good intra-rater reliability and inter-rater reliability and good internal validity.

3. Assessment

1. Sitting to standing

INSTRUCTIONS: Please stand up. Try not to use your hands for support

4	able to stand without using hands and stabilize independently
3	able to stand independently using hands
2	able to stand using hands after several tries
1	needs minimal aid to stand or to stabilize
0	needs moderate or maximal assist to stand

2. Standing unsupported

INSTRUCTIONS: Please stand for two minutes without holding

4	able to stand safely for 2 minutes
3	able to stand for 2 minutes with supervision
2	able to stand for 30 seconds unsupported
1	needs several tries to stand for 30 seconds unsupported
0	unable to stand for 30 seconds unassisted

3. Sitting with back unsupported but feet supported on floor or on a stool

INSTRUCTIONS: Please sit with arms folded for 2 minutes

4	able to sit safely and securely for 2 minutes
3	able to sit for 2 minutes under supervision
2	able to sit for 30 seconds
1	able to sit for 10 seconds
0	unable to sit without support for 10 seconds

4. Standing to sitting

INSTRUCTIONS: Please sit down

4	sits safely with minimal use of hands
3	controls descent by using hands
2	use back of legs against chair to control descent
1	sits independently but has uncontrolled descent
0	needs assistance to sit

5. Transfers

INSTRUCTIONS: Arrange chair(s) for a pivot transfer. Ask subject to transfer one way toward a seat with armrests and one way toward a seat without armrests. You may use two chairs, (one with and one without armrests), or a bed and a chair.

4	able to transfer safely with minor use of hands
3	able to transfer safely definite need of hands
2	able to transfer with verbal cueing and/or supervision
1	needs one person to assist
0	needs two people to assist or supervise to be safe

6. Standing unsupported with eyes closed

INSTRUCTIONS: Please close your eyes and stand still for 10 seconds

4 able to stand 10 seconds safely
3 able to stand 10 seconds with supervision
2 able to stand 3 seconds
1 unable to keep eyes closed 3 seconds but stays steady
0 needs help to keep from falling

7. Standing unsupported with feet together
INSTRUCTIONS: Place your feet together and stand without holding

4 able to place feet independently and stand for 1 minute safely
3 able to place feet together and stand for 1 minute with supervision
2 able to place feet together independently to hold for 30 seconds
1 need help to attain position but able to stand 15 seconds feet together
0 needs help to attain position and unable to hold for 15 seconds

8. Reaching forward with outstretched arm while standing
INSTRUCTIONS: Lift arm to 90º. Stretch out your fingers and reach forward as far as you can. (Examiner places a ruler at end of fingertips when arm is at 90º. Fingers should not touch the ruler while reaching forward). The recorded measure is the distance forward that the finger reaches while the subject is in the most forward lean position. (When possible, ask subject to use both arms when reaching to avoid rotation of the trunk.)

4 can reach forward confidentially >25 cm (10 inches)
3 can reach forward >12.5 cm safely (5 inches)
2 can reach forward >5cm safely (2 inches)
1 reaches forward but needs supervision
0 loses balance while trying/requires external support

9. Pick up object from the floor from a standing position
INSTRUCTIONS: Pick up the shoe/slipper, which is placed in front of your feet.

4 able to pick up slipper safely and easily
3 able to pick up slipper but needs supervision
2 unable to pick up, reaches 2-5cm (1-2 inches) from slipper, keeps balance
1 unable to pick up and needs supervision while trying
0 unable to try/needs assist to keep from losing balance or falling

10. Turning to look behind over left and right shoulders while standing
INSTRUCTIONS: Turn to look directly behind you over toward left shoulder. Repeat to the right. Examiner may pick an object to look at directly behind the subject to encourage a better twist turn.

4 looks behind from both sides and weight shifts well
3 looks behind one side only, turn to other side demonstrates less weight shift
2 turns sideways only but maintains balance
1 needs supervision when turning
0 needs assist to keep from losing balance or falling

10. Turn 360 degrees
INSTRUCTIONS: Turn completely around in a full circle. Pause. Then turn a full circle in the other direction.

4 able to turn 360 degrees safely in 4 seconds or less
3 able to turn 360 degrees safely one side only in 4 seconds or less
2 able to turn 360 degrees safely but slowly
1 needs close supervision or verbal cueing
0 needs assistance while turning

12. Placing alternate foot on step or stool while standing unsupported
INSTRUCTIONS: Place each foot alternately on the step/stool. Continue until each foot has touched the step/stool four times.

4	able to stand independently and safely and complete 8 steps in 20 seconds
3	able to stand independently and complete 8 steps >20 seconds
2	able to complete 4 steps without aid with supervision
1	able to complete >2 steps needs minimal assist
0	needs assistance to keep from falling/unable to try

13. Standing unsupported one foot in front

INSTRUCTIONS: (DEMONSTRATE TO SUBJECT)
Place one foot directly in front of the other. If you feel that you cannot place your foot directly in front, try to step far enough ahead that the heel of your forward foot is ahead of the toes of the other foot. (To score 3 points, the length of the step should exceed the length of the other foot and the width of the stance should approximate the subject's normal stride width)

4	able to place foot tandem independently and hold 30 seconds
3	able to place foot ahead of other independently and hold 30 seconds
2	able to take small step independently and hold 30 seconds
1	needs help to step but can hold 15 seconds
0	loses balance while stepping or standing

14. Standing on one leg

INSTRUCTIONS: Stand on one leg as long as you can without holding.

4	able to lift leg independently and hold >10 seconds
3	able to lift leg independently and hold 5 – 10 seconds
2	able to lift leg independently and hold ≥ 3 seconds
1	tries to lift leg, unable to hold 3 seconds but remains standing independently
0	unable to try or needs assist to prevent fall

TOTAL SCORE **(Maximum = 56)**

Interpretation of Berg Scores

Please take note that these values are based on the Berg score alone and the patient mobilising without the assistance of a walking device. They do not take into account other falls risk factors

- A score of 45 or less indicates a greater risk of falls
- In the range of 56-54 each 1 point drop was associated with a 3-4% increase in falls risk
- In the range of 54-46 each point drop was associated with a 6-8% falls risk
- Below 36 falls risk is close to 100%

References

Wood-Dauphinee S, Berg K, Bravo G, Williams JI: The Balance Scale: Repsonding to clinically meaningful changes. Canadian Journal of Rehabilitation 10:35-50,1997

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Berg K, Maki B, Williams JI, Holliday P, Wood-Dauphinee S: A comparison of clinical and laboratory measures of postural balance in an elderly population. Arch Phys Med Rehabil 73: 1073-1083, 1992

Berg K, Wood-Dauphinee S, Williams JI, Maki B: Measuring balance in the elderly: validation of an instrument. Can. J. Pub. Health July/August supplement 2:S7-11, 1992

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Appendix 12

The Barthel Index

مقياس بارثل

Bowels

آلأمعاء

0 = incontinent (or needs to be given enemata)

عدم المقدرة على التحكم في عملية إخراج البراز (او الاحتياج للأداة اللازمة)

1 = occasional accident (once/week)

تحدث عرضيا (مره بالأسبوع)

2 = continent

قادر على ضبط النفس

Patient's Score:

Bladder

المثانة

0 = incontinent, or catheterized and unable to manage

عدم المقدرة على التحكم بالبول أو بحاجة لتسليك المسالك البولية

1 = occasional accident (max. once per 24 hours)

تحدث عرضيا (كحد أقصى مرة باليوم لكل ٢٤ ساعة)

2 = continent (for over 7 days)

قادر على التحكم

Patient's Score:

Grooming

التهندم (الاعتناء بالنفس)

0 = needs help with personal care

الحاجة بالإعتناء بالنفس

1 = independent face/hair/teeth/shaving (implements provided)

الإستقلالية بالإعتناء بالشعر والأسنان والحلاقة (في حال توفر الأدوات)

Patient's Score:

Toilet use

إستخدام دورة المياه

0 = dependent

الإعتماد على الآخرين

1 = needs some help, but can do something alone

يحتاج إلى مساعدة ولكنه يستطيع بالقيام لبعض الأشياء

2 = independent (on and off, dressing, wiping)

الإستقلالية (بالغسيل الذاتي، واللبس)

Patient's Score:

Feeding

تناول الطعام

0 = unable

غير قادر

1 = needs help cutting, spreading butter, etc.

أحتاج لمساعدة في التقطيع

2 = independent (food provided within reach)

الإستقلالية في تناول الطعام بنفسه

Patient's Score:

Transfer

الإنتقال

0 = unable – no sitting balance

غير قادر على الإنتقال ـ مختل التوازن

1 = major help (one or two people, physical), can sit

يحتاج لمساعدة أساسية من شخص أو أكثر حتى يجلس

2 = minor help (verbal or physical)

مساعدة محدودة (سواء بالكلام او الفعل)

3 = independent

مستقل ويمكنه القيام بالإنتقال بنفسه

Patient's Score:

Mobility

الحركة

0 = immobile

غير قادر على الحركة

1 = wheelchair independent, including corners, etc.

لا يعتمد على الكرسي المتحرك

2 = walks with help of one person (verbal or physical)

يمشي بمساعدة لفظية او جسدية مع شخص آخر

3 = independent (but may use any aid, e.g., stick)

يقدر على الحركة ولكن ربما يستخدم ادوات مساعده كالعصا والخ

Patient's Score:

Dressing

اللبس / إرتداء الملابس

0 = dependent

يعتمد على الآخرين

1 = needs help, but can do about half unaided

يحتاج مساعدة ولكن يمكن القيام بنفس المهمة دون مساعدة

2 = independent (including buttons, zips, laces, etc.)

مستقل وقادر على القيام (باللبس والخ)

Patient's Score:

Stairs

السلالم

0 = unable

غير قادر على ذلك

1 = needs help (verbal, physical, carrying aid)

يحتاج إلى مساعدة (كالتشجيع اللفظي أو مد يد العون+ إستخدام سلالم متحركة)

2 = independent up and down

بإمكانه الصعود او الهبوط بمفردة

Patient's Score:

Bathing

الإستحمام

0 = dependent

يعتمد على الآخرين

1 = independent (or in shower)

يعتمد على نفسه

Patient's Score: Total Score:

Appendix 13

Hospital Anxiety and Depression Scale (HADS)

Patients are asked to choose one response from the four given for each interview. They should give an immediate response and be dissuaded from thinking too long about their answers. The questions relating to anxiety are marked "A", and to depression "D". The score for each answer is given in the right column. Instruct the patient to answer how it currently describes their feelings.

A	**I feel tense or 'wound up':**	
	Most of the time	3
	A lot of the time	2
	From time to time, occasionally	1
	Not at all	0

D	**I still enjoy the things I used to enjoy:**	
	Definitely as much	0
	Not quite so much	1
	Only a little	2
	Hardly at all	3

A	**I get a sort of frightened feeling as if something awful is about to happen:**	
	Very definitely and quite badly	3
	Yes, but not too badly	2
	A little, but it doesn't worry me	1
	Not at all	0

D	**I can laugh and see the funny side of things:**	
	As much as I always could	0
	Not quite so much now	1
	Definitely not so much now	2
	Not at all	3

A	**Worrying thoughts go through my mind:**	
	A great deal of the time	3
	A lot of the time	2
	From time to time, but not too often	1
	Only occasionally	0

D	**I feel cheerful:**	
	Not at all	3
	Not often	2
	Sometimes	1
	Most of the time	0

A	**I can sit at ease and feel relaxed:**	
	Definitely	0
	Usually	1
	Not Often	2
	Not at all	3

D	**I feel as if I am slowed down:**	
	Nearly all the time	3
	Very often	2
	Sometimes	1
	Not at all	0

A	**I get a sort of frightened feeling like 'butterflies' in the stomach:**	
	Not at all	0
	Occasionally	1
	Quite Often	2
	Very Often	3

D	**I have lost interest in my appearance:**	
	Definitely	3
	I don't take as much care as I should	2
	I may not take quite as much care	1
	I take just as much care as ever	0

A	**I feel restless as I have to be on the move:**	
	Very much indeed	3
	Quite a lot	2

	Not very much	1
	Not at all	0

D	**I look forward with enjoyment to things:**	
	As much as I ever did	0
	Rather less than I used to	1
	Definitely less than I used to	2
	Hardly at all	3

A	**I get sudden feelings of panic:**	
	Very often indeed	3
	Quite often	2
	Not very often	1
	Not at all	0

D	**I can enjoy a good book or radio or TV program:**	
	Often	0
	Sometimes	1
	Not often	2
	Very seldom	3

	Scoring (add the As = Anxiety. Add the Ds = Depression). The norms	

	below will give you an idea of the level of Anxiety and Depression.	
	0-7 = Normal	
	8-10 = Borderline abnormal	
	11-21 = Abnormal	

Reference:

Zigmond and Snaith (1983)

Appendix 14.a

Exercise Monitoring Form

MS Exercise Study

Patient code:

Exercise Prescription and progression notes:

Age = Resting HR =

Temperature=

Patient code:

Week		Weight of subject	Total intensity	Heart Rate		Temperature		RPE	CR10	Notes
Week no.	Date			Pre	Post	Pre	Post			
W1	D1-									
	D2-									
	D3-									
W2	D1-									
	D2-									
	D3-									
W3	D1-									
	D2-									
	D3-									

W4	D1-									
	D2-									
	D3-									
W5	D1-									
	D2-									
	D3-									
W6	D1-									
	D2-									
	D3-									
W7	D1-									
	D2-									
	D3-									

W8	D1-									
	D2-									
	D3-									
W9	D1-									
	D2-									
	D3-									
W10	D1-									
	D2-									
	D3-									
W11	D1-									
	D2-									
	D3-									

W12	D1-									
	D2-									
	D3-									

Appendix 14.b

Subject code	Date of contacting	Date of consenting	Date of MS diagnosis	Date of starting study	Type of MS (0Benign; 1 Primary progressive; 2 Relapsing & Remitting; 3Secondary Progressive)	patient status (1 drop,2 only assess,3 all)	Exercise type Exercise type (0 no exercise,1 resistance , 2 endurance , 3 Mixed)	Gender (0 female; 1 male)	Age
1	6/20/13	6/20/13	Jan-13	10/21/13	0	3	3	0	40
2	6/20/13	6/20/13	Apr-12	10/21/13	1	3	1	0	36
3	7/4/13	7/4/13	May-13	10/21/13	2	3	3	0	23
4	6/23/13	6/23/13	Sep-12	10/21/13	1	2	0	0	36
5	6/20/13	6/20/13	Nov-10	10/21/13	1	2	0	1	33
6	6/17/13	6/17/13	Mar-12	10/21/13	1	3	3	0	27
7	7/1/13	7/1/13	Mar-13	10/21/13	0	3	3	1	40
8	6/17/13	6/17/13	Nov-97	10/21/13	2	1	0	0	40
9	7/1/13	7/17/13	Jun-12	10/21/13	3	2	0	0	36
10	7/1/13	7/1/13	Mar-01	10/21/13	2	3	3	0	30
11	6/27/13	6/27/13	Jan-11	10/21/13	١	3	3	1	41
12	6/13/13	6/13/13	Oct-12	drop	1	1	0	1	30
13	6/13/13	6/13/13	Apr-05	10/21/13	٢	3	3	0	30
14	6/13/13	6/13/13	Jan-08	10/21/13	2	3	3	1	26
15	7/4/13	7/4/13	May-10	10/21/13	١	3	3	0	27
16	6/27/13	6/27/13	May-11	10/21/13	2	3	3	0	32
17	7/1/13	7/1/13	Sep-12	10/21/13	١	3	3	0	38
18	6/27/13	7/27/13	Nov-09	10/21/13	1	3	3	0	45
19	7/1/13	7/1/13	Mar-06	10/21/13	1	3	3	0	41
20	7/1/13	7/1/13	Sep-98	10/21/13	1	3	3	0	52
21	7/1/13	7/1/13	Jun-06	drop	1	2	0	1	35

22	7/1/13	7/1/13	May-98	drop	2	1	0	0	40
23	7/1/13	7/17/13	Feb-92	10/21/13	1	3	3	1	54
24	6/20/13	6/20/13	May-05	10/21/13	1	3	3	0	44
25	6/25/13	6/25/13	May-05	drop	3	1	0	1	35
26	6/25/13	6/25/13	Jan-10	drop	2	1	0	0	35

Nationality (1 kuwati, 2 other)	height	weight-bl1	weight-bl2	weight-12w	weight-16w	MFIS-bl1	MFIS-bl2	MFIS-12w	MFIS-16w	HADS-bl1	HADS-bl2	HADS-W12
1	160	68	67	60.2	61.4	26	26	36	23	5	5	9
1	162	59.5	60	63.9	65.2	45	46	43	42	22	22	22
1	151	55	55	54	53.9	36	36	26	36	13	13	10
1	168	72	71	79.1	77.6	78	36	69	84	69	69	26
1	183	79	75	78	79	45	36	31	33	3	3	10
1	154	49	47	49.4	49.1	58	46	65	64	15	15	21
1	180	109	105	108.9	109.7	7	6	14	12	1	2	9
1	163	67	61			67	67			67	67	
1	154	35	35	42.2	39.2	73	73	75	59	21	22	22
1	154	35	35	37	36.3	29	29	17	8	12	12	7
1	180	119	115	118.3	118.3	45	45	28	18	11	11	11
1	170	78	75			9	24			10	10	
1	173	64	63	64	63.7	31	31	15	22	17	17	19
1	181	79	78	79.9	78.2	51	51	29	29	15	15	11
1	170	104	103	103.4	100.1	70	70	33	31	34	34	12
2	154	56	55	56.3	57.3	42	43	31	31	20	20	18
1	162	61	59	58.8	59.2	74	74	20	71	29	29	68
1	155	45	65	56.3	٦٣.٧	18	18	16	14	8	8	9
1	158	80	79	81.8	80	52	52	40	39	22	22	19
1	169	71	66	73	70.1	28	29	25	29	18	17	20
1	179	90	91	91.8	89.2	51	51	8	24	18	18	16

1						55	55			17	17	
1	182	95	92	93.6	90.6	32	32	16	19	4	4	7
1	154	70	71	71	71.5	48	48	45	45	16	17	19
1		70	85			45	45			16	17	
1		60	65			57	57			14	14	

HADS-W16	EDSS-bl1	EDSS-bl2	EDSS=12w	EDSS-16w	barthel-bl1	barthel-bl2	barthel-12w	barthel-16w	TUG-bl2	TUG-12w	TUG-16w	10m-bl2_S.S.V
7	5	5	5	5	20	20	20		8.5	7.9	7.98	6.5
21	5.5	5.5	5.5	5.5	17	17	20	20	9.8	7.8	9.1	4.8
18	4	4	4	4	20	20	20	20	6.5	5.59	5.5	5.5
35	6.5	6.5	6.5	6.5	19	19	20	20	9.7	7.4	8.68	6.9
10	5.5	5.5	5.5	5.5	19	19	18	20	7.1	5.98	7	5.5
21	5.5	5.5	5.5	5.5	18	18	20	20	5.8	6.33	5.95	4.3
4	3.5	3.5	3.5	3.5	15	15	20	20	5.6	4.88	5.45	10.1
	5.5	5.5			13	13			14			V.
26	7	7	7	7	19	19	17	20	8.5	6.2	6.56	5.4
0	5	5	5	5	20	20	20	20	10.1	7.65	8.11	5.7
11	5	5	5	5	20	20	20	20	7.1	6.83	6.29	3.7
	6	6			19	8			7.7			5
17	6.5	6.5	6.5	6.5	15	15	13	16	14.1	9.4	10.9	5.9
19	6	6	6	6	20	20	20	19	10.9	6.23	6.9	16.1
14	5	5	5	5	20	20	20	20	7.3	6.1	6.9	4
16	6	6	6	6	18	18	19	19	8.6	7.5	7.34	5.5
28	5	5	5	5	15	15	19	20	8.7	5.4	6.04	7.9
7	6	6	6	6	20	20	20	20	7.2	6.6	7.63	5.4
19	5.5	5.5	5.5	5.5	17	17	18	19	8	6	5.5	5.5
12	5	5	5	5	20	20	20	20	5.7	5.9	5.99	4
13	5.5	5.5	5.5	5.5	20	20	20	20	5.1	5.96	4.94	5.5

	6	6			18	17			5.8			6.5
6	6	6	6	6	18	18	20	20	6.2	6.03	6.78	4.8
15	5	5	5	5	19	19	19	19	7.2	6.85	6.8	3.4
	7.5	7.5			15	15			6.9			5.4
	7	7			14	14			7.8			6.5

10m-bl2_F.V	10m-12w_S.S.V	10m-12W_F.V	10m-16w_S.S.V	10m-16W_F.V	6m-bl2	6m-12w	6m-16	bbs-bl2	bbs-12w	bbs-16w	nhptR-bl2	nhptL-bl2
4.59	5.66	4	4.6	3.9	360	400	392	56	56	56	13.03	9.06
3.8	5.5	3.9	5.76	4.9	300	410	379	48	49	51	22.7	29.8
3.5	4.65	2.74	3	3	430	456	454	56	56	56	9.19	9.5
4.8	6	4	7.31	5.5	380	400	180	38	54	54	33.1	36.2
3.3	5.93	2.45	5.65	2.33	433	420	400	55	56	56	11.6	15.1
2.6	4.58	3.45	4.44	3.25	438	460	444	56	53	56	11.7	13.6
6.5	2.36	3.7	3.27	2.68	423	500	490	55	56	53	16.7	17.9
4.5					203			42			29	27
4.5	5.2	3.5	5.48	3.46	345	450	385	55	48	55	12.4	14.2
4.8	5.2	4.3	4.47	4.42	302	363	336	47	46	55	22.8	25.1
3.1	4.41	2.68	4.56	2.61	470	512	522	55	56	56	13.8	13.7
3.6					392			54			21.2	26.5
4.8	6.6	4.9	5.73	4.58	202	230	169	44	46	42	20.6	30.8
4.3	4.33	3.06	3.91	3.6	375	448	393	47	55	50	15.5	16.1
3.8	5	3.4	4.25	3.6	373	440	380	53	55	56	16.7	22
4.5	6.7	4.3	4.47	3.6	363	356	408	48	47	53	19.7	23.2
5.1	6.2	3.9	4.78	3.56	280	424	397	48	56	56	20.2	19.9
3.8	5.6	3.4	4.78	3.6	403	435	402	54	56	56	18	18.8
4.4	4.9	3.5	4	3.2	380	412	415	54	55	55	20	23.8
3.5	4.6	3.5	3.94	3.21	475	490	493	51	55	55	16.7	27.7
2.3	4.66	2.28	4.98	2.01	446	508	554	56	56	56	12.4	17.1

3.4					395			56			18.8	21.4
3.4	3.68	2.97	4.01	2.86	452	435	448	45	51	52	21.1	34.9
4.1	4.03	3.33	4.07	3.35	455	470	462	55	56	56	11	13.6
3.5					364			38			24.6	45.2
5					490			53			18.4	22.1

nhptR-12w	nhptL-12w	nhptR-16w	nhptL-16w	gripbl2R_1	gripbl2R_2	gripbl2R_3	max_gripbl2R	gripbl2L_1	gripbl2L_2	gripbl2L_3	max_gripblL2	grip12W_R_1
12.45	13.68	12.56	12.55	12	12	10	12	9	12	12	12	10
21	23.7	22.33	24.34	11	11	10	11	11	11	10	11	11
9.68	9.59	9.32	11.07	14	14	14	14	16	15	15	16	16
21.9	23.9	24.36	26.53	12	12	10	12	9	12	12	12	12
14.37	14.05	14	13.89	28	32	29	32	24	26	28	28	38
21	24.7	13.65	13.95	21	19	18	21	14	14	16	16	15
11.88	13.88	13.1	12.95	30	28	26	30	36	30	30	36	34
				14	10	12	14	12	12	10	12	
13.16	16.52	13.31	17.03	16	16	16	16	16	14	14	16	13
23.1	24.5	22.24	23.46	16	18	14	18	12	12	12	12	14
13.08	13	14.59	15.6	29	30	30	30	36	32	36	36	31
				26	20	20	26	20	20	14	20	
18.9	28	21.5	30.01	20	18	20	20	18	22	26	26	22
16.95	16.95	15.14	16.77	14	16	18	18	14	13	11	14	31
15.3	16.5	16.91	16.96	16	13	20	20	22	20	18	22	18
19.3	22.3	10.36	12.48	14	12	18	18	12	14	13	14	16
18.5	19	10.81	12.99	7	10	11	11	5	4	12	12	14
18.3	19.9	16.65	20.5	17	17	18	18	18	19	17	19	17
17.7	25.4	16.88	23.1	18	10	14	18	5	10	14	14	14
15.9	28.5	9.85	19.73	14	15	16	16	14	13	16	16	13
14.03	14.5	11.27	13.52	18	35	26	35	32	32	31	35	38

				19	19	20	20	20	20	20	20	
12.76	12.56	13.02	19.34	20	24	24	24	12	20	16	20	22
11.56	15.03	10.66	12.35	10	9	10	10	14	8	9	14	16
				22	23	24	24	24	21	25	25	
				15	15	16	16	13	12	13	13	

grip12w_R_2	grip12W_R_3	max_grip12W_R	grip12W_L_1	grip12W_L_2	grip12W_L_3	max_grip12W_L	grip16W_R_1	grip16w_R_2	grip16W_R_3	max_grip16W_R	grip16W_L_1	grip16W_L_2
14	11	14	13	13	13	13	16	13	13	16	14	13
11	11	11	12	11	9	12	13	10	12	13	11	10
16	15	16	16	14	14	16	16	14	12	16	15	14
18	14	18	14	12	12	14	8	8	6	8	15	14
38	31	38	26	24	23	26	33	38	38	38	26	26
12	14	15	13	12	12	13	19	14	14	19	16	11
31	19	34	44	44	39	44	37	34	31	37	40	38
12	12	13	11	11	11	11	16	16	17	17	16	15
14	13	14	12	11	10	12	14	15	15	15	15	10
33	31	33	36	29	33	36	37	35	35	37	36	36
23	24	24	25	25	25	25	23	20	21	23	26	26
32	27	32	19	19	17	19	23	26	22	26	17	15
23	13	23	19	18	22	22	20	17	14	20	20	22
16	15	16	13	12	13	13	18	20	17	20	20	18
16	14	16	14	13	14	14	11	13	14	14	14	12
19	19	19	18	18	18	18	24	22	22	24	26	26
14	16	16	13	14	16	16	14	17	15	17	15	15
16	16	16	14	16	17	17	18	17	18	18	20	18
38	36	38	40	32	30	40	42	44	38	44	45	41

30	28	30	22	20	20	22	26	27	27	27	22	20
13	11	16	15	17	13	17	10	10	12	12	13	9

grip16W_L_3	max_grip16W_L	max_kfR-bl2	max_kfL-bl2	max_kfR-12w	max_kfL-12w	max_kfR-16w	max_kfL-16w	max_kextR-bl2	max_kextL-bl2	max_kextR-12w	max_kextL-12w	max_kextR-16w
10	14	66.7	63.8	61.9	60.5	68.5	68.1	65.3	62.1	77.3	78.7	70.9
10	11	67.1	66.1	66.6	64.5	66	64.8	68.6	67.5	66.5	68.4	74.9
14	15	65.6	68.8	72.1	71.5	73.6	70.1	62.9	64	73.8	75.4	80.1
13	15	54.4	54.3	62.2	63.1	60.9	57.5	55.6	54.5	62.3	64	60.5
25	26	70.2	70.9	72	81.7	73.6	81	69.6	67.4	84.2	77.8	82.2
10	16	64.4	62.2	66.6	65.7	64.6	64.3	66.3	65.9	72.8	67.6	76
36	40	73.7	71.8	76.9	76.8	82.5	86.6	77.5	73.6	91.1	89.7	95.1
		57.3	56.5					56.8	56.1			
14	16	61.4	62	64.9	64.2	67	68.9	65.1	65.1	64.2	63.9	69.7
12	15	55	56.5	66.7	64.2	70	67.1	52.8	55.1	64.7	66.5	68.6
35	36	72.4	73.9	72.8	69.2	81.9	80.5	75.4	74.4	94.6	88	89.2
		57.3	61.4					58.5	60.2			
25	26	57.7	57.5	64	64	66.3	66.9	58.4	57.6	62.9	60.4	82.9
19	19	70.1	67.8	77.1	74.2	74.5	71.6	65.2	60	93.9	89.3	79.2
19	22	60.7	60.8	67.8	67.8	75.4	73.2	61.3	59.7	68.8	69.8	79.7
16	20	58.4	58.7	64.3	62.5	64.8	63.8	54.9	55	68	65.6	82.2
14	24	59.2	59.6	64.7	63.2	69.2	64.1	59	57.9	68.1	64.9	74.4
24	26	64.1	63.1	67.5	66.1	69.4	68.3	62.1	61.1	68.7	68.7	82.4
16	16	57.5	59.2	67.7	60.1	69.2	64.1	59.9	60	64.9	63	68.6
16	20	65.7	62.2	67.3	69.8	68.5	72.9	64.7	65.9	66	66.5	84.2
41	45	66.8	67.8	75.6	80.7	89.9	88.6	69.1	70.1	89.9	84.9	90.2

		59.8	58.7					68	69.5			
18	22	64	64.6	78.9	72.9	84.3	85.1	65.5	63.2	83	85.3	92.4
10	13	65.9	66.4	62	77.3	65.1	68.7	66.7	64.1	80.5	74	76.4
		67.8	76.8					69	66.2			
		69.8	69.2					60.5	59.9			

max_kextL-16w	max_hipflx-R-bl2	max_hipflx-L-bl2	max_hipflx-R-12w	max_hipflx.L-12w	max_hipflx-R_16w	max_hipflx-L_16w	max_hipext-R-bl2	max_hipext-L-bl2	max_hipext-R-12w	max_hipext.L-12w	max_hipext-R_16w	max_hipext-L_16w
67.5	67.6	64.7	65.9	62.2	64.8	63.1	57.3	57.9	62.5	59.8	62.2	61.7
69.6	56.2	66.2	62.3	64.4	59.9	64.8	60.5	60.9	60.3	59.4	61.2	70.8
74.9	68.6	70.1	74.5	76.7	70.6	73	61.1	59	67	68	65.6	64.4
56.9	54.9	54.5	36	63.3	56.9	61.3	54.1	54	60.8	60.6	59	61.7
77.5	73.9	75.3	78	81.7	69	70.2	75.2	72.6	83.4	85.6	81.7	85.6
70	67.4	66.7	68.2	66.8	71	67.7	68.6	68.2	70.7	66	69.7	66
87.4	73.5	74.2	78.7	77.8	75.3	77.4	74.3	74.1	79.7	76.8	79.6	71.2
	55.8	55.1					55.2	53.1				
67.8	60.9	59.3	66.7	65.7	61.2	62.8	57.6	59.8	67.5	66	67.2	68.5
74.5	55.7	55.1	65	64.6	66.8	65.7	54.3	54.3	60.8	61.9	67	64.1
85.7	71.8	71.5	79.2	79.9	79.3	84.7	70.1	72.2	70.8	69.7	71.3	71.9
	59.9	60.6					55.8	56.2				
85.3	58.4	58.6	64	64	66	65.2	57.2	54.6	66.2	66.2	67.4	65.3
89.5	63.8	55.7	76	70	68.9	63.1	58.5	59.8	66.2	70.7	68.7	63.1
76.7	61.7	61.4	67.8	65.8	69.2	69.4	56.1	56.8	62.8	61.4	68.1	66.1
83.7	59.7	58.7	65	62.9	62.3	66.5	58.6	59.8	63.9	62.8	68.4	67.2
75.7	58.2	57.4	64.9	62.1	65	63.2	57.4	57.2	62.7	61.4	64.3	65.5
78.9	64.7	63.9	63.7	65	62.6	62	59.6	60.7	61.8	61.9	67.6	69.7
64.5	59.8	59.8	64.9	65.8	69.5	69.4	57.2	57	61.5	62.5		
82.9	64.5	64.8	69.1	69.8	65.5	70.5	61	61.4	62	61.9	67.6	68.4
88.3	76.8	71.9	75.7	80.1	80	83.5	75.7	77.9	78.6	75.4	83.1	86.5

	63.4	61.7					61.8	62.7				
89.2	61.7	62.6	70	71.9	71.9	71.3	64	59.3	74.5	70.3	66.7	67.7
72.5	62.8	64.7	63.1	64.3	65.7	69.3	57.1	56.6	60.9	66.6	67.6	76.4
	64.3	60.7					64.4	63.1				
	57.2	57.3					60.1	56.8				

max_shldflx-R-bl2	max_shldflx-L-bl2	max_shldflx-R-12w	max_shldflx_L-12w	max_shldflx-R_16w	max_shldflx-L_16w	max_shldabd-R-bl2	max_shldabd-L-bl2	max_shldabd-R-12w	max_shldabd_L-12w	max_shldabd-R_16w	max_shldabd-L_16w	max_elbflx-R-bl2
61.2	62.9	63.7	64.7	71.8	73.2	61.7	61.8	61.3	65.4	68.8	70.3	58.9
61.5	61.9	62.1	62	62.5	53.3	62.2	60.9	62.2	60.8	57.9	57.2	63.6
59.2	60.7	63.2	67.7	64.1	64.6	58.7	58	65.8	64.3	63.5	65	64.7
54.3	53.7	62.6	60.8	59.5	57	56.2	53.3	61.6	61.8	59.5	57	52.3
74.9	73.9	73.6	77.7	72.6	73.4	72.8	72.7	74.7	73.1	69	72.5	84.4
61.9	61.5	61.3	62.5	65.1	62.2	62	60.9	62.3	62	59.7	61.4	62.7
78.3	81	74.8	85.9	76.7	79.2	72.1	69.7	79.7	75	77.3	77.6	82
56.4	55.1					56.2	55					52.6
59.2	58.8	60.3	63	62.7	62.4	59.8	60.1	63	64.3	61.7	62.2	62
54.4	54.4	61.1	61.5	62.4	63.2	54.5	54.4	60.9	64.1	63.3	63	52.6
69.8	74.6	71.1	74.9	72.6	80.2	67.1	75.6	72.4	79.1	69	72.5	76.6
56.9	55.7					58	58.7					56
57.3	55.4	63.6	65.4	62.9	65.8	55.9	55.6	67.5	66.6	65.6	63	57.3
71	63.2	67.5	67.6	71.8	73.2	65.3	65.1	66.8	68.1	68.8	70.3	67
57.3	57.7	60.9	60.5	66.1	64.9	56.9	57.4	63.8	64.2	63	64.8	59.4
56.7	46	62.9	62.9	66	63.5	58.8	56.8	62.3	62.3	66.3	62.7	58.8
55.6	56.7	58.8	56.5	59.5	62.9	56.9	57.4	62.4	60.7	60.9	60.5	58.8
60.8	60	63.1	61.9	62.3	67	59.2	60.6	63.4	63.6	63.1	63.1	63.3
58.3	57.5	60	61.3	62.3	67	58.3	57.4	61.1	61.8	63.1	63.1	58.1
60.5	62.2	62.7	64.5	66.8	70.2	60.8	62.3	64.8	65.1	67.8	62.3	60.1
73.4	76.7	77.1	80.7	85.4	81.9	71.8	76.5	79.1	82.5	78.3	79.7	77.4

61.9	61.6					69.9	61.6					63.4
63.9	64.4	76.5	75.6	77.7	74.9	62.9	64	70.1	69.1	71.1	72.8	61.7
63.5	61.8	67.1	67.9	62.5	64.7	60.8	62.3	64.2	65.9	66.5	62.8	67.8
65.5	63.7					64	64.6					62.9
56.9	56.1					60	59.1					56.5

max_elbflx-L-bl2	max_elbflx-R-12w	max_elbflx_L-12w	max_elbflx-R_16w	max_elbflx-L_16w	max_elbext-R-bl2	max_elbext-L-bl2	max_elbext-R-12w	max_elbext_L-12w	max_elbext-R_16w	max_elbext-L_16w
61.5	65	65.7	72.2	70.8	60.8	61.6	65.6	63.9	68.6	67
64	61.8	62.1	61.5	62.6	61.9	64	62.4	63.6	59.5	60.6
61.8	67.2	65.1	61.4	67.6	66.3	67.3	64.9	63.8	63.3	64.3
53.6	59.6	61.6	62	64.5	53.5	53.8	60.1	62	58.3	61.8
80.6	73.1	82.1	72.2	70.8	69.5	66.9	73.1	76.9	72.9	75.6
61.3	67	60.6	66.7	63.1	63.3	64.5	60.7	60.9	61.3	62.3
82.8	82.4	80.5	79.7	84.4	73.1	72.3	69.2	75.7	74.7	75.1
58.4					53.5	55.2				
62.9	60.4	36.6	72.2	70.8	60.1	60.9	62.2	61.9	68.6	67
53.2	59.2	61.8	63.1	67.8	54.5	53.4	62.1	60.3	61	60.2
80.4	80.5	83.5	80	84	74.3	78.7	78.3	78.6	82.9	77.6
53.4					56.3	55.9				
56.7	63.2	64.9	66.7	68	55.8	53.5	61.7	62.7	61.4	66.7
63.9	69	71.3	72.2	70.8	64.7	61.9	74.7	72.3	68.6	67
59.8	61.3	63	70	66.7	60.3	60.6	65	63.4	66	67.2
57.6	62.3	61.3	64.8	36.8	58.9	59.6	61.3	65.1	64	65.7
57.7	62.4	61.2	61.2	63.5	58.4	58.8	61.9	61.4	63	60
60.4	65.3	59.9	67.2	68.9	64.2	64.1	62.3	60.8	64.4	66.5
58.8	62	61.4	61.2	63.5	59.8	60.1	62	61	63	60
58.1	62.7	64.4	68.7	70.6	58.6	57.8	61.2	64.7	66.4	67.4
78.1	82.3	91	87.6	87.3	72.8	78.8	84.5	80.2	84.4	79.6

61.7					61.7	62.7				
62.6	85.1	84.2	78.9	81.8	64	59.3	70.5	72.3	71.8	73.4
69.7	67.1	70.7	64.8	69.6	65.2	67.7	64.6	96.7	67	67.5
64.2					66.8	65.8				
54.8					59.7	58.7				

Appendix 14.c

p	daycode	day	mass (kg)	Hrtarget	Rest HR	Mid HR	End HR	maxHR
1	w1d1	1	62.6	**122**	64		71	71
1	w1d2	3		**122**	76		71	71
1	w1d3	5		**122**	75		76	76
1	w2d1	8	62.5	**122**	64		71	71
1	w2d2	10		**122**	67		71	71
1	w2d3	12		**122**	69		76	76
1	w3d1	15		**122**				0
1	w3d2	17	61.8	**122**	61		68	68
1	w3d3	19		**122**	69		75	75
1	w4d1	22		**122**	64		64	64
1	w4d2	24	59	**122**	71		73	73
1	w4d3	26		**122**	68		65	65
1	w5d1	29	60	**122**	68		76	76
1	w5d2	31		**122**	78		81	81
1	w5d3	33		**122**	75		76	76
1	w6d1	36	60.5	**122**	75		76	76
1	w6d2	38		**122**	64		73	73
1	w6d3	40		**122**	71		73	73
1	w7d1	43		**122**				0
1	w7d2	45	61	**122**	65		68	68
1	w7d3	47		**122**				0
1	w8d1	50	٦١.١	**122**	65	64	76	76
1	w8d2	52		**122**	65	72	76	76
1	w8d3	54		**122**	68	75	78	78
1	w9d1	57	61.2	**122**	68	83	83	83
1	w9d2	59		**122**	73	75	91	91
1	w9d3	61		**122**	76	83	81	83
1	w10d1	64		**122**	0	0	0	0
1	w10d2	66	62.5	**122**	68	98	91	98

1	w10d3	68		**122**	76	96	89	96
1	w11d1	71		**122**	75	81	73	81
1	w11d2	73		**122**	67	75	76	76
1	w11d3	75		**122**	75	89	101	101
1	w12d1	78	61.9	**122**	75	98	89	98
1	w12d2	80		**122**	80	83	85	85
1	w12d3	82		**122**				0
2	w1d1	1	65	**140**	78		95	95
2	w1d2	3		**140**	86		104	104
2	w1d3	5		**140**	76		89	89
2	w2d1	8	63	**140**	83		95	95
2	w2d2	10		**140**	83		100	100
2	w2d3	12		**140**	79		96	96
2	w3d1	15	64.4	**140**	75		95	95
2	w3d2	17		**140**	82		95	95
2	w3d3	19		**140**	82		100	100
2	w4d1	22	64.7	**140**	84		95	95
2	w4d2	24		**140**	85		110	110
2	w4d3	26		**140**	78		95	95
2	w5d1	29	65.2	**140**	75		95	95
2	w5d2	31		**140**	75		95	95
2	w5d3	33		**140**	75		95	95
2	w6d1	36	64.7	**140**	73		78	78
2	w6d2	38		**140**	91		95	95
2	w6d3	40		**140**	75		95	95
2	w7d1	43	64.1	**140**	87		90	90
2	w7d2	45		**140**	96		90	90
2	w7d3	47		**140**	87		92	92
2	w8d1	50	64.7	**140**	86		82	82
2	w8d2	52		**140**	88		83	83

2	w8d3	54		**140**	81	92	92
2	w9d1	57	64.7	**140**	88	99	99
2	w9d2	59		**140**	87	99	99
2	w9d3	61		**140**	84	94	94
2	w10d1	64	64.9	**140**	84	90	90
2	w10d2	66		**140**	82	87	87
2	w10d3	68		**140**	76	90	90
2	w11d1	71	64.9	**140**	80	78	78
2	w11d2	73		**140**	85	84	84
2	w11d3	75		**140**	89	90	90
2	w12d1	78					0
2	w12d2	80					0
2	w12d3	82					0
3	w1d1	1	55	**136**	81	95	95
3	w1d2	3		**136**	79	99	99
3	w1d3	5		**136**	81	101	101
3	w2d1	8	55.8	**136**	81	101	101
3	w2d2	10		**136**	85	102	102
3	w2d3	12		**136**	85	99	99
3	w3d1	15	55.6	**136**	75	95	95
3	w3d2	17		**136**	83	99	99
3	w3d3	19		**136**	87	100	100
3	w4d1	22	55	**136**	75	95	95
3	w4d2	24		**136**	75	99	99
3	w4d3	26		**136**	72	98	98
3	w5d1	29	55	**136**	75	105	105
3	w5d2	31		**136**	79	95	95
3	w5d3	33		**136**	80	97	97
3	w6d1	36	54.4	**136**	74	115	115
3	w6d2	38		**136**	75	85	85

3	w6d3	40		**136**	69		100	100
3	w7d1	43	53.6	**136**	77	111	101	111
3	w7d2	45		**136**	77	127	95	127
3	w7d3	47		**136**	75	125	98	125
3	w8d1	50	53.6	**136**	77	126	116	126
3	w8d2	52		**136**	70	111	99	111
3	w8d3	54		**136**	73	100	123	123
3	w9d1	57	54.1	**136**	88	97	95	97
3	w9d2	59		**136**	88	98	127	127
3	w9d3	61		**136**	90	93	111	111
3	w10d1	64	54.2	**136**	85	100	117	117
3	w10d2	66		**136**	87	127	109	127
3	w10d3	68		**136**	96	110	110	110
3	w11d1	71						0
3	w11d2	73						0
3	w11d3	75						0
3	w12d1	78						0
3	w12d2	80						0
3	w12d3	82						0
4	w1d1	1						0
4	w1d2	3						0
4	w1d3	5						0
4	w2d1	8						0
4	w2d2	10						0
4	w2d3	12						0
4	w3d1	15						0
4	w3d2	17						0
4	w3d3	19						0
4	w4d1	22						0
4	w4d2	24						0

4	w4d3	26	0
4	w5d1	29	0
4	w5d2	31	0
4	w5d3	33	0
4	w6d1	36	0
4	w6d2	38	0
4	w6d3	40	0
4	w7d1	43	0
4	w7d2	45	0
4	w7d3	47	0
4	w8d1	50	0
4	w8d2	52	0
4	w8d3	54	0
4	w9d1	57	0
4	w9d2	59	0
4	w9d3	61	0
4	w10d1	64	0
4	w10d2	66	0
4	w10d3	68	0
4	w11d1	71	0
4	w11d2	73	0
4	w11d3	75	0
4	w12d1	78	0
4	w12d2	80	0
4	w12d3	82	0
5	w1d1	1	0
5	w1d2	3	0
5	w1d3	5	0
5	w2d1	8	0
5	w2d2	10	0

5	w2d3	12	0
5	w3d1	15	0
5	w3d2	17	0
5	w3d3	19	0
5	w4d1	22	0
5	w4d2	24	0
5	w4d3	26	0
5	w5d1	29	0
5	w5d2	31	0
5	w5d3	33	0
5	w6d1	36	0
5	w6d2	38	0
5	w6d3	40	0
5	w7d1	43	0
5	w7d2	45	0
5	w7d3	47	0
5	w8d1	50	0
5	w8d2	52	0
5	w8d3	54	0
5	w9d1	57	0
5	w9d2	59	0
5	w9d3	61	0
5	w10d1	64	0
5	w10d2	66	0
5	w10d3	68	0
5	w11d1	71	0
5	w11d2	73	0
5	w11d3	75	0
5	w12d1	78	0
5	w12d2	80	0

5	w12d3	82						0
6	w1d1	1	49	**135**	76		90	90
6	w1d2	3		**135**	77		85	85
6	w1d3	5		**135**	70		128	128
6	w2d1	8	48.5	**135**	78		91	91
6	w2d2	10		**135**	80		96	96
6	w2d3	12		**135**	84		90	90
6	w3d1	15	49	**135**	84		111	111
6	w3d2	17		**135**	75		96	96
6	w3d3	19		**135**	75		94	94
6	w4d1	22	48	**135**	75		82	82
6	w4d2	24		**135**	83		94	94
6	w4d3	26		**135**	77		99	99
6	w5d1	29	48.7	**135**	75		80	80
6	w5d2	31		**135**	78		93	93
6	w5d3	33		**135**	75		81	81
6	w6d1	36	48.7	**135**	76		96	96
6	w6d2	38		**135**	78		85	85
6	w6d3	40		**135**	85		110	110
6	w7d1	43	48	**135**	85		100	100
6	w7d2	45		**135**	84	109	96	109
6	w7d3	47		**135**	81	100	81	100
6	w8d1	50	48	**135**	88	100	118	118
6	w8d2	52		**135**	84	100	101	101
6	w8d3	54		**135**	90	110	110	110
6	w9d1	57	48.1	**135**	80	110	100	110
6	w9d2	59		**135**	75	118	120	120
6	w9d3	61		**135**	87	128	120	128
6	w10d1	64						0
6	w10d2	66						0

6	w10d3	68						0
6	w11d1	71						0
6	w11d2	73						0
6	w11d3	75						0
6	w12d1	78						0
6	w12d2	80						0
6	w12d3	82						0
7	w1d1	1	115	**151**	75		122	122
7	w1d2	3		**151**	95		125	125
7	w1d3	5		**151**	75		129	129
7	w2d1	8	115	**151**	75		120	120
7	w2d2	10		**151**	79		112	112
7	w2d3	12		**151**	78		138	138
7	w3d1	15	114	**151**	75		135	135
7	w3d2	17		**151**	85		126	126
7	w3d3	19		**151**	86		111	111
7	w4d1	22	113.5	**151**	85		114	114
7	w4d2	24		**151**	83		118	118
7	w4d3	26		**151**	85		120	120
7	w5d1	29	112.4	**151**	85		110	110
7	w5d2	31		**151**	75		121	121
7	w5d3	33		**151**	76		122	122
7	w6d1	36	110.3	**151**	85		121	121
7	w6d2	38		**151**	75		120	120
7	w6d3	40		**151**	79		116	116
7	w7d1	43	110.8	**151**	80		129	129
7	w7d2	45		**151**	85		127	127
7	w7d3	47		**151**	90	115	115	115
7	w8d1	50	110	**151**	118	97	113	113
7	w8d2	52		**151**	92	109	113	113

7	w8d3	54		**151**	97	98	122	122
7	w9d1	57	109	**151**	91	142	108	142
7	w9d2	59		**151**	75	118	125	125
7	w9d3	61		**151**	105	115	135	135
7	w10d1	64	110	**151**	97	100	112	112
7	w10d2	66		**151**	100	129	118	129
7	w10d3	68		١٥١	120	120	141	141
7	w11d1	71	110.3	**151**	86	119	120	120
7	w11d2	73						0
7	w11d3	75						0
7	w12d1	78						0
7	w12d2	80						0
7	w12d3	82						0
8	w1d1	1						0
8	w1d2	3						0
8	w1d3	5						0
8	w2d1	8						0
8	w2d2	10						0
8	w2d3	12						0
8	w3d1	15						0
8	w3d2	17						0
8	w3d3	19						0
8	w4d1	22						0
8	w4d2	24						0
8	w4d3	26						0
8	w5d1	29						0
8	w5d2	31						0
8	w5d3	33						0
8	w6d1	36						0
8	w6d2	38						0

8	w6d3	40	0
8	w7d1	43	0
8	w7d2	45	0
8	w7d3	47	0
8	w8d1	50	0
8	w8d2	52	0
8	w8d3	54	0
8	w9d1	57	0
8	w9d2	59	0
8	w9d3	61	0
8	w10d1	64	0
8	w10d2	66	0
8	w10d3	68	0
8	w11d1	71	0
8	w11d2	73	0
8	w11d3	75	0
8	w12d1	78	0
8	w12d2	80	0
8	w12d3	82	0
9	w1d1	1	0
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9	w3d2	17	0
9	w3d3	19	0
9	w4d1	22	0
9	w4d2	24	0

9	w4d3	26					0
9	w5d1	29					0
9	w5d2	31					0
9	w5d3	33					0
9	w6d1	36					0
9	w6d2	38					0
9	w6d3	40					0
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9	w7d2	45					0
9	w7d3	47					0
9	w8d1	50					0
9	w8d2	52					0
9	w8d3	54					0
9	w9d1	57					0
9	w9d2	59					0
9	w9d3	61					0
9	w10d1	64					0
9	w10d2	66					0
9	w10d3	68					0
9	w11d1	71					0
9	w11d2	73					0
9	w11d3	75					0
9	w12d1	78					0
9	w12d2	80					0
9	w12d3	82					0
10	w1d1	1	35	**152**	113	113	113
10	w1d2	3		**152**	85	99	99
10	w1d3	5		**152**	99	112	112
10	w2d1	8	36.9	**152**	73	108	108
10	w2d2	10		**152**	75	107	107

10	w2d3	12		**152**	75		91	91
10	w3d1	15	35.6	**152**	80		97	97
10	w3d2	17		**152**	73		112	112
10	w3d3	19		**152**	75		85	85
10	w4d1	22	35.6	**152**	73		89	89
10	w4d2	24		**152**	75		92	92
10	w4d3	26		**152**	90		86	86
10	w5d1	29	35.7	**152**	75		105	105
10	w5d2	31		**152**	75		99	99
10	w5d3	33		**152**	75		86	86
10	w6d1	36	35.8	**152**	85		105	105
10	w6d2	38		**152**	75		99	99
10	w6d3	40		**152**	75		86	86
10	w7d1	43	35.6	**152**	95	86	89	89
10	w7d2	45		**152**	92	87	97	97
10	w7d3	47		**152**	93	89	115	115
10	w8d1	50	36.5	**152**	87	90	99	99
10	w8d2	52		**152**	93	93	96	96
10	w8d3	54		**152**	85	90	86	90
10	w9d1	57	37.5	**152**	74	90	115	115
10	w9d2	59		**152**	93	100	100	100
10	w9d3	61		**152**	89	92	95	95
10	w10d1	64	37.6	**152**	85	83	92	92
10	w10d2	66		**152**	97	86	97	97
10	w10d3	68						0
10	w11d1	71						0
10	w11d2	73						0
10	w11d3	75						0
10	w12d1	78						0
10	w12d2	80						0

10	w12d3	82						0
11	w1d1	1	119	**128**	76		95	95
11	w1d2	3		**128**	75		115	115
11	w1d3	5		**128**	73		113	113
11	w2d1	8	119	**128**	76		114	114
11	w2d2	10		**128**	78		100	100
11	w2d3	12		**128**	75		114	114
11	w3d1	15	118	**128**	75		109	109
11	w3d2	17		**128**	75		110	110
11	w3d3	19		**128**	82		112	112
11	w4d1	22	119	**128**	85		126	126
11	w4d2	24		**128**	74		104	104
11	w4d3	26		**128**	85		108	108
11	w5d1	29	119	**128**	89		116	116
11	w5d2	31		**128**	87		115	115
11	w5d3	33		**128**	89		109	109
11	w6d1	36	119.4	**128**	95		120	120
11	w6d2	38		**128**	98		116	116
11	w6d3	40		**128**	87		100	100
11	w7d1	43	118.6	**128**	90		111	111
11	w7d2	45		**128**	81		120	120
11	w7d3	47		**128**	86		108	108
11	w8d1	50	118.9	**128**	83		105	105
11	w8d2	52		**128**	84	120	115	120
11	w8d3	54	118	**128**	81	112	122	122
11	w9d1	57		**128**	80	99	100	100
11	w9d2	59		**128**	92	118	120	120
11	w9d3	61		**128**	87	120	119	120
11	w10d1	64						0
11	w10d2	66						0

11	w10d3	68	0
11	w11d1	71	0
11	w11d2	73	0
11	w11d3	75	0
11	w12d1	78	0
11	w12d2	80	0
11	w12d3	82	0
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12	w3d2	17	0
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12	w4d2	24	0
12	w4d3	26	0
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12	w5d2	31	0
12	w5d3	33	0
12	w6d1	36	0
12	w6d2	38	0
12	w6d3	40	0
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12	w7d2	45	0
12	w7d3	47	0
12	w8d1	50	0
12	w8d2	52	0

12	w8d3	54					0
12	w9d1	57					0
12	w9d2	59					0
12	w9d3	61					0
12	w10d1	64					0
12	w10d2	66					0
12	w10d3	68					0
12	w11d1	71					0
12	w11d2	73					0
12	w11d3	75					0
12	w12d1	78					0
12	w12d2	80					0
12	w12d3	82					0
13	w1d1	1	63	**139**	80	95	95
13	w1d2	3		**139**	75	97	97
13	w1d3	5		**139**	75	98	98
13	w2d1	8	63.8	**139**	77	89	89
13	w2d2	10		**139**	76	100	100
13	w2d3	12		**139**	80	87	87
13	w3d1	15	64.6	**139**	83	1034	1034
13	w3d2	17		**139**	79	86	86
13	w3d3	19		**139**	75	99	99
13	w4d1	22	63.8	**139**	79	104	104
13	w4d2	24		**139**	72	99	99
13	w4d3	26		**139**	76	92	92
13	w5d1	29	64.5	**139**	87	95	95
13	w5d2	31		**139**	77	88	88
13	w5d3	33		**139**	89	91	91
13	w6d1	36	64.5	**139**	65	101	101
13	w6d2	38		**139**	75	104	104

13	w6d3	40		**139**	68	98	98
13	w7d1	43	63.4	**139**	76	88	88
13	w7d2	45		**139**	76	80	80
13	w7d3	47		**139**	80	85	85
13	w8d1	50	63.4	**139**	76	102	102
13	w8d2	52		**139**	82	99	99
13	w8d3	54		**139**	89	122	122
13	w9d1	57	62.8	**139**	94	105	105
13	w9d2	59		**139**	85	107	107
13	w9d3	61		**139**	99	115	115
13	w10d1	64	64.3	**139**	67	90	90
13	w10d2	66		**139**	86	99	99
13	w10d3	68		**139**	76	109	109
13	w11d1	71	64.1	**139**	80	96	96
13	w11d2	73		**139**	56	111	111
13	w11d3	75		**139**	71	99	99
13	w12d1	78	64	**139**	83	90	90
13	w12d2	80					0
13	w12d3	82					0
14	w1d1	1	79	**132**	69	73	73
14	w1d2	3		**132**	69	77	77
14	w1d3	5		**132**	78	80	80
14	w2d1	8	79.2	**132**	66	100	100
14	w2d2	10		**132**	67	95	95
14	w2d3	12		**132**	92	95	95
14	w3d1	15	79.5	**132**	72	91	91
14	w3d2	17		**132**	70	84	84
14	w3d3	19		**132**	72	104	104
14	w4d1	22	80.1	**132**	75	95	95
14	w4d2	24		**132**	64	108	108

14	w4d3	26		**132**	72		99	99
14	w5d1	29	78.8	**132**	69		108	108
14	w5d2	31		**132**	69		99	99
14	w5d3	33		**132**	70		99	99
14	w6d1	36	79.7	**132**	65		99	99
14	w6d2	38		**132**	79		102	102
14	w6d3	40		**132**	73		83	83
14	w7d1	43	79.9	**132**	66		80	80
14	w7d2	45		**132**	75		92	92
14	w7d3	47		**132**	80		93	93
14	w8d1	50	78.9	**132**	66		96	96
14	w8d2	52		**132**	79	121	92	121
14	w8d3	54		**132**	67	96	88	96
14	w9d1	57	79.9	**132**	67	96	100	100
14	w9d2	59		**132**	69	81	99	99
14	w9d3	61		**132**	66	88	107	107
14	w10d1	64	78.5	**132**	80	90	115	115
14	w10d2	66		**132**	77	90	115	115
14	w10d3	68		**132**	106	115	106	115
14	w11d1	71	78.8	**132**	74	95	98	98
14	w11d2	73						0
14	w11d3	75						0
14	w12d1	78						0
14	w12d2	80						0
14	w12d3	82						0
15	w1d1	1	106	**140**	87		100	100
15	w1d2	3		**140**	81		95	95
15	w1d3	5		**140**	83		95	95
15	w2d1	8	105	**140**	75		95	95
15	w2d2	10		**140**	86		87	87

15	w2d3	12		**140**	84		104	104
15	w3d1	15	105.9	**140**	85		95	95
15	w3d2	17		**140**	86		95	95
15	w3d3	19		**140**	83		99	99
15	w4d1	22	107.2	**140**	85		105	105
15	w4d2	24		**140**	79		95	95
15	w4d3	26		**140**	75		105	105
15	w5d1	29	106.7	**140**	94		99	99
15	w5d2	31		**140**	75		109	109
15	w5d3	33		**140**	85		90	90
15	w6d1	36	106.2	**140**	82		95	95
15	w6d2	38		**140**	79		105	105
15	w6d3	40		**140**	80		107	107
15	w7d1	43	106.2	**140**	75		100	100
15	w7d2	45		**140**	76	90	104	104
15	w7d3	47		**140**	86	98	96	98
15	w8d1	50		**140**	78	91	94	94
15	w8d2	52	105.7	**140**	77	93	80	93
15	w8d3	54		**140**	74	96	120	120
15	w9d1	57	104.7	**140**	78	96	98	98
15	w9d2	59		**140**	77	111	104	111
15	w9d3	61		**140**	82	96	91	96
15	w10d1	64						0
15	w10d2	66						0
15	w10d3	68						0
15	w11d1	71						0
15	w11d2	73						0
15	w11d3	75						0
15	w12d1	78						0
15	w12d2	80						0

15	w12d3	82						0
16	w1d1	1	55	**127**	65		85	85
16	w1d2	3		**127**	65		90	90
16	w1d3	5		**127**	75		95	95
16	w2d1	8	57.2	**127**	77		90	90
16	w2d2	10		**127**	68		95	95
16	w2d3	12		**127**	75		100	100
16	w3d1	15	57.5	**127**	64		85	85
16	w3d2	17		**127**	73		95	95
16	w3d3	19		**127**	79		100	100
16	w4d1	22	57.1	**127**	71		95	95
16	w4d2	24		**127**	72		90	90
16	w4d3	26		**127**	71		77	77
16	w5d1	29	56.6	**127**	79		95	95
16	w5d2	31		**127**	63		64	64
16	w5d3	33		**127**	72		100	100
16	w6d1	36	57.7	**127**	67		73	73
16	w6d2	38		**127**	74		95	95
16	w6d3	40		**127**	71	75	79	79
16	w7d1	43	57	**127**	73	99	99	99
16	w7d2	45		**127**	75	81	84	84
16	w7d3	47		**127**	72	80	99	99
16	w8d1	50	57.1	**127**	82	85	95	95
16	w8d2	52		**127**	68	85	95	95
16	w8d3	54						0
16	w9d1	57						0
16	w9d2	59						0
16	w9d3	61						0
16	w10d1	64						0
16	w10d2	66						0

16	w10d3	68	0
16	w11d1	71	0
16	w11d2	73	0
16	w11d3	75	0
16	w12d1	78	0
16	w12d2	80	0
16	w12d3	82	0
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17	w1d2	3	0
17	w1d3	5	0
17	w2d1	8	0
17	w2d2	10	0
17	w2d3	12	0
17	w3d1	15	0
17	w3d2	17	0
17	w3d3	19	0
17	w4d1	22	0
17	w4d2	24	0
17	w4d3	26	0
17	w5d1	29	0
17	w5d2	31	0
17	w5d3	33	0
17	w6d1	36	0
17	w6d2	38	0
17	w6d3	40	0
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17	w7d2	45	0
17	w7d3	47	0
17	w8d1	50	0
17	w8d2	52	0

17	w8d3	54					0
17	w9d1	57					0
17	w9d2	59					0
17	w9d3	61					0
17	w10d1	64					0
17	w10d2	66					0
17	w10d3	68					0
17	w11d1	71					0
17	w11d2	73					0
17	w11d3	75					0
17	w12d1	78					0
17	w12d2	80					0
17	w12d3	82					0
18	w1d1	1	65	**122**	69	90	90
18	w1d2	3		**122**	73	100	100
18	w1d3	5		**122**	65	90	90
18	w2d1	8	65	**122**	67	95	95
18	w2d2	10		**122**	70	100	100
18	w2d3	12		**122**	64	93	93
18	w3d1	15	64	**122**	67	91	91
18	w3d2	17		**122**	60	99	99
18	w3d3	19		**122**	67	95	95
18	w4d1	22	64	**122**	65	90	90
18	w4d2	24		**122**	75	93	93
18	w4d3	26		**122**	72	90	90
18	w5d1	29	64.4	**122**	68	90	90
18	w5d2	31		**122**	71	93	93
18	w5d3	33		**122**	71	90	90
18	w6d1	36	65.1	**122**	73	89	89
18	w6d2	38		**122**	70	86	86

18	w6d3	40		**122**	78	97	98	98
18	w7d1	43	64.2	**122**	78	99	79	99
18	w7d2	45		**122**	78	90	90	90
18	w7d3	47		**122**	73	94	90	94
18	w8d1	50	64.6	**122**	73	91	92	92
18	w8d2	52		**122**	56	89	84	89
18	w8d3	54						0
18	w9d1	57						0
18	w9d2	59						0
18	w9d3	61						0
18	w10d1	64						0
18	w10d2	66						0
18	w10d3	68						0
18	w11d1	71						0
18	w11d2	73						0
18	w11d3	75						0
18	w12d1	78						0
18	w12d2	80						0
18	w12d3	82						0
19	w1d1	1	80	**122**	65		80	80
19	w1d2	3		**122**	66		99	99
19	w1d3	5		**122**	78		80	80
19	w2d1	8	82	**122**	76		75	75
19	w2d2	10		**122**	69		75	75
19	w2d3	12		**122**	67		64	64
19	w3d1	15	81.5	**122**	69		97	97
19	w3d2	17		**122**	69		90	90
19	w3d3	19		**122**	70		97	97
19	w4d1	22	81.9	**122**	61		80	80
19	w4d2	24		**122**	79		90	90

19	w4d3	26		**122**	64	99	99
19	w5d1	29	81.9	**122**	69	72	72
19	w5d2	31					0
19	w5d3	33					0
19	w6d1	36					0
19	w6d2	38					0
19	w6d3	40					0
19	w7d1	43					0
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19	w7d3	47					0
19	w8d1	50					0
19	w8d2	52					0
19	w8d3	54					0
19	w9d1	57					0
19	w9d2	59					0
19	w9d3	61					0
19	w10d1	64					0
19	w10d2	66					0
19	w10d3	68					0
19	w11d1	71					0
19	w11d2	73					0
19	w11d3	75					0
19	w12d1	78					0
19	w12d2	80					0
19	w12d3	82					0
20	w1d1	1	73	**126**	75	100	100
20	w1d2	3		**126**	88	95	95
20	w1d3	5		**126**	83	100	100
20	w2d1	8	73	**126**	75	100	100
20	w2d2	10		**126**	86	103	103

20	w2d3	12		**126**	78		92	92
20	w3d1	15	73.3	**126**	81		105	105
20	w3d2	17		**126**	75		101	101
20	w3d3	19		**126**	77		100	100
20	w4d1	22	73.5	**126**	75		105	105
20	w4d2	24		**126**	75		105	105
20	w4d3	26		**126**	73		100	100
20	w5d1	29	74.6	**126**	80		105	105
20	w5d2	31		**126**	80		103	103
20	w5d3	33		**126**	75		109	109
20	w6d1	36	73.3	**126**	81		105	105
20	w6d2	38		**126**	78		103	103
20	w6d3	40		**126**	81		109	109
20	w7d1	43	73.8	**126**	80		109	109
20	w7d2	45		**126**	77		109	109
20	w7d3	47		**126**	77		95	95
20	w8d1	50	73.3	**126**	75	93	85	93
20	w8d2	52		**126**	81	104	97	104
20	w8d3	54		**126**	93	106	92	106
20	w9d1	57	73.2	**126**	82	124	98	124
20	w9d2	59		**126**	82	111	98	111
20	w9d3	61		**126**	86	118	92	118
20	w10d1	64	73.1	**126**	75	115	115	115
20	w10d2	66		**126**	81	107	116	116
20	w10d3	68		**126**	75	105	99	105
20	w11d1	71	73.8	**126**	83	110	101	110
20	w11d2	73		**126**	85	112	112	112
20	w11d3	75						0
20	w12d1	78						0
20	w12d2	80						0

20	w12d3	82	0
21	w1d1	1	0
21	w1d2	3	0
21	w1d3	5	0
21	w2d1	8	0
21	w2d2	10	0
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21	w3d2	17	0
21	w3d3	19	0
21	w4d1	22	0
21	w4d2	24	0
21	w4d3	26	0
21	w5d1	29	0
21	w5d2	31	0
21	w5d3	33	0
21	w6d1	36	0
21	w6d2	38	0
21	w6d3	40	0
21	w7d1	43	0
21	w7d2	45	0
21	w7d3	47	0
21	w8d1	50	0
21	w8d2	52	0
21	w8d3	54	0
21	w9d1	57	0
21	w9d2	59	0
21	w9d3	61	0
21	w10d1	64	0
21	w10d2	66	0

21	w10d3	68	0
21	w11d1	71	0
21	w11d2	73	0
21	w11d3	75	0
21	w12d1	78	0
21	w12d2	80	0
21	w12d3	82	0
22	w1d1	1	0
22	w1d2	3	0
22	w1d3	5	0
22	w2d1	8	0
22	w2d2	10	0
22	w2d3	12	0
22	w3d1	15	0
22	w3d2	17	0
22	w3d3	19	0
22	w4d1	22	0
22	w4d2	24	0
22	w4d3	26	0
22	w5d1	29	0
22	w5d2	31	0
22	w5d3	33	0
22	w6d1	36	0
22	w6d2	38	0
22	w6d3	40	0
22	w7d1	43	0
22	w7d2	45	0
22	w7d3	47	0
22	w8d1	50	0
22	w8d2	52	0

22	w8d3	54						0
22	w9d1	57						0
22	w9d2	59						0
22	w9d3	61						0
22	w10d1	64						0
22	w10d2	66						0
22	w10d3	68						0
22	w11d1	71						0
22	w11d2	73						0
22	w11d3	75						0
22	w12d1	78						0
22	w12d2	80						0
22	w12d3	82						0
23	w1d1	1	92	**122**	75		95	95
23	w1d2	3		**122**	77		96	96
23	w1d3	5		**122**	74		96	96
23	w2d1	8	93.6	**122**	86		100	100
23	w2d2	10		**122**	77		91	91
23	w2d3	12		**122**	83		100	100
23	w3d1	15	93	**122**	88		105	105
23	w3d2	17		**122**	80		100	100
23	w3d3	19		**122**	72		100	100
23	w4d1	22	93	**122**	79		99	99
23	w4d2	24		**122**	79		91	91
23	w4d3	26		**122**	80		95	95
23	w5d1	29	93	**122**	77	95	97	97
23	w5d2	31		**122**	80	88	95	95
23	w5d3	33		**122**	86	99	105	105
23	w6d1	36	94	**122**	80	88	96	96
23	w6d2	38		**122**	73	90	99	99

23	w6d3	40		**122**	79	86	101	101
23	w7d1	43	94	**122**	74	89	99	99
23	w7d2	45		**122**	79	95	94	95
23	w7d3	47		**122**	80	93	93	93
23	w8d1	50	94.2	**122**	72	93	93	93
23	w8d2	52		**122**	74	96	96	96
23	w8d3	54		**122**	73	95	90	95
23	w9d1	57						0
23	w9d2	59						0
23	w9d3	61						0
23	w10d1	64						0
23	w10d2	66						0
23	w10d3	68						0
23	w11d1	71						0
23	w11d2	73						0
23	w11d3	75						0
23	w12d1	78						0
23	w12d2	80						0
23	w12d3	82						0
24	w1d1	1	75	**131**	85		95	95
24	w1d2	3		**131**	75		95	95
24	w1d3	5		**131**	75		95	95
24	w2d1	8	74	**131**	84		95	95
24	w2d2	10		**131**	85		100	100
24	w2d3	12		**131**	84		90	90
24	w3d1	15	74.5	**131**	87		95	95
24	w3d2	17		**131**	83		100	100
24	w3d3	19		**131**	73		120	120
24	w4d1	22	74.9	**131**	82		125	125
24	w4d2	24		**131**	75		100	100

24	w4d3	26		**131**	87		100	100
24	w5d1	29	73.3	**131**	82		121	121
24	w5d2	31		**131**	84		122	122
24	w5d3	33		**131**	74		100	100
24	w6d1	36	70.9	**131**	76		95	95
24	w6d2	38		**131**	75		100	100
24	w6d3	40		**131**	75	80	79	80
24	w7d1	43	70.8	**131**	90	99	90	99
24	w7d2	45		**131**	82	98	90	98
24	w7d3	47		**131**	76	87	83	87
24	w8d1	50	71.6	**131**	83	85	90	90
24	w8d2	52		**131**	83	85	90	90
24	w8d3	54		**131**	80	88	95	95
24	w9d1	57	70.9	**131**	80	96	99	99
24	w9d2	59		**131**	86	85	90	90
24	w9d3	61		**131**	81	97	97	97
24	w10d1	64	71	**131**	78	99	89	99
24	w10d2	66		**131**	84	103	95	103
24	w10d3	68		**131**	82	87	94	94
24	w11d1	71						0
24	w11d2	73						0
24	w11d3	75						0
24	w12d1	78						0
24	w12d2	80						0
24	w12d3	82						0
25	w1d1	1						0
25	w1d2	3						0
25	w1d3	5						0
25	w2d1	8						0
25	w2d2	10						0

25	w2d3	12	0
25	w3d1	15	0
25	w3d2	17	0
25	w3d3	19	0
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25	w4d2	24	0
25	w4d3	26	0
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25	w5d3	33	0
25	w6d1	36	0
25	w6d2	38	0
25	w6d3	40	0
25	w7d1	43	0
25	w7d2	45	0
25	w7d3	47	0
25	w8d1	50	0
25	w8d2	52	0
25	w8d3	54	0
25	w9d1	57	0
25	w9d2	59	0
25	w9d3	61	0
25	w10d1	64	0
25	w10d2	66	0
25	w10d3	68	0
25	w11d1	71	0
25	w11d2	73	0
25	w11d3	75	0
25	w12d1	78	0
25	w12d2	80	0

25	w12d3	82	0
26	w1d1	1	0
26	w1d2	3	0
26	w1d3	5	0
26	w2d1	8	0
26	w2d2	10	0
26	w2d3	12	0
26	w3d1	15	0
26	w3d2	17	0
26	w3d3	19	0
26	w4d1	22	0
26	w4d2	24	0
26	w4d3	26	0
26	w5d1	29	0
26	w5d2	31	0
26	w5d3	33	0
26	w6d1	36	0
26	w6d2	38	0
26	w6d3	40	0
26	w7d1	43	0
26	w7d2	45	0
26	w7d3	47	0
26	w8d1	50	0
26	w8d2	52	0
26	w8d3	54	0
26	w9d1	57	0
26	w9d2	59	0
26	w9d3	61	0
26	w10d1	64	0
26	w10d2	66	0

26	w10d3	68	0
26	w11d1	71	0
26	w11d2	73	0
26	w11d3	75	0
26	w12d1	78	0
26	w12d2	80	0
26	w12d3	82	0
			0

HR%	TempPre	TempPost	TempChange	cardio Speed	Time	weights	Resistance dur.	RPE	CR10
58	37	37	0		15	4	15	13	13
58	36.1	36.4	-0.3	2.3	15	2	15	13	13
62	36.9	37.1	-0.2	3	15	3	15	13	13
58	37.1	36.4	0.7	2.4	15	2	15	15	14
58	37.2	37.1	0.1	2.2	15	4	15	13	14
62	36.9	36.9	0	2.7	15	1	15	15	17
0			0						
56	36.4	36.6	-0.2	2	15	2	15	14	15
61	37.1	36.4	0.7	3	15	1	15	13	15
52	36.2	36.2	0	3	15	1	15	13	15
60	36.3	36.2	0.1	3	15	1	15	13	15
53	36.7	36	0.7	3	15	1	15	13	15
62	36.2	36.4	-0.2	3.3	15	1	15	13	17
66	36.5	36.2	0.3	3.5	15	2	15	11	15
62	36.7	36.5	0.2	3.5	15	1	15	13	15
62	36.6	36.2	0.4	3.7	15	2	15	13	17
60	36.6	36.2	0.4	3.7	15	2	15	15	17
60	36.6	36.2	0.4	3.8	15	2	15	13	18
0			0						
56	36.6	36.2	0.4	3	15	1	15	15	15
0			0						
62	36.5	36.9	-0.4	4	15	2	15	11	13
62	36.5	36.5	0	3	15	1.36	15	11	17
64			0						
68	36.5	35.9	0.6	4.5	15	2	15	11	17
75			0						
68	35.9	35.9	0	5	15	2	15	13	17
0			0						
80	35.9	36.6	-0.7	5	15	2	15	13	15

79	36.5	36.9	-0.4	5	15	2	15	13	15
66	36.9	36.4	0.5	5	15	2	15	13	16
62	37	36.4	0.6	5	15	2.5	15	12	15
83	36.4	36.5	-0.1	5.5	15	1.25	15	11	16
80	36.5	36	0.5	5	15	2	15	11	15
70	36.6	36	0.6	5	15	2	15	11	15
0			0						
68	37	36	1			0.5	30		14
74	37	36	1			0.5	30		14
64	37	36	1			2	30		16
68	37	37	0			1	30		13
71	37	36	1			1	30		14
69	37	37	0			2	30		12
68	36	36	0			2	30		13
68	37	36	1			1	30		13
71	36	36	0			1	30		13
68	36	36	0			1	30		12
79	36	36	0			1	30		13
68	36	36	0			1	30		13
68	36	36	0			1	30		12
68	36	36	0			1	30		13
68	36	36	0			2	30		12
56	37	36	1			1	30		12
68	37	36	1			1	30		12
68	37	36	1			1	30		12
64	36	36	0			1	30		13
64	36.7	36.5	0.2			2	30		13
66	36.6	36.5	0.1			0.5	30		12
59	36.5	36.2	0.3			3	30		13
59	36.6	36.5	0.1			1	30		12

66	37.1	37.9	-0.8			2	30		12
71	36.9	36.9	0			1.5	30		12
71	36.8	37	-0.2			2	30		12
67	37.3	36.9	0.4			1.5	30		12
64	37.2	36.9	0.3			2	30		12
62	37.1	37	0.1			1.3	30		12
64	37	36.4	0.6			2	30		12
56	36.7	36.5	0.2			3	30		12
60	36.9	36.7	0.2			3	30		12
64	36.9	36.3	0.6			2	30		10
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70	36	36	0	0.7	15	1	15	13	13
73	37	37	0	2.9	15	1	15	13	13
74	37	37	0	7.5	15	2	15	11	14
74	37	37	0	2.9	10	2	15	12	15
75	37	36	1	3.4	15	2	15	12	15
73	36	36	0	5	15	1	15	12	14
70	37	36	1	5	15	2	15	14	13
73	37	37	0	9	15	1	15	12	12
74	37	37	0	5	15	2	15	12	12
70	36	36	0	2	14	0.5	15	13	14
73	37	36	1	2.5	15	2	15	14	13
72	37	36	1	4	15	2	15	12	14
77	36	36	0	2.4	15	3	15	12	15
70	37	36	1	6	15	3	15	10	15
71	37	36	1	2	15	2	15	13	12
85	37	36	1	2.2	15	1	15	12	14
63	73	36	37	3	15	3	15	12	14

74	37	37	0	3.2	15	2	15	13	14
82	37	37	0	4	9	1	15	11	13
93	37	36	1	3.2	9	2	15	14	14
92	36.7	36.8	-0.1	6.3	15	1	15	12	12
93	36.7	36.5	0.2	3.9	15	2	15	14	14
82	36.8	36.6	0.2	3.6	15	1	15	13	12
90	37	36.5	0.5	4	15	1.6	15	13	13
71	37.2	37	0.2	5	15	2	15	13	12
93	36.9	36.5	0.4	3.3	15	3	15	11	12
82	37.1	36.8	0.3	3.3	15	2	15	11	12
86	36.9	36.7	0.2	3.5	15	2	15	12	13
93	36.8	36.7	0.1	3.8	15	2.5	15	12	12
81	3701	36.9	3664.1	3.8	15	3	15	12	13
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67	37	37	0	1	13	0.5	15	12	13
63	37	37	0	3.5	15	1	15	11	11
95	37	37	0	1	15	1	15	11	11
67	37	37	0	3.5	15	1	15	10	10
71	37	37	0	3.4	15	1	15	13	19
67	37	37	0	4.3	15	2.5	15	11	13
82	37	37	0	4.4	15	1	15	13	15
71	37	37	0	5	15	1	15	13	15
70	37	37	0	2.5	15	1	15	10	11
61	37	37	0	2	15	1	15	11	11
70	37	37	0	3.5	15	1	15	13	15
73	37	37	0	3.7	15	1	15	11	15
59	37	37	0	3.6	15	2	15	10	15
69	37	37	0	4	15	2	15	10	18
60	37	37	0	4	15	2	15	11	12
71	37	37	0	3.5	15	1	15	11	12
63	37	37	0	7	15	1	15	11	13
81	37	37	0	3.5	15	1	15	11	15
74	37	37	0	3.5	15	1	15	11	15
81	37.9	38.1	-0.2	4.5	15	3	15	14	15
74	37.7	37.5	0.2	4.3	15	1	15	12	15
87	37.2	37.2	0	4.1	15	3	15	10	15
75	37	37.3	-0.3	4.2	15	2	15	11	15
81	37	37.5	-0.5	4.5	15	3	15	12	12
81	37	37.2	-0.2	7.1	15	2	15	10	13
89	36.6	37.4	-0.8	4.5	15	3	15	14	10
95	37.5	37.3	0.2	5	15	2.5	15	11	12
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81	36	36	0	2.5	15	2	15	12	12
83	37	37	0	2.3	15	2	15	12	13
85	36	37	-1	3.5	15	2.5	15	11	12
79	36	37	-1	3.5	15	2.5	15	11	11
74	36	36	0	3	15	2.5	15	11	11
91	36	37	-1	3	15	2.5	15	11	12
89	36	36	0	4.1	15	2.5	15	11	11
83	36	36	0	4.1	15	2.5	15	11	10
74	36	36	0	2	15	2.5	15	11	12
75	36	36	0	4	15	2.5	15	10	11
78	36	36	0	4.5	15	2.5	15	10	11
79	37	37	0	5	15	2.5	15	11	11
73	36	36	0	5.3	15	5	15	12	13
80	36	36	0	5.5	15	5	15	12	12
81	37	36	1	5.2	15	2.5	15	13	12
80	36	36	0	5.2	15	5	15	12	12
79	36	36	0	5.6	15	5	15	12	11
77	36	36	0	5.3	15	5	15	12	12
85	36	36	0	5.3	15	2.5	15	12	12
84	36	36	0	5.5	15	5	15	12	13
76	36.2	36.4	-0.2	6.5	15	2.5	15	12	14
75	36.3	36.6	-0.3	5.5	15	5	15	12	14
75	36.8	36.6	0.2	5.5	15	5	15	11	12

81	36.7	36.5	0.2	5.4	15	5	15	11	11
94	36.7	36.6	0.1	6.2	15	6.2	15	11	11
83	36.7	36.7	0	5.5	15	5	15	11	11
89	36.7	36.2	0.5	6.6	15	5	15	11	11
74	36.6	36.6	0	6.3	15	5	15	11	11
85	36.6	36.8	-0.2	6.6	15	5	15	11	11
93	36.6	36.6	0	5.7	15	2.5	15	11	11
79	36.4	36.5	-0.1	6	15	5	15	11	10
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71	36	36	0	2.9	15	0.5	15	12	11
70	37	37	0	2	15	0.5	15	13	13

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64	36	36	0	1.5	15	1	15	13	11
74	36	36	0	1.5	15	0.5	15	12	12
56	36	36	0	1.3	15	2	15	12	11
59	37	36	1	1.5	15	5	15	12	12
61	36	36	0	1.5	15	1	15	11	11
57	36	37	-1	1.5	15	0.5	15	12	13
69	36	36	0	1.5	15	0.5	15	11	11
65	36	36	0	1.6	15	1	15	11	11
57	37	36	1	1.7	15	1	15	12	12
69	36	36	0	1.6	15	1	15	11	12
65	36	36	0	1.8	15	1	15	13	11
57	36	36	0	1.9	15	0.5	15	13	12
59	36.8	36.9	-0.1	1.7	15	0.5	15	12	11
64	37	36.8	0.2	2.2	15	0.5	15	12	12
76	37.2	36.4	0.8	2.2	15	1	15	11	11
65	36.9	36.8	0.1	2.3	15	1.5	15	13	12
63	36.7	36.3	0.4	2.3	15	1.2	15	12	12
59	36.6	35.8	0.8	2.3	15	1	15	11	11
76	36.6	35.8	0.8	2.4	15	1.9	15	11	11
66	36.6	36	0.6	2.2	15	2.5	15	12	13
63	36.5	36.1	0.4	2.4	15	5	15	12	12
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64	36.7	36.07	0.63	2.5	15	2	15	11	9
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86	36	37	-1	5.5	15	5	15	11	12
88	37	36	1	5.5	15	5	15	11	11
98	36	37	-1	5.5	15	5	15	11	11
81	36	36	0	5.5	15	5	15	11	12
84	36	37	-1	5.5	15	5	15	12	11
91	36	36	0	5.5	15	5	15	13	11
90	36	37	-1	5.5	15	2.5	15	12	12
85	36	36	0	5.5	15	5	15	12	12
94	36	36	0	5.5	15	2.5	15	12	11
91	36	36	0	5.5	15	5	15	12	12
78	36	36	0	5.5	15	5	15	11	11
87	36	36	0	5.5	15	5	15	11	11
94	36	36	0	5.5	15	2.5	15	11	11
84	36	36	0	5.5	15	5	15	10	10
82	36	36	0	5.5	15	5	15	10	11
94	36.1	36.7	-0.6	5.5	15	5	15	11	11
95	36.9	36.3	0.6	5.5	15	5	15	11	11
78	37	36.8	0.2	6	15	5	15	11	11
94	36.9	36.8	0.1	5.5	15	5	15	11	11
94	36.4	36.6	-0.2	5.6	15	5	15	11	11
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64	37	37	0			1	30		11
72	36	37	-1			1	30		11
63	37	37	0			1	30		11
744	36	37	-1			1	30		11
62	36	37	-1			2	30		11
71	37	37	0			1	30		13
75	36	37	-1			1	30		11
71	37	37	0			0.5	30		12
66	36	37	-1			1	30		11
68	36	37	-1			1	30		13
63	36	37	-1			2	30		11
65	36	36	0			1	30		12
73	37	37	0			2	30		11
75	36	37	-1			1	30		15

71	37	37	0			2	30		11
63	36	37	-1			1	30		15
58	37	37	0			1	30		11
61	36	37	-1			2	30		13
73	36	37	-1			2.5	30		13
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88	37	37.2	-0.2			1	30		12
76	37.2	37.2	0			2	30		11
77	37.1	37	0.1			2	30		12
83	36.4	36.9	-0.5			2	30		11
65	37.2	36.9	0.3			2	30		13
71	37.6	37.4	0.2			2	30		11
78	37.7	37.6	0.1			2	30		13
69	37.5	37.4	0.1			2	30		11
80	37.5	37.5	0			2	30		12
71	37.3	37.2	0.1			2	30		11
65	37.6	37.6	0			4	30		13
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76	36.5	36.8	-0.3	3.2	15	1	15	15	15
72	36.7	36.5	0.2	3.5	15	3	15	13	13
72	36.4	36.5	-0.1	3.1	15	1	15	13	13
69	36.5	36.8	-0.3	3.3	15	3	15	15	16
64	36.7	36.8	-0.1	3.1	15	3	15	16	17
79	36.6	37.3	-0.7	3.5	15	2	15	17	17
72	36.3	36	0.3	3.2	15	1.5	15	11	12
82	36.3	37	-0.7	3.1	15	2	15	14	14

75	36.1	36.9	-0.8	3.4	15	1	15	15	14
82	36	37	-1	3.3	15	1	15	15	15
75	36.1	36.7	-0.6	3.6	15	2.5	15	15	17
75	36.2	36.4	-0.2	3.5	15	2.5	15	15	15
75	36.3	36.7	-0.4	3.7	15	2.5	15	13	16
77	36.2	36.6	-0.4	3.7	15	2.5	15	15	16
63	35.5	36.8	-1.3	3.7	15	2.5	15	15	13
61	36	36.6	-0.6	3.5	15	2.5	15	13	12
70	36.2	36.8	-0.6	3.8	15	2	15	15	15
70	36	36.8	-0.8	3.4	15	2.5	15	15	17
73	35.9	36.2	-0.3	3.4	15	1.5	15	17	14
92	36	36.8	-0.8	3.4	15	2.5	15	15	15
73	36.2	36.6	-0.4	3.3	13	2.5	15	13	16
76	36	36.6	-0.6	3.2	15	2	15	15	16
75	36.1	36.3	-0.2	3.3	13	2.5	15	13	15
81	36.1	36.3	-0.2	3.3	15	2.5	15	13	15
87	36.2	36.8	-0.6	3.3	15	2.5	15	14	14
87	36.2	36.1	0.1	3.3	13	2.5	15	14	14
87	36.7	36.8	-0.1	3	15	5	15	14	14
74	36.3	36	0.3	3.3	15	2.5	15	14	14
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62	37	37	0	3	15	3.5	15	12	11

74	37	37	0	3.5	15	4	15	11	12
68	36	37	-1	4.5	15	3	15	11	12
68	37	37	0	4.5	15	1	15	13	13
71	37	37	0	4.5	15	3	15	13	12
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68	37	37	0	4.5	15	3	15	13	11
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64	37	37	0	4.8	15	3	15	13	11
68	37	37	0	5	15	3	15	13	15
75	37	37	0	5	15	3	15	16	15
76	37	37	0	5	15	3	15	15	12
71	37	37	0	5	15	4	15	13	11
74	37	36.8	0.2	5	15	2.5	15	13	15
70	37.4	37.4	0	4.5	15	3	15	12	12
67	37.4	37.2	0.2	5	15	3	15	12	13
66	37.3	37	0.3	6	15	3	15	11	9
86	37.3	36.5	0.8	3	15	3	15	9	11
70	37.9	36.9	1	3	15	3	15	11	15
79	36.9	36.8	0.1	5	15	3	15	11	9
69	36.9	36.8	0.1	5	15	4	15	11	9
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75	37	37	0	2.2	15	0.5	13	13	11
71	37	37	0	2.2	15	0.5	13	11	11
75	37	36	1	2.2	15	0.5	13	13	11
79	37	37	0	2.2	15	2	16	13	15
67	36	36	0	2.2	15	2	15	13	15
75	36	36	0	2.2	15	0.5	13	13	13
79	36	37	-1	2.2	15	0.5	11	11	13
75	36	37	-1	2.2	15	1	12	12	13
71	37	37	0	2.2	15	0.5	13	13	12
61	36	37	-1	2.2	15	1	12	12	13
75	36	36	0	2.2	15	0.5	11	11	12
50	37	37	0	2.2	15	1	11	11	12
79	37	37	0	2.2	15	0.5	15	10	11
57	36	37	-1	5	15	1	15	11	12
75	36	36	0	2.2	15	1	15	11	11
62	36.7	36.9	-0.2	2.2	15	1	15	11	12
78	36.7	36.6	0.1	2.5	15	1	15	12	11
66	36.7	37.2	-0.5	2.2	15	1	15	13	11
78	37.1	37.1	0	2.4	15	0.5	15	11	11
75	37.1	37.4	-0.3	2.4	15	1.3	15	10	11
75	37	37.2	-0.2	2.4	15	1	15	10	12
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74	37	36	1	2.5	15	1.5	15	13	12
78	36	37	-1	3	15	1.5	15	11	20
82	36	37	-1	2.5	15	1	15	15	15
76	36	36	0	2.5	15	1.5	15	13	9
75	36	37	-1	2.8	15	2	15	14	13
81	36	36	0	3.5	15	2	15	20	16
78	36	36	0	3.5	15	2	15	11	10
74	36	36	0	3.5	15	2	15	10	15
76	36	37	-1	3.6	9	1	15	11	11
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74	37	36	1	3.5	15	2	15	13	10
76	37	37	0	3.7	15	1	15	11	12
74	36	36	0	3.7	15	2	15	10	8
73	36	36	0	3.5	15	2	15	8	8
70	37.3	37.5	-0.2	3.7	15	3	15	11	11

80	36.9	37	-0.1	3.7	15	1	15	12	12
81	36.6	36.6	0	3.5	15	2	15	12	12
74	36.9	37.1	-0.2	3.7	15	3	15	11	9
77	36.8	36.8	0	3.9	15	3	15	11	12
75	37.1	36.7	0.4	3.3	15	2	15	9	9
73	36.5	36.8	-0.3	3.4	15	3	15	9	8
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81	36	36	0	3	15	1	15	12	17
66	36	37	-1	1	15	2	15	15	19
61	36	36	0	2.4	15	1	15	13	13
61	36	36	0	2.5	15	1	15	14	13
52	36	36	0	2	15	0.5	15	15	17
80	36	36	0	1.8	15	1	15	12	13
74	36	36	0	2.3	15	1	15	15	17
80	36	37	-1	2.5	15	2	15	15	11
66	36	36	0	2.3	15	2	15	12	14
74	37	36	1	2.5	15	1	15	11	13

81	37	36	1	2.5	15	1	15	12	11
59	36.9	36.7	0.2	2.5	15	1	15	11	13
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79	37	37	0	3	15	2	15	8	13
79	37	37	0	3.5	15	2	15	9	11
82	37	36	1	3.5	15	3	15	9	8

73	37	37	0	3.9	15	2.5	15	8	8
83	37	37	0	4.4	15	3	15	11	11
80	37	37	0	4	15	4	15	10	11
79	36	37	-1	4	15	4	15	8	9
83	37	37	0	4	15	1	15	11	12
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83	37	37	0	4.3	15	2	15	11	10
82	37	37	0	4.3	15	4	15	10	11
87	37	37	0	5	15	3	15	11	12
83	37	37	0	5	15	2	15	11	11
82	37	36	1	5.3	15	2	15	14	13
87	37	37	0	5.5	15	1	15	13	8
87	37	36	1	5.7	15	5	15	11	10
87	36	37	-1	5.7	15	2	15	11	8
75	36	36	0	5.5	15	3	15	10	10
74	37.1	36.9	0.2	4.5	15	2.5	15	11	11
83	36.9	37.2	-0.3	4.5	15	3	15	11	11
84	37.3	36.8	0.5	5	15	2	15	11	11
98	36.9	36.9	0	4.5	15	3	15	11	11
88	36.7	37.1	-0.4	4.5	15	3	15	12	10
94	37	37	0	5	15	3	15	13	11
91	36.9	37	-0.1	3	15	3	15	11	11
92	37.3	37.1	0.2	5	15	3	15	11	11
83	37.2	36.9	0.3	6	15	1.5	15	11	11
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89	37.5	37.4	0.1	5	15	4	15	9	11
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75	36	36	0	3.4	15	5	15	13	15
82	36	36	0	4	15	2.5	15	12	12
86	36	36	0	4.4	15	5	15	12	12
82	36	36	0	3.4	15	2.5	15	13	13
82	36	36	0	3.4	15	5	15	11	12
81	36	35	1	3.4	15	2.5	15	11	13
75	36	36	0	3.5	15	2.5	15	11	11
78	36	36	0	3.4	15	2.5	15	11	13
80	36.1	36.1	0	4	15	2.5	15	12	13
78	36.7	36.3	0.4	4	15	2.5	15	12	13
86	36.4	36.4	0	4	15	2.5	15	14	11
79	36.3	36.3	0	4	15	2.5	15	13	12
81	36.5	36.3	0.2	4	15	2.5	15	11	13

83	35.9	36.2	-0.3	4	15	2.5	15	12	13
81	36.4	36.4	0	4	15	2.5	15	13	11
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95	36	37	-1	3.4	15	2	15	13	13
76	36	36	0	3.4	15	2	15	13	13

76	36	36	0	3.4	15	1	15	11	11
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76	36	36	0	3.7	15	0.5	15	9	13
61	35.8	35.5	0.3	3.8	15	1	15	11	12
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75	36.2	36.4	-0.2	4	15	1	15	11	9
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69	36.5	37	-0.5	4.1	15	1.5	15	8	9
69	36.4	36.5	-0.1	4.1	15	1.81	15	8	11
73	36.2	35.9	0.3	4.1	15	1	15	11	13
76	36	36.3	-0.3	5	15	1.8	15	11	11
69	36.6	36.4	0.2	4.1	15	1.8	15	11	11
74	36.3	35.9	0.4	4.1	15	2.5	15	11	12
76	36.5	36.5	0	4.2	15	1	15	8	9
79	36.6	36.3	0.3	4.4	15	1.8	15	8	8
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Appendix 15

Interview script: Participant Y (Literal translation of the participant's account. R=Researcher)

R: Could you describe your foot trip?
Y: I started the journey with my family early Thursday morning. We walked all day stopping only for rest and food, say about 20 minutes after each hour of walking. We slept in the open air that night and marched the next day non-stop and arrived at our destination on Friday just after midnight. We did the 85 kilometer walk in exactly 55 hours.
R: Did you feel tired before the journey?
Y: Not at all. I was actually feeling refreshed after a good night sleep.
R: How tired did up you feel during and after the trip?
Y: Beginning with day 1, tiredness started building up as the day progressed, but it was bearable possibly because we used to have some rest every hour. Strangely enough, although I used to feel in need of long rest in the afternoon, I carried on walking that day and had only the usual short breaks. After sunset, I was feeling really exhausted, and I immediately went to sleep.
R: How was your sleep? How did you feel?
Y: My sleep is usually disturbed. Not that night. I did feel some pain in my muscles, but I ignored it and slept for nearly 8 hours without interruption. Maybe because I was tired. When I woke up in the morning, I was still feeling tired but I knew I still had a long way to go, and I continued the journey. I was determined to get to my destination, no matter what.
R: Did you not think that the exercise effort might trigger a relapse? Y: Not at all. Had it happened, I would have welcomed it. The harder the better, you know (smiling). By the way, we had a wheel-chair with us, but it was for my mother-in-law, and she refused to use it most of the way.
R: What about the weather? Any effect?
Y: It was not bad. Say about 25°c. We got a bit wet one night though. It was drizzly.
R: Did you take any precautions?
Y: No precautions whatsoever. Had any of us been blessed by death, others would have carried his dead body to Karbala to be buried there.
R: Apart from tiredness, did you experience any other symptoms?
Y: Not really. I did stumble twice or three times, but it was the usual thing. Like everybody else may, I also used to feel a bit dizzy at the end of the day. It is the sort of situation when you have no time to think about yourself. You see the old, the frail, people in wheel-chairs or with crutches or walking sticks. All are determined, marching and chanting. Then you say to yourself, thank God I am healthy and well.
R: What about your ability to concentrate? For example when preparing your meals?
Y: Food was provided free of charge all the way. I was focused only on one thing: to make it to the holy shrine in Karbala.
R: You started talking about the first day of the journey. What about the second?
Y: Just like the day before, although the distance was longer.
R: Did you feel more tired than the day before?
Y: Yes, in the beginning. But when I got to Karbala, you would be surprised if I told you that fatigue vanished altogether. It was a feeling I cannot describe. I slept for only three

hours or so. I was so excited and waiting impatiently for the dawn to break and start the celebrations. On Saturday, the day of Ashura, we spent all day praying and walking inside and around the shrine. Nearly eight hours non-stop and without food. I came to realise how tired I was only when everything was over. But I did promise Imam Hussein, peace be upon him, to go and see him again next year. I have been doing this for the past seven years, you know.

R: How tired did you feel after the pilgrimage? Can you describe that?

Y: I did actually feel very tired. But after some good rest and sleep, fatigue went back to its normal levels. As usual, I do sometimes feel tired during the day, especially in the afternoon. But that is bearable.

R: Yours is an extraordinary story. Some will find it hard to believe.

Y: It is up to the others to think or believe what they want. In my view, nothing stands in the way of true faith. I am not saying that only as a Muslim. A Hindu or a Christian would feel and tell you the same.

Appendix 16

Interview guiding questions

The pre-training interview was focused on the nature of MS fatigue, and the post-training interview was meant to gauge participants' attitude towards training. Both were semi-structured interviews. What follows are only the guiding questions.

Pre-training interview

1. Can you describe the difference in fatigue between pre-diagnosis and post-diagnosis with MS?
2. Is MS fatigue permanent or transient?
3. How does fatigue progress during the day?
4. How would you describe the fatigue you experience in the morning/afternoon/at night?
5. In your view, what are the factors that alleviate fatigue?
6. What are the factors that reduce fatigue?
7. Can you describe the relationship between fatigue and anxiety (depression, pain, sleep disorders)?
8. What is the impact of fatigue on your daily living activities?
9. What is the impact of fatigue on your social activities (and work)?
10. How do you deal with fatigue?

Post training interview

1. What was your view about exercise before the trail?
2. What motivated you to join the training programme?
3. What do you think about training after you had joined the programme?
4. What are the positive outcomes of the training programme?
5. What are its negative outcomes?
6. What do you think about the training programme in terms of its leaders (participants)?
7. What are your suggestions to improve future training programmes?
8. What are the factors that hinder the participation of MS patients in training?

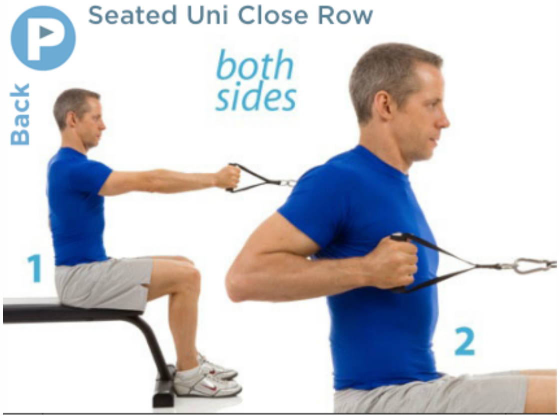
Appendix 17.a

RESISTANCE PROGRAM

1. **Sit on the gym ball in a good posture.**
2. **Lift weights to your shoulders, alternating sides.**
3. **Fully straighten your elbows between lifts.**
4. **Repeat 10-20 times (as advised by your supervisor)**

1. **Begin with your arms straight over your head.**
2. **Slowly lower the weights over your head by bending your elbows. Do not move your elbows.**
3. **Straighten your elbows.**
4. **Repeat 10-20 times (as advised by your supervisor)**

1. **Sit on the gym ball in a good posture.**
2. **Keeping your back straight, pull the band back, bringing your shoulder blades together.**
3. **Slowly release the band back to the starting position.**
4. **Repeat 10-20 times (as advised by your supervisor). Keep your shoulders down and away from your ears.**



1. **Stand against the wall with your feet a little out from it.**
2. **Slowly lower into a seated position.**
3. **Push back up into a standing position. Keep your upper back against the wall at all times. Keep your head up and gaze level.**
4. **Repeat 10-20 times (as advised by your supervisor)**

Appendix 17.b

1. Stand at the wall, you may hold on to it for balance.
2. Keeping your knees beside each other (not touching) bend your knee, lifting your heel up as far as you can.
3. Slowly lower.
4. Repeat 10-20 times (as advised by your supervisor)

1. Stand against the wall, holding hand weights.
2. Raise onto your toes, slowly lower all the way down.
3. Repeat 10-20 times (as advised by your supervisor)

1. Lie on your back on the exercise mat with your knees bent and feet slightly apart.
2. Squeeze your bottom, then raise your bottom off the floor.
3. Keep the squeeze on your bottom as you slowly lower all the way down.
4. Repeat 10-20 times (as advised by your supervisor)

Lie on your back on the exercise mat with your arms and legs in the air as shown in the image.

1. Slowly lower opposite arm and leg to the floor while breathing OUT (e.g. right arm-left leg).
2. Raise back up into starting position.
3. Repeat with the opposite arm and leg.
4. Repeat 10-20 times (as advised by your supervisor)

1. Lie on your front with your forehead on a rolled-up towel.
2. Raise opposite arm and leg in the air as if you are swimming as you breathe OUT. Slowly lower.
3. Repeat 10-20 times (as advised by your supervisor)