APPLYING THE BEHAVIOURAL EPIDEMIOLOGY FRAMEWORK TO INVESTIGATE SEDENTARY BEHAVIOUR AND PHYSICAL ACTIVITY IN RHEUMATOID ARTHRITIS

By

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ABSTRACT

Rheumatoid Arthritis (RA) is a chronic autoimmune disease, characterised by high-grade inflammation. People with RA experience pain, fatigue, functional disability and compromised psychological well-being. These patients typically spend long periods of the day engaged in sedentary behaviour, which may exacerbate negative RA health outcomes.

This thesis was guided by the Behavioural Epidemiology Framework, and provided novel evidence in the field of sedentary behaviour research in RA. Primarily, the activPAL and ActiGraph accelerometer were validated for measurement of sedentary time and physical activity (PA) in RA (Chapter 2). These devices were subsequently employed in the longitudinal study comprising Chapters 4-6. In Chapter 4, longitudinal associations were revealed between several clinically- and patient-important RA outcomes with sedentary, standing and stepping time. These relationships were largely bi-directional. Grounded in self-determination theory, Chapter 5 demonstrated that autonomous motivation to reduce sedentary behaviour was negatively associated with sedentary time, and positively related to time engaged in standing, stepping and light-intensity PA in RA. Chapter 6 tested hypothesised models of sedentary behaviour change, which suggested fostering autonomous motivation to reduce sedentary behaviour in people with RA, may promote changes in sedentarity to the extent that it might attenuate the burden of disease in this patient group.

I would like to dedicate this thesis to my family,

Peter, Sherie, Sinead and Lisa O’Brien

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CONTENTS LISTING

LIST OF PAPERS

Ciara O'Brien conducted study design, recruitment, data collection, statistical analysis and writing. Dr Sally Fenton, Professor Joan Duda and Professor George Kitas advised on study design and statistical analysis, and provided feedback on all written work. Biomedical scientists (Jacqueline Smith and Janet Imeson-Wood) at Russells Hall Hospital assisted with analysis of blood samples. Co-authors, where listed, advised on statistical analysis and paper editing.

Chapter 2 of this thesis is comprised of the following paper.

1. **O'Brien, C. M.,** Duda, J. L., Kitas, G. D., Veldhuijzen van Zanten, J. J. C. S., Metsios, G. S., & Fenton, S. A. M. (under review). Objective measurement of sedentary time and physical activity in people with rheumatoid arthritis: an accelerometer and activPAL validation study. *Arthritis & Rheumatology.*

During the period of PhD study within the School of Sport, Exercise and Rehabilitation Sciences at the University of Birmingham, the following papers and conference abstracts were accepted for publication/presentation.

Publications

1. **O'Brien, C. M.,** Duda, J. L., Kitas, G. D., & Fenton, S. A. M. (2018). *Sedentary Time*. Encyclopedia of Behavioral Medicine: Springer, New York, NY.

2. **O'Brien, C. M.,** Duda, J. L., Kitas, G. D., Veldhuijzen van Zanten, J. J. C. S., Metsios, G. S., & Fenton, S. A. M. (2018). Correlates of sedentary behaviour and light physical activity in people living with rheumatoid arthritis: protocol for a longitudinal study. *Mediterranean Journal of Rheumatology*, *29*(2), 106-117.

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Conference Presentations

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3. **O'Brien, C. M.,** Duda, J. L., Kitas, G. D., Veldhuijzen van Zanten, J. J. C. S., Metsios, G. S., & Fenton, S. A. M. Health-related and psychosocial correlates of sedentary behaviour in people living with rheumatoid arthritis: a longitudinal study. *24thAnnual Congress of the European College of Sports Science, Prague, Czech Republic, July 2019* (awarded 2nd prize in the ECSS Young Investigators Award and invited to present at the *75th Annual Congress of the Japanese Society of Physical Fitness and Sports Medicine, Kagoshima City, Japan, September 2020*)

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CHAPTER 1

GENERAL INTRODUCTION

Overview

Rheumatoid Arthritis (RA) is a chronic autoimmune disease, characterised by high-grade systemic inflammation. The heightened inflammatory burden of RA contributes to debilitating joint pain, fatigue and functional disability, symptomatic of the condition (Smolen, Aletaha, & McInnes, 2016a; Uhlig, Moe, & Kvien, 2014), as well as increased risk of cardiovascular disease (CVD) (Avina-Zubieta, Thomas, Sadatsafavi, Lehman, & Lacaille, 2012). Further, people with RA are at high risk of psychological comorbidities (e.g., depression) (Matcham, Rayner, Steer, & Hotopf, 2013). According to a report by the National Rheumatoid Arthritis Society (NRAS), over half of people with RA leave employment within 6 years of diagnosis (NRAS, 2010).

RA is the most common inflammatory arthritis, with a global prevalence of 0.5-1% (Uhlig et al., 2014; Wasserman, 2018). The clinical treatment of RA currently targets the control of inflammatory disease activity ('treat to target'), with the aim of decelerating joint damage, alleviating symptoms of pain, improving physical function and preventing the onset of chronic diseases (e.g., CVD) (Smolen et al., 2017). This approach involves the use of pharmacological methods, including the prescription of disease-modifying anti-rheumatic drugs (DMARDs) (Ferro, Elefante, Luciano, Talarico, & Todoerti, 2017; Smolen et al., 2017). These therapeutic agents are initiated as early as possible in the disease course to achieve these targets (Smolen et al., 2017).

However, there remains an 'unmet need' on behalf of patients with RA regarding these specific treatment objectives. Firstly, sometimes control of RA disease activity by drug treatment is not achieved (Taylor, Moore, Vasilescu, Alvir, & Tarallo, 2016). Secondly, even when medication *is* successfully controlling RA disease activity, patients may still report pain, fatigue, functional disability and compromised mental health, or experience a 'flare-up' in

which a bout of heightened inflammation worsens symptoms (Santos et al., 2019; Taylor et al., 2016). Thus, treatment regimens that serve to tightly control inflammation (e.g., pharmacological intervention) *and* promote self-management to attenuate important RA symptoms (e.g., non-pharmacological intervention), might be warranted (Santos et al., 2019; Taylor et al., 2016).

Non-pharmacological methods of managing RA outcomes include physical activity (PA) (Santos et al., 2019), and the ideology of 'exercise as medicine' has been explored in this population. A growing body of research has investigated associations between engagement in PA, with disease outcomes in RA. The available evidence indicates beneficial associations to exist between PA of a moderate-to-vigorous intensity (MVPA, ≥3 metabolic equivalents [METs]), with outcomes such as systemic inflammation, disease activity, functional disability, pain, fatigue, psychological well-being and CVD risk in this population (Cooney et al., 2011; de Jong et al., 2003; Hammam, Ezeugwu, Rumsey, Manns, & Pritchard-Wiart, 2019; Loppenthin et al., 2015; Metsios & Kitas, 2018; Metsios, Stavropoulos-Kalinoglou, & Kitas, 2015; Plasqui, 2008; Rahnama & Mazloum, 2012; Rongen-van Dartel et al., 2015; Verhoeven et al., 2016). Despite this, evidence suggests that people with RA are physically inactive. That is, they do not engage in sufficient levels of MVPA to accrue the reported benefits to health (Lee et al., 2012; Sokka et al., 2008; Tierney, Fraser, & Kennedy, 2012; Yu et al., 2015b).

Over the last decade, an increasing amount of research attention has focused on sedentary behaviour, defined as any waking behaviour expending energy ≤1.5 METs whilst in a sitting/reclining/lying posture (Sedentary Behaviour Research Network [SBRN], 2012; Tremblay et al., 2017) (e.g., sitting whilst watching television, reading a book or travelling in a vehicle), and its role in the development of poor health in non-RA individuals (Biswas et al., 2015; Carson et al., 2014; de Rezende, Rey-Lopez, Matsudo, & do Carmo Luiz, 2014; Ford &

Caspersen, 2012; Healy, Matthews, Dunstan, Winkler, & Owen, 2011; Okely et al., 2019; Rosenberg et al., 2016; Santos et al., 2012). Sedentary behaviour is a distinct construct from physical inactivity, demonstrating independent health risks (e.g., all-cause, CVD and cancer mortality) in different populations (Patterson et al., 2018). Levels of accelerometer-assessed sedentary time have been reported to exceed 9h/day in people with RA (Fenton, Veldhuijzen van Zanten, Duda, Metsios, & Kitas, 2018b), with cross-sectional studies reporting associations between high levels of sedentary time with higher disease activity, functional disability and CVD in these patients (Fenton et al., 2018b; Fenton et al., 2017; Hammam et al., 2019).

Reasons cited for lack of engagement in MVPA among people with RA include pain, fatigue and functional disability (Larkin, Kennedy, Fraser, & Gallagher, 2017; Tan, Pugh, Humby, & Morrissey, 2019; Veldhuijzen van Zanten et al., 2015). A recent qualitative study (Larkin et al., 2017) remarked on how the symptoms of RA (e.g., pain and fatigue) were reported as barriers to participation. One patient stated, “sometimes the pain is so bad you just don’t know you know and I’m just thinking how the hell am I going to get upstairs today”. Patients in this study also acknowledged their physical limitations, and described the importance of ‘pacing’ themselves with regard to PA engagement. The authors highlighted that PA guidelines for the RA population should consider the pragmatisms with meeting optimum PA recommendations among these patients.

This has led to research exploring the potential of light-intensity PA (LPA [1.6-2.9 METs]) for improving health in RA. It has been noted that populations with reduced physical function (e.g., older adults) may find LPA participation more realistic than MVPA to achieve (Buman et al., 2010; Ekwall, Lindberg, & Magnusson, 2009; Manns, Dunstan, Owen, & Healy, 2012). Although very much in their infancy, cross-sectional studies have demonstrated

associations between higher LPA with lower disease activity and functional disability, attenuated CVD risk and enhanced psychological well-being in RA (Fenton et al., 2018c; Hammam et al., 2019; Khoja, Almeida, Chester Wasko, Terhorst, & Piva, 2016). In addition, research has demonstrated a strong inverse correlation between LPA with sedentary time in RA (Fenton, et al., 2017) which further highlights the potential of LPA for improving health in this patient group. Specifically, increasing LPA whilst simultaneously reducing sedentary time could induce positive health outcomes relevant to this patient group.

With this in mind, interventions targeting sedentary behaviour change in RA might offer a non-pharmacological method of managing important disease outcomes. However, the low quantity and quality of previous research in this field hinders the development of such interventions. The Behavioural Epidemiology Framework (BEF) (Sallis, Owen, & Fotheringham, 2000) specifies a series of steps that are required to inform the development of evidence-based behaviour change interventions (Figure 1.1). This framework underlines the importance of validating measures to assess the behaviour in question (e.g., sedentary behaviour) and subsequently employing validated measures to; 1) establish associations between behaviour with health, and 2) identify determinants of the behaviour that can be targeted by intervention. Importantly, each stage of this framework should be addressed in the target population to optimise the potential efficacy of the resulting intervention.

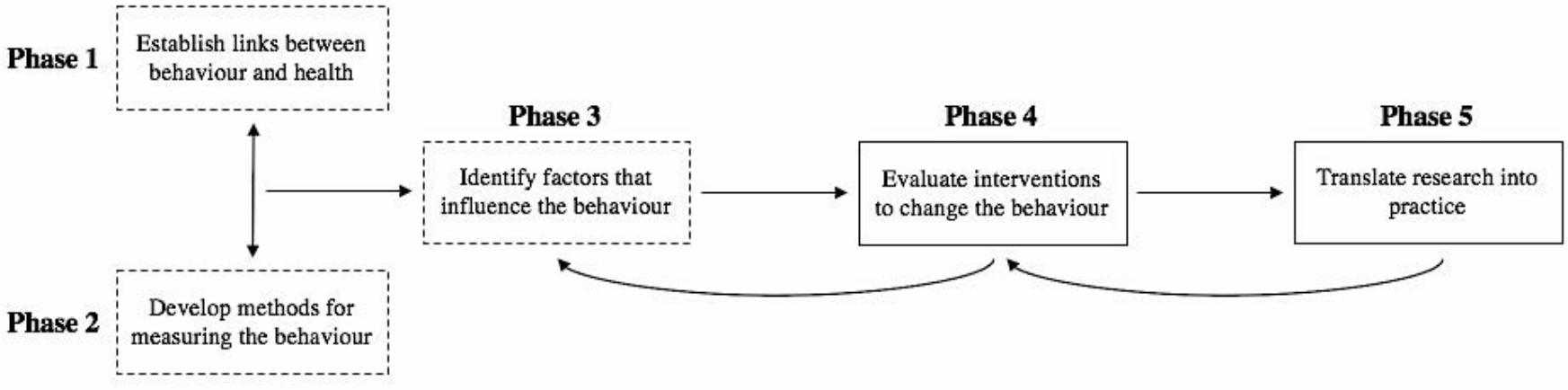

Figure 1.1 The Behavioural Epidemiology Framework (Sallis et al., 2000). The aims of the current thesis will focus on the first 3 'phases' of this framework, in order to inform 'Phase 4'.

Note: ⟷ Reciprocal link

→ Next phase

- - - - Aims of the current thesis (based on these phases)

A major limitation of RA studies seeking to establish the health consequences and determinants of sedentary behaviour and PA in these patients, is the employment of a cross-sectional design. Cross-sectional studies cannot infer cause and effect in the examined relationships. Longitudinal studies can provide insight into how change in one variable (e.g., sedentary time) relates to change in another (e.g., pain in RA) over time, and these relationships can be tested with experimental studies further down the line (Carlson & Morrison, 2009; Solem, 2015). Additionally, until recently, our understanding of the levels, health outcomes and determinants of sedentary time and PA in RA has largely been based on studies employing self-report methods to quantify engagement in these behaviours (Fenton et al., 2018b), which are limited in their validity and reliability (Atkin et al., 2012; Healy et al., 2011a; Sylvia, Bernstein, Hubbard, Keating, & Anderson, 2014). Device-based measures are being increasingly used in RA studies to objectively measure sedentary time and PA, but have not been validated specifically for use in this population. Research which validates these devices is critical in order to accurately determine levels of sedentary time and PA, and understand the relationships between health with these behaviours in RA. Additionally, it is important to establish the determinants of sedentary behaviour and PA in these patients, to develop modifiable targets for intervention.

Investigation into the determinants of sedentary behaviour has certainly not been forthcoming in RA, but studies have begun to explore the factors influencing PA in this patient group. Importantly, the debilitating features of RA disease have been suggested to be causes, as well as consequences, of sedentary behaviour and PA levels in this patient group (Thomsen et al., 2015; Veldhuijzen van Zanten et al., 2015). Nevertheless, the potential bi-directional nature of these relationships has not been tested in people with RA. Psychosocial factors (e.g., motivation) have also been suggested as determinants of PA among people with RA

(Hurkmans et al., 2010; Yu et al., 2015a), but little research exists in this domain for sedentary behaviour. In a qualitative study by Thomsen et al. (2015), participants reported that sedentary behaviour engagement was a consequence of "when symptoms dominate", such as pain and fatigue. In addition, enhancing motivation for reducing sedentary behaviour in RA patients, was suggested as a strategy to elicit sedentary behaviour change in this population.

When research questions seek to establish the modifiable determinants of sedentary behaviour and PA in people with RA, such as motivation, they should be theoretically informed (Hurkmans et al., 2010; Michie et al., 2008; Yu et al., 2015a). Self-determination theory (SDT) (Deci & Ryan, 1985) may offer a framework for understanding the motivational processes underpinning engagement in these behaviours among RA patients. SDT is a theory of motivation increasingly applied to the context of PA promotion (Teixeira, Carraca, Markland, Silva, & Ryan, 2012), and postulates that variability in the reasons 'why' individuals choose to engage in behaviour holds implications for levels of participation (Deci & Ryan, 1987, 2000, 2008a, 2008b; Ryan & Deci, 2000). This 'why' is referred to as 'quality of motivation', with more autonomous reasons for engagement (high quality, e.g., engaging in behaviour because it is personally important, or for enjoyment) being linked to higher levels of PA, with the reverse true for more controlled reasons for engagement (low quality, e.g., engaging in behaviour for others' approval, or to avoid guilt). To date, there are a couple of cross-sectional RA studies demonstrating that more autonomous motivation to engage in PA promotes higher levels of self-reported PA in these patients (Hurkmans et al., 2010; Yu et al., 2015a). Studies are yet to employ an SDT lens to explore the role of quality of motivation as a determinant of sedentary behaviour in RA.

It is clear that there is a requirement for intervention development targeting changes in sedentary behaviour and PA in people with RA, but the current state of evidence is not

sufficient to design them to high quality. With this in mind, the overarching aim of this thesis was to develop the evidence base required to inform development of interventions targeting sedentary behaviour and PA, in people living with RA. In line with the BEF, specific aims were first, to validate devices (the ActiGraph accelerometer and activPAL3$^{\mu TM}$) for measurement of sedentary time and PA among RA patients (Chapter 2). Then, in a longitudinal study, employ these devices in order to; 1) determine associations between pertinent aspects of RA health with objectively-assessed sedentary time and PA in RA – exploring the presence of bi-directional relationships (Chapter 4), and 2) investigate relationships between autonomous and controlled motivation to reduce sedentary behaviour, with objectively-assessed sedentary time and PA in RA (Chapter 5). Finally, informed by Chapters 4 and 5, to test models of sedentary behaviour change to examine sequential relationships between quality of motivation to reduce sedentary behaviour, with objectively-assessed behaviours, and in turn, important RA outcomes (Chapter 6).

Rheumatoid arthritis

Disease characteristics, prevalence and diagnosis

Rheumatoid Arthritis (RA) is a chronic autoimmune disease, characterised by elevated inflammatory load. Articular disease manifestations, resulting from high-grade inflammation, include joint pain, stiffness and swelling, musculoskeletal deterioration, and functional disability in this patient group (Smolen et al., 2016a; Uhlig et al., 2014). Further, people with RA can experience debilitating fatigue, increased risk of cardiovascular disease (CVD) and compromised psychological well-being (Avina-Zubieta et al., 2012; Katz, 2017b; Matcham et al., 2013). Most likely stemming from the physical and psychological implications of RA, unemployment is not an uncommon consequence of the disease for some patients (Berner et

al., 2018; Cross et al., 2014; Hansen et al., 2016), with over half the population leaving work within 6 years of diagnosis (NRAS, 2010).

Affecting 0.5-1% of adults worldwide, RA is particularly prevalent in individuals aged 30-50 years old, women, smokers and those with a genetic predisposition (family history) of the disease (Deane et al., 2017; Smolen et al., 2016a; Uhlig et al., 2014; Wasserman, 2018). The pathophysiology of RA is unclear, but a combination of genetic and environmental factors has been proposed to initiate chronic sequela of RA. An interplay of several cell types (e.g., fibroblast-like synoviocytes, macrophages, T lymphocytes) at the synovial membrane of the affected person's joint, is believed to cause over-expression of inflammatory biomarkers (e.g., high-sensitivity C-reactive protein [hsCRP], erythrocyte sedimentation rate [ESR]) at the site (Angelotti et al., 2017). Thus, such inflammatory biomarkers are considered in the process of clinical diagnosis, and subsequently targeted in the treatment of the disease (Demoruelle, Deane, & Holers, 2014; Shrivastava et al., 2015).

RA is clinically diagnosed according to the American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) (Aletaha et al., 2010). Specifically, a person is diagnosed with RA if they have synovitis (inflammation at the synovial membrane) in ≥1 joint, with no alternate explanation for the synovitis, and a score ≥6 (range = 1-10) based on 4 domains; 1) number and location of affected joint/s (score: 0 = 1 large joint [shoulders, elbows, hips, knees, ankles]; 1 = 2-10 large joints; 2 = 1-3 small joints [metacarpophalangeal joints, proximal interphalangeal joints, 2nd-5th metatarsophalangeal joints, thumb interphalangeal joints, wrists] with/without involvement of large joints; 3 = 4-10 small joints with/without involvement of large joints; 5 = >10 joints [can involve other joints not listed, e.g., temporomandibular] with at least 1 small joint), 2) abnormal serology results (score: 0 = negative rheumatoid factor and negative anti–citrullinated protein antibody; 2 = low-positive

rheumatoid factor or low-positive anti−citrullinated protein antibody; high-positive rheumatoid factor or high-positive anti−citrullinated protein antibody), 3) abnormal levels of CRP and ESR (score: 0 = normal CRP and normal ESR; 1 = abnormal CRP or abnormal ESR), and 4) duration of experiencing symptoms (score: 0 = <6 weeks; 1 = ≥6 weeks).

Treatment and management of rheumatoid arthritis

The treatment of RA involves tight control and close monitoring of inflammatory disease activity. Pharmacological intervention is the first-line treatment of RA, and has significantly advanced during the last 30 years (Smolen et al., 2017). Termed 'treat-to-target', therapeutic agents, such as disease-modifying anti-rheumatic drugs (DMARDs), are prescribed to RA patients as early as possible in the course of disease (Smolen et al., 2017). The aim is to regulate inflammation and in turn, attenuate the burden of pain and functional disability, as well as decreasing the risk of comorbidities, such as CVD (Ferro et al., 2017; Saag et al., 2008; Singh et al., 2016; Smolen et al., 2017; Taylor et al., 2016). RA disease activity is routinely measured in clinical practice via the extensively validated Disease Activity Score-28 (DAS-28), and is used to inform clinical decisions regarding pharmacological treatment (e.g., initiating, continuing and/or adjusting patient medication) (Prevoo et al., 1995; Smolen et al., 2016b; van Gestel, Haagsma, & van Riel, 1998; Weinblatt et al., 2006).

Rheumatoid arthritis and health

Broadly speaking, research with a focus on health in RA investigate the prevalence, aetiology and treatment of well-established patient-reported outcomes, such as pain, fatigue, physical function and psychological well-being (Boers et al., 2014; Kirwan et al., 2007; van Tuyl & Boers, 2015), which may all contribute to the individual's quality of life.

Pain. Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Merksey, Lindblom, & Mumford, 1979). Pain is the most frequently reported symptom in patients with RA, and can lead to the development of other disease outcomes, such as fatigue, quality of life and psychological well-being (Brandstetter et al., 2017; Madsen, Danneskiold-Samsoe, Stockmarr, & Bartels, 2016; Walsh & McWilliams, 2014).

Fatigue. Fatigue in RA is perceived by patients as distinct from typical experiences of tiredness, described as “exhausting”, “overwhelming”, “frustrating” and often “unpredictable” (Hewlett et al., 2005; Repping-Wuts, Uitterhoeve, van Riel, & van Achterberg, 2008). Fatigue has a debilitating impact on overall well-being and quality of life, and exacerbates challenges of managing additional RA symptoms (Katz, 2017a). After pain, fatigue is the second most commonly reported symptom among people with RA, with management of fatigue regarded by patients as paramount for remission (Katz, 2017a). It has been reported that severe fatigue affects 41% of people with RA (Overman, Kool, Da Silva, & Geenen, 2016), with multifaceted symptoms of fatigue experienced between 88%-98% of patients (Hewlett et al., 2005).

Physical function. Impaired physical function in RA comprises reversible (e.g., joint pain and swelling) and irreversible (e.g., structural joint damage and deformity) components (Aletaha, Smolen, & Ward, 2006). Reduced physical function has a profound impact on psychological well-being and quality of life in people with RA (Englbrecht, Kruckow, Araujo, Rech, & Schett, 2013; Radner, Smolen, & Aletaha, 2011; Uhlig et al., 2014; Wan et al., 2016). Physical function is assessed widely in clinical practice, using the Health Assessment Questionnaire (HAQ) (Fries, Spitz, Kraines, & Holman, 1980).

Psychological well-being. The health burden of RA often compromises a patient's psychological well-being (Gettings, 2010; Isik, Koca, Ozturk, & Mermi, 2007; Lok, Mok, Cheng, & Cheung, 2010; Matcham et al., 2013). Indeed, it has been reported that depressive symptoms, characterised by persistent low mood, and loss of pleasure and interest in activities (World Health Organisation [WHO], 2019a), may be affecting 66% of the RA population, with 17% of patients currently diagnosed with major depressive disorder (Fiest et al., 2017). RA and comorbid depression pose a significant risk in terms of mortality within this population (Margaretten, Julian, Katz, & Yelin, 2011).

Quality of life. Quality of life has been defined as "a broad ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment" (WHO, 2019b). Pain, fatigue, impaired physical function and compromised psychological well-being in RA, mean that people living with this disease typically report low quality of life (Matcham et al., 2014; Rosa-Goncalves, Bernardes, & Costa, 2018; Senra et al., 2017; Uhlig et al., 2014; Wan et al., 2016). Although both physical and mental factors comprising quality of life are adversely affected in RA, it has been reported that the physical aspects (e.g., pain, physical function) are compromised to a greater extent than mental aspects, in this patient group (Matcham et al., 2014).

The role of inflammation. The aforementioned RA disease outcomes have been associated with increased inflammation in RA, although multiple mechanisms have been proposed. Predominantly, inflammatory disease activity is reported to play a critical role in the reversible (e.g., joint pain and swelling) and irreversible (e.g., structural joint damage and deformity) RA disease manifestations that affect physical function (Hazes, 2003; Walsh &

McWilliams, 2014). The aetiology of fatigue in RA is unclear, but recent reviews in the area have alluded to a link between RA disease activity with fatigue in this patient group (Katz, 2017a, 2017b; Madsen et al., 2016). Indeed, studies have demonstrated associations between biomarkers of inflammation (e.g., CRP) and DAS-28, with fatigue in RA (Madsen et al., 2016; van Steenbergen, Tsonaka, Huizinga, Boonen, & van der Helm-van Mil, 2015). Similarly to pain, it has been accepted that the role of inflammation does not independently contribute to fatigue in these patients. For example, mediators including pain, functional disability and depression, between RA disease activity and fatigue have been demonstrated in the literature, as well as continual reporting of fatigue symptoms among patients with well-controlled RA disease activity (Druce, Jones, Macfarlane, & Basu, 2015; Olsen, Lie, Kvien, & Zangi, 2016).

It has also been hypothesised that heightened inflammation in RA is associated with depressive symptoms in this patient group (Nerurkar, Siebert, McInnes, & Cavanagh, 2019). Research has demonstrated that elevated systemic inflammatory biomarkers (e.g., CRP) are related to depression in the general population (Chamberlain et al., 2019; Strawbridge et al., 2015), and that the relationship between inflammation and depression is bi-directional (Kiecolt-Glaser, Derry, & Fagundes, 2015). A recent review published in the Lancet (Nerurkar et al., 2019) supports the contention that although pain and fatigue do have a role to play in the development of depressive symptomology, the mechanistic action of inflammatory mediators on the hypothalamic-pituitary-adrenal axis in RA, may also contribute to depression in these patients. Although prescribed medication aims to reduce the negative inflammatory effects of RA, there are 2 main challenges of relying on such medication for the simultaneous treatment of RA and depressive symptoms; 1) we do not wholly understand the link between inflammation and depression in RA, and 2) people with RA and depression demonstrate lack of compliance to prescribed medication (Margaretten et al., 2011).

Finally, recent research has shown an inverse association between disease activity and quality of life in RA, that is, lower disease activity is linked to more highly-rated quality of life (Rosa-Goncalves et al., 2018). This is unsurprising, as disease activity is well-established as a fundamental determinant of pain, fatigue, impaired physical function and compromised psychological well-being in this patient group, all of which impact quality of life (Matcham et al., 2014; Rosa-Goncalves et al., 2018; Senra et al., 2017; Uhlig et al., 2014; Wan et al., 2016).

Sometimes, the 'treat-to-target' approach via pharmacological intervention is not successful in controlling inflammatory disease activity (Taylor et al., 2016). Additionally, patients with well-controlled disease activity may still experience pain, fatigue, functional disability and compromised psychological well-being, or a bout of inflammation ('flare-up') may occur which exacerbates symptoms (Santos et al., 2019; Taylor et al., 2016). Further, these health-related factors may interact, and simultaneously contribute to the patient experience of RA (Englbrecht et al., 2013; Kojima et al., 2009; Kwan, Koh, Leong, & Wee, 2014). This, together with pharmacological treatment entailing high overall healthcare costs (advancements in medication have incurred a 300% increase in direct healthcare costs) (Chaudhari, 2008), has led to non-pharmacological intervention warranting attention (Santos et al., 2019; Taylor et al., 2016). Indeed, a combination of pharmacological (to control inflammatory disease activity) and non-pharmacological (potentially addressing more than just inflammatory disease activity, and offering RA self-management techniques) intervention, might be a sound approach to the management of RA.

Physical activity (PA) offers a non-pharmacological method of disease management and improvement in RA, and has been recently recommended for this purpose by ACR and EULAR (Rausch Osthoff et al., 2018). These are highly-regarded scientific and educational associations, providing evidence-based recommendations to be applied to clinical practice and

daily management of rheumatic and musculoskeletal diseases. Indeed, accumulating evidence underlines the benefits of PA of a moderate-to-vigorous intensity (MVPA, ≥3 metabolic equivalents [METs]) for improving RA outcomes, for example, reduced systemic inflammation and disease activity, improved functional disability, pain and fatigue, and enhanced psychological well-being (Cooney et al., 2011; de Jong et al., 2003; Loppenthin et al., 2015; Metsios & Kitas, 2018; Metsios et al., 2015; Plasqui, 2008; Rahnama & Mazloum, 2012; Rongen-van Dartel et al., 2015; Verhoeven et al., 2016). Additionally, MVPA shows potential to reduce the overall healthcare costs inherent to pharmacological RA treatment and is completely safe (Hernandez-Hernandez & Diaz-Gonzalez, 2017; Metsios & Kitas, 2018; Metsios et al., 2011). Until recently, the focus in such recommendations has been on PA, but EULAR has recently remarked on emerging evidence that sedentary behaviour is adversely associated with RA outcomes, and that there is a requirement to build upon the scarce evidence base that currently exists in this area (Agca et al., 2017; Rausch Osthoff et al., 2018). For example, sedentary behaviour has been associated with higher RA disease activity and functional disability (Fenton et al., 2018b).

Against this backdrop, the primary aim of this thesis is to investigate the correlates of sedentary behaviour in people with RA. A large body of research has examined the correlates of MVPA in this patient group, but sedentary behaviour is distinct from MVPA, and shown to have independent hazards to health in the general population (Biswas et al., 2015; Carson et al., 2014; de Rezende et al., 2014; Ford & Caspersen, 2012; Healy et al., 2011b; Rosenberg et al., 2016; Santos et al., 2012). With this in mind, MVPA will be introduced in this thesis to provide context, but sedentary behaviour will remain the central focus.

Sedentary behaviour

Sedentary behaviour has been defined as any waking behaviour characterised by energy expenditure ≤1.5 METs while in a sitting, reclining, or lying posture (SBRN, 2012; Tremblay et al., 2017) (Figure 1.2). There exists a wealth of opportunities for sedentary behaviour across life domains (e.g., travelling in a vehicle, working at a computer, watching television, reading a book) (Ainsworth et al., 2011), and technological innovation has facilitated increased sedentary behaviour in recent decades (Bailey, 2017).

A common error previously made in this field, is the incorrect inference of sedentariness from physical inactivity. Sedentary behaviour and physical inactivity are distinct behaviours, with the latter defined as insufficient purposeful participation in MVPA (van der Ploeg & Hillsdon, 2017). Indeed, an individual can be classed as both sedentary *and* physically inactive, sedentary *and* physically active, or non-sedentary *and* physically inactive (Owen, Sparling, Healy, Dunstan, & Matthews, 2010; van der Ploeg & Hillsdon, 2017). For example, an individual who spends the majority of their day sitting, and who also fails to meet recommended guidelines for participation in MVPA (150min/week in MPA or 75min/week in VPA) (Chief Medical Officer [CMO], 2019), would be classed as <u>sedentary and physically inactive</u>. In contrast, a person would be considered <u>sedentary and physically active</u> where sitting constitutes a large part of their day, but they still manage to meet recommended guidelines for participation in MVPA. Alternatively, by failing to engage in recommended levels of MVPA, but spending time in light-intensity PA (LPA), an individual can be classed as <u>non-sedentary and physically inactive</u>. This revised line of thinking has led to researchers investigating the independent and simultaneous contributions of different behavioural components across the entire movement continuum (Figure 1.2), to health in different populations.

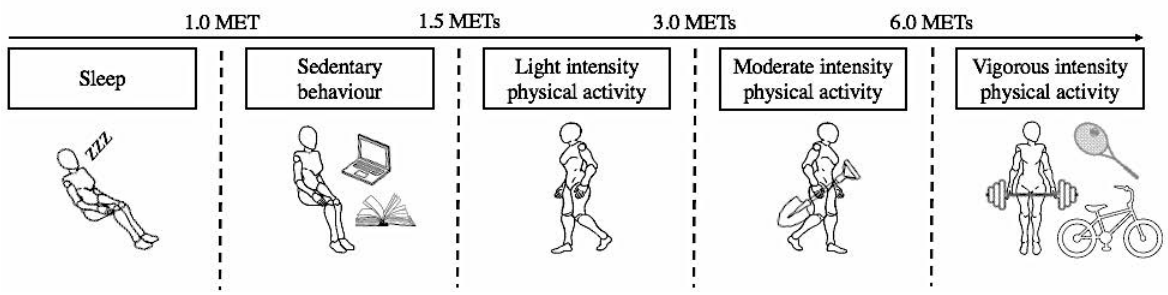

Figure 1.2 The movement continuum – energy requirements of sleep, sedentary behaviour, light-intensity physical activity, moderate-intensity physical activity and vigorous-intensity physical activity.

Sedentary behaviour and health

The problem of sedentariness is receiving increased attention due to high prevalence of this behaviour among youth, adults and older adults, coupled with growing evidence for the role of sedentary time in the development of poor health. For example, epidemiological research indicates that adolescents accumulate 6h/day of accelerometer-assessed sedentary time, and sedentary time estimates increase with age (Collings et al., 2014). For adults, the National Health and Nutrition Examination Survey (NHANES) (Healy et al., 2011b) indicated that sedentary time represents around 50-60% of waking hours when measured with accelerometry. Still, older adults (≥60 years old) represent the most sedentary age group, with sedentary time estimates of approximately 9h/day (Harvey, Chastin, & Skelton, 2015).

Research examining the health consequences of sedentary behaviour has mostly been conducted among adults. Recent findings have indicated associations between increased sedentary time with heightened mortality and morbidity, and that these are independent from the accrual of MVPA participation (Biswas et al., 2015). In this regard, sedentary time has been consistently linked with increased inflammation in clinical and non-clinical populations, and it has been proposed that this may represent a mechanism through which sedentary behaviour leads to greater risk of poor health (Carson et al., 2014; Carter, Hartman, Holder, Thijssen, &

Hopkins, 2017; Falconer et al., 2014; Ford & Caspersen, 2012; Healy et al., 2011b; Henson et al., 2013). Indeed, prospective studies have demonstrated high levels of sedentary time to associate with worsened cardiometabolic health, of which heightened systemic inflammation is an established factor (Biswas et al., 2015; Carson et al., 2014; Fitzgerald et al., 2015; Hamilton, Hamilton, & Zderic, 2014). Further, a recent systematic review and dose-response meta-analysis have reported that total sitting time and television viewing time, were associated with greater risk of several major chronic disease outcomes, including all-cause, CVD and cancer mortality, as well as incident diabetes (Patterson et al., 2018).

Sedentary behaviour has also been deemed hazardous for health in older adults, of whom exhibit similar levels of accelerometer-assessed sedentary time to people with RA. Indeed, it has been reported that RA patients spend approximately 9h/day engaged in sedentary behaviour (Fenton et al., 2018b). Interestingly, numerous studies with older adults have demonstrated links between sedentary time with deleterious health consequences very relevant to disease outcomes experienced by RA patients. For example, sedentary time accumulated by older adults has been associated with poorer cardiometabolic health, increased pain and fatigue, and reduced physical function, depression and all-cause mortality, often independent from MVPA participation (Balboa-Castillo, Leon-Munoz, Graciani, Rodriguez-Artalejo, & Guallar-Castillon, 2011; de Rezende et al., 2014; Dogra & Stathokostas, 2012; Okely et al., 2019; Park, Thogersen-Ntoumani, Veldhuijzen van Zanten, & Ntoumanis, 2018; Rosenberg et al., 2016; Santos et al., 2012; Sardinha, Santos, Silva, Baptista, & Owen, 2015; Seguin et al., 2012; van der Berg et al., 2014).

A more recent review to that of Biswas et al. (2015), showed that mortality risk resulting from sedentarity, decreased in physically active individuals (Ekelund et al., 2016). Specifically, Ekelund and colleagues (2016) indicated that 60-75min/day of MVPA is the optimal target to

diminish this deleterious consequence associated with sedentary time. However, achieving this quantity of daily MVPA might be challenging, particularly in populations with reduced physical function (e.g., RA). Certainly, people with RA typically do not achieve recommended levels of MVPA per week (Tierney et al., 2012). This is both unfortunate and concerning, considering the large body of research promoting MVPA for improving important RA outcomes.

It has been proposed that RA symptomology, including pain, fatigue and disability, contribute to the perception among RA patients that MVPA is unachievable, resulting in low participation (Larkin et al., 2017; Tan et al., 2019; Veldhuijzen van Zanten et al., 2015). Indeed, in their systematic review, Veldhuijzen van Zanten and colleagues (2015) found that several quantitative and qualitative studies reported “pain”, “fatigue”, “mobility” and “stiffness” as key RA-specific barriers to PA and exercise. In a recent qualitative study, barriers to PA was an emerging theme among RA patients (Larkin et al., 2017). Consistent with findings by Veldhuijzen van Zanten et al. (2015), a participant explained, “you could be on top of the mountain, feeling just wonderful and then you know you’d get sick and you’ve such a setback, you’re back down at the bottom again”, and another reported, “sometimes the pain is so bad you just don’t know you know and I’m just thinking how the hell am I going to get upstairs today”. An additional theme emerging from this study was “limits and pacing”, whereby participants recognised their limits when it came to engaging in PA. This has led to research exploring the potential of LPA participation for improving health in RA (Fenton et al., 2018c; Khoja et al., 2016).

Cross-sectional studies have demonstrated associations between LPA with improved disease activity, physical function and psychological well-being in people with RA (Fenton et al., 2018c; Khoja et al., 2016). In addition, LPA demonstrates a strong inverse correlation with

sedentary time in people with RA (Fenton et al., 2017), and therefore demonstrates greater potential than MVPA for replacing sedentary time in day-to-day life (Paul et al., 2014). Further, LPA engagement might be viewed as more feasible for these patients (Manns et al., 2012). Research examining associations between LPA and health have been conducted in populations with reduced mobility, including older adults (Buman et al., 2010; Ekwall et al., 2009), people with osteoarthritis (White, Lee, Song, Chang, & Dunlop, 2017) and individuals who have suffered from a stroke or spinal cord injury (Manns et al., 2012). Such studies list benefits LPA pose to health in these populations (e.g., better physical function and quality of life) but do not recommend excluding MVPA participation from daily activity. Rather, LPA is viewed a 'stepping stone' to improved health and perhaps, future participation in higher-intensity PA.

Promoting MVPA participation is an unsuccessful intervention strategy to reduce sedentary time (Martin et al., 2015; Prince, Saunders, Gresty, & Reid, 2014). With this in mind, interventions targeting sedentary behaviour change in RA might focus on increasing LPA, offering a non-pharmacological method of managing important disease outcomes. However, the low quantity and quality of previous research in this field hinders the development of such interventions. Thus, more high-quality research should be conducted to ascertain relationships between sedentary behaviour, LPA and health in RA.

Measurement of free-living sedentary behaviour and physical activity

Studies examining relationships between sedentary behaviour and PA with health outcomes in different populations, rely on accurate measurement of these behaviours. The implications of unreliable and invalid measurement of these behaviours are concerning, particularly when confirming population prevalence of these behaviours, the dose-response relationships between behaviour and health, and the efficacy of behaviour change interventions, that guide policy. The sections that follow will provide a description and critical

evaluation of common measures employed to quantify these behaviours, outlining their employment in RA studies to provide evidence for the link between sedentary behaviour, LPA and health, to date.

Current measurement techniques that attempt to assess sedentary behaviour and PA are split broadly into self-report measures and objective measures. Self-report methods encompass questionnaires (e.g., International Physical Activity Questionnaire [IPAQ]) (Craig et al., 2003) and diaries (e.g., Bouchard Physical Activity Record) (Bouchard et al., 1983). Questionnaires, such as the IPAQ, are the most frequently-employed measure of sedentary behaviour and PA in large-scale epidemiological and observational studies, due to ease of application, relatively low cost and low burden on participants (Atkin et al., 2012; Healy et al., 2011a; Sylvia et al., 2014). Device-based measures being increasingly employed to objectively quantify habitual levels of time spent sedentary and in PA in the general population, include accelerometers (e.g., ActiGraph accelerometer [ActiGraph, LLC., Pensacola, Florida, USA]) and posture sensors (e.g., activPAL™ [PAL Technologies Ltd., Glasgow, UK]) (Atkin et al., 2012; Edwardson et al., 2017; Healy et al., 2011a; Sylvia et al., 2014; Wijndaele et al., 2015). Accelerometers are typically small and lightweight, and afford the ability to continuously monitor free-living sedentary time and PA (Atkin et al., 2012; Healy et al., 2011a; Sylvia et al., 2014). The activPAL™ is also small and lightweight, capable of quantifying free-living sitting/lying (sedentary), standing and stepping time (Edwardson et al., 2017). Consequently, accelerometers and the activPAL™ have been administered in large-scale studies for surveillance of time spent sedentary and in PA in various countries, including the UK (e.g., UK Biobank, 1970 British Birth Cohort), USA (e.g., NHANES, Woman's Health Study), Canada (e.g., Canadian Health Measures Survey) and Australia (e.g., AusDiab) (Colley et al.,

2011; Dall et al., 2018; Doherty et al., 2017; Healy et al., 2011b; Healy et al., 2008; Lee & Shiroma, 2014; Troiano et al., 2008; Troiano, McClain, Brychta, & Chen, 2014).

The decision to employ self-report and/or device-based measures to assess free-living sedentariness and PA in a population of interest, must be informed by a number of factors. First, prior to employing certain methods to measure behaviour, the specific characteristics of the behaviour should be considered. Indeed, sedentary behaviour, by definition, has 2 fundamental components; 1) waking activity requiring ≤1.5 METs, and 2) activity undertaken in a sitting/reclining/lying posture (SBRN, 2012; Tremblay et al., 2017). Thus, sedentary behaviour research methodology should employ measures which accurately assess both energy expenditure *and* posture. Further, it is essential that measures accurately capture the energy requirements of behaviour to quantify PA intensity.

Second, the manner in which sedentary behaviour is accumulated throughout the day holds variable implications for health. Specifically, longer sedentary bouts (the duration of uninterrupted sedentary time) and less sedentary breaks (the frequency of interruptions in sedentary time) have been associated with negative health outcomes in clinical and non-clinical populations (de Rezende et al., 2014; Healy et al., 2011b). Measures of sedentariness should therefore enable accurate assessment of these patterns.

Third, an understanding of the context of sedentary behaviour and PA is important to assist in developing more targeted interventions (Kim & Welk, 2015a). For example, one domain of sedentary behaviour may hold worse implications for health compared to another (e.g., sitting, watching television vs. sitting, reading) (Hallgren et al., 2019; Hallgren et al., 2018). Additionally, work-based interventions targeting reductions in sedentary time might not be appropriate for those in the teaching profession, but perhaps more suited to employees working at a computer for most of the day (Thivel et al., 2018).

Correspondingly, principles representing the multifaceted components of sedentary behaviour and PA relevant for health, have been proposed. Following suit from the reputable 'FITT' acronym (Montoye, 2000), which relates to the multidimensional nature of PA, the 'SITT' acronym (Tremblay, Colley, Saunders, Healy, & Owen, 2010) has been developed for sedentary behaviour. 'SITT' informs the researcher of the various characteristics that should be considered when measuring sedentary behaviour.

Components of sedentary behaviour – SITT:

- S = sedentary behaviour frequency (number of sedentary bouts of a certain duration)
- I = interruptions (number of sedentary breaks during sedentary time)
- T = time (duration of sedentary behaviour)
- T = type (context of sedentary behaviour)

Presently, no single measurement tool exists that fulfils the aforementioned criteria in its entirety. Certainly, self-report (e.g., questionnaires and diaries) and device-based assessments (e.g., accelerometers and posture sensors) attempt to capture free-living sedentary behaviour, but only measure the 'SITT' principles in part. Questionnaires and diaries typically attempt to gauge the duration of engagement in sedentary behaviour ($_{SI}T_{T}$)[1]. Self-report diaries also offer a measure of the context in which these behaviours occurred ($_{SIT}T$). However, these measures fail to capture sedentary bouts (S_{ITT}) and breaks ($_{S}I_{TT}$).

[1] This is termed 'sedentary time'. *Sedentary time* refers to the sum of all sedentary behaviours that are undertaken throughout the course of a day. For example, time spent travelling to work by car, sitting working at an office desk, and watching television during leisure time all represent different sedentary behaviours, but accumulate to contribute towards 'total sedentary time' (O'Brien, Duda, Kitas, & Fenton, 2018).

Device-based measures seemingly address more 'SITT' principles compared to self-report (SIT_T), but cannot capture the context of sedentary behaviour ($_{SIT}T$). Accelerometers and posture sensors afford the ability to continuously assess behaviour throughout the day, in order that estimates of free-living sedentary time ($_{SI}T_T$), as well as sedentary bouts (S_{ITT}) and sedentary breaks ($_SI_{TT}$), can be determined. Further, sleep and sedentariness can be distinguished by applying suitable research-informed analytical procedures to these data, allowing inclusion of solely waking behaviour in subsequent analysis.

Self-report and device-based measurement methods succumb to several limitations, which are unique from one another, relating to validity and reliability when attempting to capture sedentary behaviour (and PA).

Self-report measures. Self-report measures are subject to social desirability bias and inaccuracies in participant recall, and require a certain level of cognitive ability which may pose a challenge to populations such as older adults (Atkin et al., 2012; Cleland, Ferguson, Ellis, & Hunter, 2018; Healy, et al., 2011a; Seymour et al., 2001; Sylvia et al., 2014). Furthermore, questionnaires that seek to capture sedentary behaviour are usually adapted from instruments designed to assess PA, or include a single item to assess sedentary time, and demonstrate poor accuracy (Dall et al., 2017).

In addition, the validity of questionnaire measures is typically based on the strength of an association (via correlation or regression analysis) between self-reported PA and sedentary behaviour with a measure entailing superior validity (e.g., accelerometry), when it is the *agreement* between these measures that provides greater insight into their accuracy (Bland & Altman, 1986). Indeed, recent studies in adults have sought to assess the agreement between questionnaire-based assessments of PA and sedentary time against accelerometers and posture sensors, respectively (Chastin et al., 2018; Wanner et al., 2016). For example, Chastin et al.

(2018) evaluated the agreement between 18 self-report measures of sedentary time vs. the activPAL™ (gold standard measure of free-living sedentary time). Bland-Altman plots showed large mean differences (ranging from approximately 8h/day underestimation to 4h/day overestimation), and wide 95% limits of agreement (LOA [ranging from approximately 10h/day to 17h/day]), between measures of self-reported sedentary time vs. activPAL™-assessed sedentary time.

Additionally, Wanner et al. (2016) used Bland-Altman analysis to determine the agreement between the IPAQ vs. a widely-employed accelerometer (ActiGraph GT3X) for measurement of PA in an adult population. Resulting Bland-Altman plots demonstrated a large mean difference (approximately 13h/week) and wide 95% LOA, approximately = -38h/week – 11h/week, between these measures of MVPA. In this instance, most data points were below zero, representing overestimation of MVPA when using the IPAQ vs. accelerometry to measure this behaviour.

Objective measures. Device-based measures offer a more objective approach to measurement of sedentary time and PA and therefore address several of the limitations posed by self-report (Atkin et al., 2012; Janz, 2006). Still, despite overcoming some shortcomings of self-report measures, research employing device-based measures of sedentary time and PA encounter challenges distinct from questionnaire- and diary-based methods. For example, the accompanying costs associated with purchasing the device can be high, and their means of attachment can often lead to low compliance (e.g., accelerometers worn on the hip) (Edwardson et al., 2017; Matthews, Hagstromer, Pober, & Bowles, 2012). Further, data reduction can be time-consuming for the researcher, and may result in data loss due to participant non-compliance (Edwardson et al., 2017; Matthews et al., 2012). Indeed, device wear criteria chosen by the researcher may discount participants from subsequent statistical analysis and

could introduce selection bias (Matthews et al., 2012). Finally, widely-used data reduction techniques (e.g., researcher-selected device wear criteria and accelerometer cut-points) for obtaining estimates of PA and sedentary time might not be generalisable to all populations (Pedisic & Bauman, 2015). Thus, more validation studies are required to ascertain the accuracy of these measures in different populations and establish population-specific analytical procedures to apply during data reduction.

With this in mind, it might be appropriate for research to employ *both* self-report and device-based measures of sedentary behaviour (and PA), in order to optimally capture free-living behaviour (Bann et al., 2015; Rosenberg et al., 2016). Importantly, the researcher should consider if the measure being deliberated, has been validated for use in the population of interest. Certainly, different populations (e.g., RA adults vs. non-RA adults) are likely to have varying perceptions, physiological requirements and activity patterns. Thus, a 'one size fits all' approach to measurement of free-living behaviour might lead to inaccurate estimates of sedentary time and PA (Aguilar-Farias, Brown, & Peeters, 2014; Copeland & Esliger, 2009; Fenton et al., 2018b; Kowalski, Rhodes, Naylor, Tuokko, & MacDonald, 2012; Santos-Lozano et al., 2013).

In the following section, current measures used to capture engagement in sedentary behaviour and PA among people with RA will be described, and the advantages and disadvantages of each measure in this specific population will be discussed.

Measurement of free-living sedentary behaviour and physical activity in rheumatoid arthritis

To date, self-report measures, such as the IPAQ, are common place in research measuring habitual PA and sedentary behaviour in people living with RA, but have been criticised due to the tendency of patients to over-report levels of PA and under-report levels of

sedentary behaviour when using these methods (Yu et al., 2015b). Indeed, Yu et al. (2015b) used Bland-Altman analysis to compare the agreement between IPAQ-assessed vs. accelerometer-assessed PA and sedentary time in people with RA. Consistent with studies in adults (Chastin et al., 2018; Wanner et al., 2016) and other populations with reduced physical function, for example older adults (Ryan et al., 2018) and patients with lower back pain (Schaller, Rudolf, Dejonghe, Grieben, & Froboese, 2016), the authors discovered that patients overestimated MPA and underestimated sedentary time when responding to a questionnaire (IPAQ), compared to the criterion of accelerometry (ActiGraph GT3X). Specifically, the mean differences between IPAQ-assessed vs. accelerometer-assessed MPA and sedentary time were approximately 1h/day and 10h/day, with data points positioned mostly below zero (representing overestimation) and above zero (representing underestimation), respectively.

As such, researchers would not be well-informed to select self-report measures for quantitative measurement of sedentary time and PA in studies with RA patients. Albeit the advantages of some self-report measures to provide contextual information regarding specific sedentary behaviours and PA settings, estimates of these behaviours should be determined using instruments that assess them more objectively in this patient group (Fenton et al., 2018b; Yu et al., 2015b). There now exists significant opportunity to employ device-based monitoring to the surveillance of sedentary time and PA in the RA population (Semanik et al., 2010). The following sections outline 2 such devices, the ActiGraph accelerometer and activPAL™, validated and subsequently employed in this thesis for measurement of these behaviours in RA.

ActiGraph accelerometer. The ActiGraph accelerometer is the most frequently employed accelerometer in field-based research (Duncan et al., 2018). The triaxial ActiGraph accelerometer (e.g., GT3X+) is typically worn on the right hip (Figure 1.3) and is a valid and reliable measure of sedentary time and PA in adults (Aadland & Ylvisaker, 2015; Santos-

Lozano et al., 2013). This device can capture human movement (accelerations) on the vertical (Y), horizontal right-left (X) and horizontal front-back (Z) axes, which can be used to determine the vector magnitude of these accelerations (vector magnitude [VM] = $\sqrt{(axisY^2 + axisX^2 + axisZ^2)}$). Accelerations are recorded over user-defined time intervals (epochs), which are converted by the manufacturer's software (Actilife) into 'activity counts'.

During 'accelerometer data reduction' (Masse et al., 2005), using Actilife, the researcher applies non-wear criteria to accelerometer data, coined as the "structural foundation in the data reduction process" (Semanik et al., 2010). Non-wear criteria determine the participant is not wearing the device, when a pre-determined (by the researcher) duration of consecutive '0' activity counts is reached. This aims to distinguish between non-wear and sedentary time, which can also be characterised by consecutive '0' activity counts (e.g., sedentary time = <100 counts/min). The researcher then decides how many valid hours constitute a 'valid day', and how many valid days comprise a 'valid week'. This determines whether the participant has worn the device for a sufficient period of time, and will be included in subsequent analysis. These decisions should be based on previous research demonstrating the optimal non-wear criteria for a specific population to gain the most accurate estimates of free-living behaviour. Seminak and colleagues (2010) supported the use of non-wear criteria = ≥60 min or ≥90 min of consecutive '0' counts, worn ≥10 h/day to constitute a valid day in people with RA. Typically in accelerometry studies with adults, ≥4 valid days/week, inclusive of ≥1 weekend day, comprise a valid week (Troiano et al., 2008). These criteria have been applied in previous RA studies (Fenton et al., 2017; Fenton et al., 2018b; Yu et al., 2015b).

Based on valid participant data, researcher-developed algorithms (referred to as 'cut-points') are applied to the accelerometer activity counts, in order to quantify time spent in different intensities of activity (sedentary behaviour, LPA, MPA and VPA). The most common

accelerometer cut-point employed to assess sedentary time is <100 counts/min (Gorman et al., 2014). This is a uniaxial (Y-axis) cut-point, which originates from a validation study of the ActiGraph accelerometer, conducted among adolescent girls (Treuth et al., 2004). Following publication, the <100 counts/min accelerometer cut-point was subsequently employed in the NHANES to estimate population prevalence of sedentary time among American adults (Matthews et al., 2008). In conjunction, uniaxial accelerometer cut-points were employed to the NHANES data to estimate the frequency and duration of LPA and MVPA (LPA, 100-2019 counts/min; MVPA, ≥2020 counts/min) among this cohort. These PA cut-points were defined by Troiano et al. (2008), on the basis of weighted averages of criteria from 4 calibration studies (Brage, Wedderkopp, Franks, Andersen, & Froberg, 2003; Freedson, Melanson, & Sirard, 1998; Leenders, Sherman, Nagaraja, & Kien, 2001; Yngve, Nilsson, Sjostrom, & Ekelund, 2003), and have since been frequently employed in studies of sedentariness and PA in RA (Fenton et al., 2017; Fenton et al., 2018c).

However, more recently, researchers have started to move away from the assumption that 'one size fits all', and there has been an increase in the number of population-specific accelerometer cut-points developed (Aguilar-Farias et al., 2014; Copeland & Esliger, 2009; Motl, Snook, Agiovlasitis, & Suh, 2009; Nero, Benka Wallen, Franzen, Stahle, & Hagstromer, 2015; Sandroff, Riskin, Agiovlasitis, & Motl, 2014; Santos-Lozano et al., 2013). Still, researchers employing accelerometry in RA studies are heavily reliant on algorithms developed in validation studies of healthy adults (Troiano et al., 2008), since no RA-specific accelerometer cut-points have been derived. This is particularly problematic when we consider that the physiology and associated activity patterns of people living with RA are likely to differ substantially to those among 'healthy adults' in the general population (e.g., a relatively higher basal metabolic rate is characteristic of RA) (Metsios et al., 2008). As such, there is an urgent

requirement for validation studies to develop RA-specific accelerometer cut-points to permit more accurate measurement of accelerometer-assessed sedentary time and PA in RA (O'Brien et al., 2019). Further, to ensure progress in this field, it is essential that the validity of these accelerometer cut-points for the measurement of free-living behaviour is established (O'Brien et al., 2019).

Despite several advantages relative to self-report, accelerometers are limited in their ability to measure posture – an important facet of the characterisation of sedentary behaviour. That is, the established definition of sedentary behaviour stipulates a consideration of both low energy expenditure (≤1.5 METs) *and* a sitting/reclining/lying posture (SBRN, 2012; Tremblay et al., 2017). Indeed, whilst cut-points can be applied to accelerometer data to provide an (indirect) measure of energy expenditure, accelerometers are less able to detect the posture at which low-energy behaviours are undertaken (An, Kim, & Lee, 2017; Kozey-Keadle, Libertine, Lyden, Staudenmayer, & Freedson, 2011). In this way, the activPAL™ posture sensor offers an advance over accelerometers for free-living assessment of sedentary time, and is currently considered the gold standard to measure sedentary time in field-based research (Chastin & Granat, 2010; Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016).

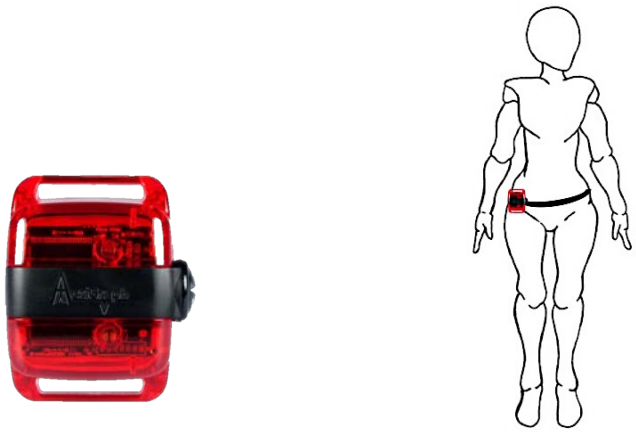

Figure 1.3 The ActiGraph GT3X+ – typical placement on the right hip of the participant

ActivPAL™ posture sensor. The activPAL™ is a small, lightweight device, typically worn attached to the front of the right thigh, in a mid-anterior position (Edwardson et al., 2017) (Figure 1.4). The activPAL™ uses proprietary algorithms to classify free-living behaviour, based on posture and acceleration, as sitting/lying (sedentary), standing and stepping over continuous 24-h time periods (Edwardson et al., 2017). The activPAL™ also attempts to monitor the number of steps and sit-stand transitions (Edwardson et al., 2017). The activPAL™ has demonstrated high validity for measurement of sedentary time in different populations when compared against the criterion of direct observation, thus is considered the gold standard measure of free-living sedentary time (Chastin & Granat, 2010; Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016). Less frequently, the activPAL™ is used to measure time spent stepping as an estimate of PA. However, the activPAL™ is limited to the extent at which these data can be accurately interpreted to determine PA intensity, which is currently estimated based on step cadence (Montoye, Pivarnik, Mudd, Biswas, & Pfeiffer, 2017; Steeves et al., 2015).

To date, only 1 study has validated the activPAL™ against direct observation in the RA population (Larkin et al., 2016). In this study, participants wore an activPAL™ whilst lying, sitting, standing, walking on a treadmill, and undertaking 10 activities of daily living (ADLs [e.g., reading a newspaper, washing and drying dishes, placing bed linens on pillows and duvet]). In analysis, *t*-tests indicated overall estimates of time spent sedentary, standing and stepping (s) from the activPAL™ vs. direct observation did not significantly differ. Linear regression also demonstrated a strong relationship between time spent sedentary (r = .74), standing (r = .86) and stepping (r = .93) derived from the activPAL™ compared to direct observation. However, Bland and Altman (1986) explained that regressions indicating the strength of a relationship does not provide scope to determine the degree of agreement between

2 methods. Indeed, it would be surprising to find non-significant comparability of methods that measure the same variables (Bland & Altman, 1986).

Lack of high quality validation studies of the activPAL™ in people with RA, coupled with the fact that this device predominantly provides a measure of sedentary time, has resulted in a small number of studies employing this device for assessment of sedentary time *and* PA in this patient group. Rather, existing RA studies have employed the activPAL™ to quantify sedentary time only (Thomsen et al., 2017). In addition, to date, most research with RA patients has been undertaken with PA as their focal point, thus have employed accelerometers for this purpose. Indeed, few studies have focused on the correlates of sedentary time in the RA population (Fenton et al., 2018b).

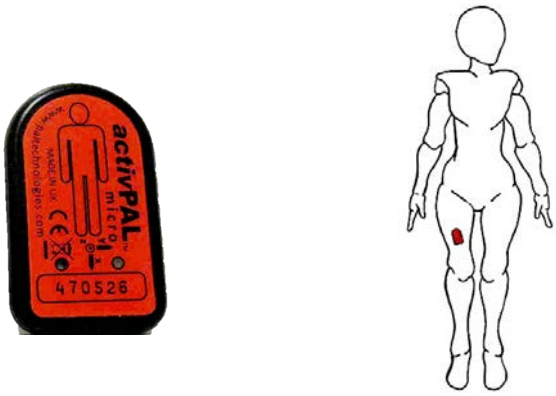

Figure 1.4 The activPAL3$^{\mu TM}$ – typical placement on the right thigh of the participant

Both the ActiGraph accelerometer and activPAL™ enable measurement of components of 'FITT' and 'SITT', but cannot capture the context of sedentary behaviour and PA. Extant studies have used a combination of objective and self-report measures of sedentariness and PA in an attempt to address this limitation (Bann et al., 2015; Rosenberg et al., 2016), but this places high burden on the participant. To date, no studies have used a combination of an accelerometer and posture sensor to simultaneously capture free-living sedentary time and PA in RA patients, which may offer the most accurate means to assess both of these behaviours.

Specifically; 1) accelerometry offers a potential 'valid' measure of LPA, MPA and VPA (where population-specific accelerometer cut-points are developed/used), but is unable to capture posture to properly assess sedentary time (An et al., 2017; Kozey-Keadle et al., 2011), and 2) the ability of the activPAL™ to ascertain the intensity of free-living behaviour is dubious, but is currently regarded as the gold standard measure of free-living sedentary time (Chastin & Granat, 2010; Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016).

It is important that levels of engagement in sedentary behaviour and PA are accurately quantified in the RA population when drawing conclusions regarding the health-related correlates of these behaviours in this patient group. Measuring both sedentariness *and* PA will lead to further knowledge regarding the associations they hold with relevant RA outcomes, such as disease activity, pain, fatigue, functional disability, psychological well-being and quality of life. Indeed, sedentariness has been shown to induce deleterious consequences to health in the general population, that are relevant to important disease features of RA (Balboa-Castillo et al., 2011; de Rezende et al., 2014; Dogra & Stathokostas, 2012; Okely et al., 2019; Park et al., 2018; Rosenberg et al., 2016; Santos et al., 2012; Sardinha et al., 2015; Seguin et al., 2012; van der Berg et al., 2014). Further, the possible links between LPA and health are particularly compelling in RA, due to the; 1) more feasible nature of LPA participation compared to MVPA in these patients (Manns et al., 2012), 2) strong likelihood that sedentary time is replaced by LPA throughout the day among people with RA (Fenton et al., 2017), and 3) demonstrated health benefits of LPA participation in other populations with reduced physical function, for example, older adults (Buman et al., 2010; Ekwall et al., 2009). Given that most research in the area is based on the wide-ranging benefits of MVPA for RA health,

there is a gap in knowledge relating to the relationships between sedentary behaviour and LPA with health outcomes in RA.

Although the methods of measuring levels of sedentary behaviour and LPA currently employed in RA studies are mixed (employing self-report and device-based measures), the following sections will present some previous research that has focused on the levels and health-related correlates of these behaviours in this patient group.

Sedentary behaviour, physical activity and health in rheumatoid arthritis

It has been reported that people with RA typically spend long periods of time engaged in sedentary behaviour, with recent accelerometry studies suggesting people with this condition can spend up to 9 waking h/day sedentary (Fenton et al., 2018b).

Research has begun to examine the implications of this behaviour for clinically- and patient-important RA outcomes, such as disease activity, pain, fatigue and physical function (Fenton et al., 2018b). Such investigations have employed either self-report or device-based methods to quantify sedentary time. The following sections describe the paucity of studies that have examined the relationships between sedentary behaviour, LPA and health, relevant to this thesis. Table 1.1 summarises these studies.

Khoja et al. (2016) designed a cross-sectional study to examine the associations between accelerometer-assessed sedentary time and LPA, with disease activity and functional disability in people with RA. The Sensewear Armband (Tierney, Fraser, Purtill, & Kennedy, 2013) was employed for measurement of sedentary time and LPA. Disease activity and functional disability were assessed with the DAS-28 and HAQ, respectively. Findings showed significant positive correlations between sedentary time with disease activity (ß = .34) and functional disability (ß = .43). Significant inverse associations were found for ‘very light-

intensity physical activity' and 'light-intensity physical activity' with disease activity (ß = -.27 and ß = -.28, respectively) and functional disability (ß = -.28 and ß = -.26, respectively).

There were some important limitations emerging from the study by Khoja and colleagues (2016). First, sedentariness was incorrectly defined as behaviour expending energy ≤1 MET, instead of ≤1.5 METs (SBRN, 2012; Tremblay et al., 2017). Second, the authors divided LPA into 2 separate behaviours, 'very light-intensity physical activity' (1.1-1.9 METs) and 'light-intensity physical activity' (2.0-2.9 METs), inconsistent with the widely-accepted characterisation of LPA as activities requiring energy expenditure between 1.6-2.9 METs (Norton, Norton, & Sadgrove, 2010). Thus, these imprecisions would have led to the authors erroneously classifying sedentary time as 'very light-intensity physical activity'. This, together with the cross-sectional design of this study, does not provide strong evidence for an association between sedentary time and LPA, with RA disease activity and functional disability. Therefore, findings should be interpreted with caution.

More recently, Summers, Booth, Brooke-Wavell, Barami and Clemes (2019) conducted a cross-sectional study to determine whether the degree of active disease in females with RA was associated with levels of ActiGraph GT3X+-assessed sedentary time, LPA and MVPA. DAS-28 was employed to classify participants as having low disease activity (DAS-28 ≤3.2) or moderate to high disease activity (DAS-28 >3.2). Summers and colleagues (2019) reported significant differences between both groups of RA patients, in terms of sedentary time and LPA. Specifically, those with low disease activity spent 10% less time engaged in sedentary behaviour and 18% more time in LPA, than patients with moderate to high disease activity. Interestingly, the proportion of sedentary time and LPA in the RA groups did not differ from a group of 'healthy controls'. However, both groups of RA patients spent 40% less time

engaged in MVPA compared to the control group. The cross-sectional design of this study reduces its quality, but it does give scope for future prospective research in this area.

In another cross-sectional study (Greene et al., 2006), participants with RA responded to a single-item on the Physical Activity and Disability Survey (PADS), reading, “On average, how many hours per day are you sitting or lying down, not counting when you sleep at night?”, in order to assess their sedentary time. Findings demonstrated positive associations between sedentary time with functional disability (ß = .28), measured by the HAQ. However, the single item in the PADS has not been validated to measure sedentary time in these patients, and may have resulted in inaccurate estimates of this behaviour (Dall et al., 2017).

Giles, Bartlett, Andersen, Fontaine and Bathon (2008) also used a cross-sectional study design, demonstrating that increased self-reported television viewing time was related to increased HAQ-assessed functional disability, in people with RA. Television viewing has been used in other RA studies as an indicator of sedentary time (Kramer, Fontaine, Bathon, & Giles, 2012), which is problematic when we consider that not all sedentary behaviours occur in this context. Thus, the quality of such studies are reduced when the selected measure fails to encapsulate the entirety of behaviour.

Fenton et al. (2018c) investigated the sequential cross-sectional associations between lower-limb functional disability (to ‘rise’ and ‘walk’) measured by the HAQ, ActiGraph GT3X-assessed LPA and psychological well-being in people with RA. Interestingly, no significant association was present between lower-limb functional disability with LPA, which builds on popular opinion that this intensity of PA might be more realistic to achieve for this patient group (Manns et al., 2012). Additional findings from the aforementioned study (Fenton et al., 2018c) revealed a significant, positive association between ActiGraph GT3X-assessed LPA with subjective vitality (ß = .27), and a significant, negative association with depressive

symptoms (ß = -.29), measured by the Subjective Vitality Scale (SVS) (Ryan & Frederick, 1997) and Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983), respectively. As such, this study generated the first evidence for the potential of LPA to improve subjective vitality and depressive symptoms, in people with RA. However, this study had a small sample size (n = 50), and only included only patients with low to moderate functional disability, meaning these findings cannot be generalised to patients with high-level functional disability.

Building on evidence from their own cross-sectional study, a longitudinal study by Prioreschi, Hodkinson, Tikly and McVeigh (2014) sought to examine the relationships between accelerometer-assessed sedentary behaviour and PA with health outcomes in RA, following DMARD treatment. Findings demonstrated a significant positive relationship between sedentary behaviour, with duration of early morning stiffness (ß = .69) in RA. Further, the authors described that with a reduction in sedentary behaviour, there was an increase in LPA. This suggested that, following DMARD treatment, sedentary time was being replaced by LPA rather than MVPA. Despite its longitudinal design, there were some limitations to this study. First, the Actical accelerometer was employed to measure sedentary behaviour, LPA, MPA and VPA, but only daily average activity counts within each 'threshold' were derived for subsequent analysis. This does not give full insight into the specific duration (e.g., mins/day) of free-living sedentary behaviour and PA. Second, although early morning stiffness is an important indicator of disease activity in this patient group, the DAS-28 offers a more comprehensive evaluation of RA disease activity. Finally, the small sample size (n = 18) and mostly 'obese' participants in this longitudinal study, limits the extent to which these results can be generalised to the wider RA population.

A randomised controlled trial has recently been conducted to test the effectiveness of a behaviour change intervention (motivational counselling and SMS reminders) to, primarily,

reduce sedentary time in people with RA (Thomsen et al., 2017). Of secondary interest in this study were RA disease outcomes, including self-reported pain (measured via visual analogue scale [VAS]), fatigue (measured via VAS and the Multidimensional Fatigue Inventory [MFI]) (Smets, Garssen, Bonke, & De Haes, 1995), functional disability (measured via the HAQ) and quality of life (measured via the 36-item Short Form Survey Instrument-Physical and Mental Component Scale) (Alonso et al., 2004). Findings demonstrated reductions in activPAL™-assessed sedentary time for patients enrolled into the intervention group vs. control group. Secondary findings revealed improvements in self-reported pain, fatigue, functional disability and quality of life alongside these reductions in activPAL™-assessed sedentary time, for patients from the intervention group vs. control group.

A strength to the study by Thomsen et al. (2017) was its randomised controlled design. However, arguably, this trial is seemingly premature in testing the efficacy of an intervention for reducing sedentary time in RA. Indeed, although research in this domain has *alluded* to links between sedentary time and RA health, these findings are still in their infancy and have been criticised for their quality. Typically, the rationale for conducting such an intervention study would rely on a solid evidence base that establishes the links between behaviour and health, as outlined by Sallis et al. (2000) in their Behavioural Epidemiology Framework (BEF [Figure 1.1]). Further, to our knowledge, there have been no studies to date that have explored the determinants of engagement in sedentary behaviour among people with RA, vital for establishing modifiable intervention targets. This point is again, outlined by Sallis and colleagues (2000) in the BEF.

Table 1.1 Overview of previous studies examining links between RA health and free-living sedentary behaviour and light-intensity physical activity

Study	Sample size (n)	Measure of free-living behaviour	Measure of health outcomes	Limitations of previous studies addressed by this thesis	How does this thesis address limitations of previous studies in the area?
Khoja et al. (2016)	98	*Objective* Sensewear Armband	*Disease activity:* DAS-28 *Physical function:* HAQ	Cross-sectional design Incorrect definition of sedentary behaviour (≤1 MET) and LPA (1.1-2.9 METs)	Longitudinal design Correct definition of sedentary behaviour (≤1.5 METs) and LPA (1.6-2.9 METs)
Summers et al. (2019)	71	*Objective* ActiGraph GT3X+	*Disease activity:* DAS-28	Cross-sectional design Female participants only ActiGraph GT3X+ - Cannot capture posture of free-living behaviour - Non-RA accelerometer cut-points	Longitudinal design Female and male participants recruited ActiGraph GT3X+ and activPAL (validated in RA) employed for measurement of free-living behaviour
Greene et al. (2006)	72	*Self-report* Physical Activity and Disability Survey	*Physical function:* HAQ	Cross-sectional design Self-report measure of behaviour - Single item – not accurate - Included OA patients in 'RA group'	Longitudinal design ActiGraph GT3X+ and activPAL (validated in RA) employed to objectively measure free-living behaviour
Giles et al. (2008)	197	*Self-report* Television viewing time	*Physical function:* HAQ	Cross-sectional design Self-report measure of behaviour -Television viewing – only measures time spent in one context of sedentary behaviour	Longitudinal design ActiGraph GT3X+ and activPAL (validated in RA) employed to objectively measure free-living behaviour
Fenton et al. (2018)	50	*Objective* ActiGraph GT3X	*Physical function:* HAQ *Depressive symptoms:* HADS *Subjective vitality:* SVS	Cross-sectional Small sample ActiGraph GT3X - Cannot capture posture of free-living behaviour - Non-RA accelerometer cut-points	Longitudinal design Larger cross-sectional sample ActiGraph GT3X+ and activPAL (validated in RA) employed to objectively measure free-living behaviour
Prioreschi et al. (2014)	18	*Objective* Actical	*Duration of early morning stiffness*	Small sample Actical - Device not validated for use in RA - Activity counts as a measure of free-living behaviour	Larger sample for longitudinal study than n = 18 ActiGraph GT3X+ and activPAL (validated in RA) employed to objectively measure free-living behaviour
Thomsen et al. (2017)	150	*Objective* ActivPAL	*Pain and fatigue:* VAS *Fatigue:* MFI *Physical function:* HAQ *Quality of life:* SF36	Intervention based on small evidence in this population Measurement of pain only captured using the VAS	Based on 'Phase 1' of BEF – building on scarce evidence base Validated questionnaires to measure pain, plus a wider range of RA health outcomes

DAS-28, Disease Activity Score-28; HAQ, Health Assessment Questionnaire; HADS, Hospital Anxiety and Depression Scale; SVS, Subjective Vitality Scale; VAS, visual analogue scale; SF36, 36-item Short Form Survey; MET, metabolic equivalent; LPA, light-intensity physical activity; RA, Rheumatoid Arthritis; OA, Osteoarthritis; BEF, Behavioural Epidemiology Framework

Contribution of this thesis

In a recent review, Fenton et al. (2018b) identified a paucity of high-quality research investigating associations between sedentary behaviour with pertinent aspects of health in RA. The authors strongly recommended that research adopt a "more rigorous approach" concerning the methodology employed, to ensure progress in this field. In addition, the potential of LPA for improving health has sparked interest, particularly among research focused on populations with reduced physical function which may prevent them from meeting recommended MVPA guidelines (Manns et al., 2012). Again, there is not enough high-quality research available to confirm whether partaking in LPA is sufficient to yield the same health benefits posed by MVPA participation in RA.

The BEF (Sallis et al., 2000) is a useful tool when gauging research progression in a particular field, setting out several 'phases' to facilitate identification of knowledge gaps that are critical to address prior to the development, delivery and evaluation of interventions to improve health in specific populations. Following these steps in the target population, ensures that resulting interventions are based on rigorous evidence and consider the unique characteristic of each population, and therefore have greater potential to be effective at promoting behaviour change.

The following sections will outline the 'phases' of the BEF specified by Sallis et al. (2000), and detail how these have formed the basis for Chapters 2-4 in the current thesis. 'Phase 1' and 'Phase 2' of this framework are reciprocally linked (Figure 1.5), and for the purposes of this thesis, are reverse-ordered. Specifically, the study comprising Chapter 2 is a validation of device-based measures of sedentary time and PA in RA, in order to 'develop methods for measuring the behaviour' ('Phase 2'). These validated measures of sedentary time and PA are then employed (general methodology – Chapter 3) in the longitudinal study comprising

Chapter 4, to establish relationships between RA health outcomes with sedentary time and PA ('Phase 1 – Establish links between behaviour and health').

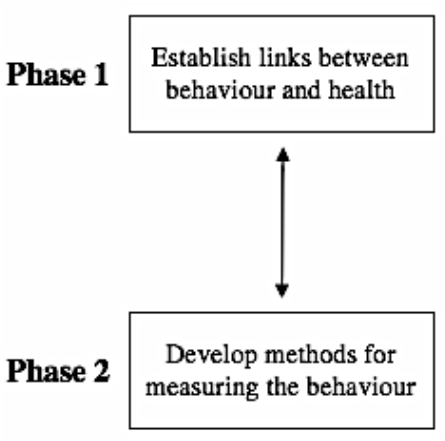

Figure 1.5 The reciprocal link between 'Phase 1' and 'Phase 2' of the Behavioural Epidemiology Framework (Sallis et al., 2000), informing Chapters 2-4 of this thesis.

'Phase 1 – Establish links between behaviour and health'. Primarily, studies should identify and record the health-related correlates of behaviour in specific populations, to emphasise the importance of future intervention and thus justify progression to the next phases (e.g., 'Phase 3 – Identify factors that influence the behaviour'). That is, 'Phase 1' establishes if there is a link between the target behaviour (e.g., sedentarity) and health (e.g., RA outcomes), leading to insight regarding whether changing behaviour is associated with change in health.

How does this thesis address 'Phase 1' of the Behavioural Epidemiology Framework? Chapter 1 of this thesis has provided an overview of previous research that has investigated associations between sedentary behaviour, PA and health in RA. Notably, there are substantially less studies examining the links between sedentary behaviour and LPA, compared with MVPA, with health in people with RA. Further, a number of studies examining the health-related correlates of sedentary behaviour and LPA are cross-sectional. Indeed, only 2 studies (1 x longitudinal and 1 x randomised controlled trial) have employed non-cross-sectional

designs for examining associations between sedentariness and LPA, with pertinent health outcomes in people with RA (Prioreschi et al., 2014; Thomsen et al., 2017). To their detriment, cross-sectional studies only provide a 'snapshot' of information (extracted from a single moment in time) and therefore offer no information relating to an individual's longer-term health and behaviour (Carlson & Morrison, 2009; Solem, 2015). Consequently, cross-sectional studies fail to offer insight into whether factors such as pain, fatigue, functional disability, quality of life and psychological well-being in RA, are causes or consequences of these behaviours, or both. Indeed, the potential bi-directional nature of these relationships has not been tested in people with RA. Although, it has been suggested that cross-sectional studies should first establish, 'quickly and easily', whether associations exist between the variables of interest (e.g., RA health with sedentary time), prior to conducting longitudinal studies (Carlson & Morrison, 2009; Caruana, Roman, Hernández-Sánchez, & Solli, 2015; Solem, 2015). Then, by gathering data beyond one moment in time, longitudinal studies offer more insight into change in one variable 'predicting' change in another variable (Carlson & Morrison, 2009; Solem, 2015).

As such, Chapter 4 of this thesis provides the first longitudinal evidence regarding associations between change in health with change in objectively-assessed sedentary time and PA, in people with RA. In addition, the presence of significant bi-directional associations in these longitudinal relationships was investigated, providing important insight into the potential causes ('predictors') *and* consequences ('outcomes') of sedentary time and PA, related to relevant aspects of RA health.

'Phase 2 – Develop methods for measuring the behaviour'. The accurate measurement of behaviour (e.g., sedentary time and PA) is crucial for inclusion in all studies that aim to establish links between these behaviours and other factors (e.g., health,

hypothesised determinants) in certain populations. Existing or new measures of behaviour should be validated for use in the population of interest.

How does this thesis address 'Phase 2' of the Behavioural Epidemiology Framework? Chapter 1 of this thesis has also outlined and critically analysed current measurement techniques utilised in previous RA studies to assess free-living sedentary behaviour and PA. Several studies have relied on self-report measures of sedentary behaviour and PA in RA. Lately, device-based measures (e.g., accelerometers and posture sensors), enabling more objective assessment of these behaviours, are becoming increasingly employed as the 'measure of choice' in this patient group (Fenton et al., 2018b; Semanik et al., 2010). Indeed, the validity and reliability of objective measures exceed that of self-report (Healy et al., 2011a; Sylvia et al., 2014). However, there is a severe lack of evidence validating device-based measures for objectively quantifying sedentary time and PA specifically in RA, limiting their application in this patient group (O'Brien et al., 2019).

Subsequently, Chapter 2 of this thesis comprehensively validated the ActiGraph accelerometer and activPAL3$^{\mu TM}$ for the objective measurement of sedentary time and PA in RA (O'Brien et al., 2019). Primarily, in the laboratory, the ActiGraph GT3X+ was calibrated against indirect calorimetry to develop the first RA-specific triaxial (VM) accelerometer cut-points for measurement of sedentary time, LPA and MPA. The activPAL3$^{\mu TM}$ was also validated in the laboratory, assessing its accuracy against direct observation for measurement of sedentary, standing and stepping time. Then, using these data, agreement between GT3X+-assessed and activPAL3$^{\mu TM}$-assessed free-living sedentary time was evaluated, employing both the novel RA-specific cut-point and the widely-used non-RA (<100 counts/min) cut-point (Troiano et al., 2008). Finally, within-person estimates of sedentary time, LPA and MPA,

quantified using RA-specific cut-points vs. the widely-used non-RA cut-points, were compared.

The validation study comprising Chapter 2, is a vital step forward in sedentary behaviour and PA research in RA, furthering knowledge regarding options for accurately measuring these behaviours in this patient group. Indeed, findings confirmed validity of the activPAL3$^{\mu TM}$ as the gold standard measure of free-living sedentary time in RA, and established the superior validity of the newly-developed RA-specific sedentary time cut-point vs. the widely-used non-RA sedentary time cut-point in this patient group. Additionally, the RA-specific cut-points were sensitive and specific for measuring sedentary time, LPA and MPA in RA. These devices were therefore subsequently employed to assess sedentary time and PA in the longitudinal study of this thesis (Chapters 4-6). The background relevant to Chapters 5 and 6 will be described in the following sections.

The determinants of sedentary behaviour and physical activity in rheumatoid arthritis

Interventions seeking to promote sedentary behaviour change (e.g., reducing sedentary time, increasing LPA) should target factors that influence these behaviours (determinants). The determinants of sedentary behaviour and LPA in RA could include both debilitating features of the disease (e.g., pain, fatigue, functional disability) (Thomsen et al., 2015; Veldhuijzen van Zanten et al., 2015) as well as psychosocial factors (e.g., motivation, self-efficacy) (Hurkmans et al., 2010; Yu et al., 2015a).

Chapter 4 of this thesis examines the former, testing whether aspects of health in RA (e.g., pain, fatigue, functional disability) are ‘predictors’ of levels of sedentary time and LPA in this patient group, as well as ‘outcomes’. If the relationships between RA health with sedentary time and LPA emerge as bi-directional, then it would follow that levels of

engagement in sedentary time and LPA may represent a consequence *and* cause of variability in health states among people with RA. In the instance that reciprocal relationships between sedentary time and LPA with RA features are observed in RA, it holds that interventions to reduce sedentary time (and promote LPA) may have the potential to improve health outcomes in these patients.

Intervening to promote sedentary behaviour change in RA is likely to be a challenging undertaking, but might be achieved if an understanding of patient *motivation* to engage in the target behaviour (e.g., sedentary behaviour, LPA) is gained. Indeed, in their critical overview of existing health-related behaviour change policies and practices, Kelly and Barker (2016) concluded that "a careful, thoughtful science that leads to a deep understanding of the nature of what motivates people", is fundamental to the development and implementation of interventions targeting health-related behaviours (e.g., sedentary behaviour). The authors also insist that this "academic" approach to behaviour change addresses the misassumption that simply providing an individual with information (verbally or written) regarding the health consequences of the target behaviour, is sufficient to promote sustained behaviour change. With this in mind, research questions exploring motivation for sedentary behaviour change in this patient group should be theoretically informed (Hurkmans et al., 2010; Michie et al., 2008; Yu et al., 2015a). Indeed, research grounded in psychological theory facilitates understanding of the psychological processes hypothesised to underlie behaviour change.

In the context of PA, several theories underpinning human motivation have guided research seeking to further knowledge and understanding regarding the motivational processes underlying PA behaviour change. For example, social cognitive theory (Bandura, 1986), theory of planned behaviour (Ajzen, 1985), achievement goal theory (Nicholls, 1989) and self-determination theory (SDT) (Deci & Ryan, 1985), have all been employed to study the role of

motivation in promoting PA behaviour change. Social cognitive theory considers that 3 interacting factors, including personal (e.g., expectations), environmental (e.g., social norms) and behavioural (e.g., self-efficacy), lead to engaging in the target behaviour (Bandura, 1986). Theory of planned behaviour postulates that an individual's intentions drive behaviour, stemming from attitude towards a target behaviour, subjective norms surrounding the target behaviour and perceptions that the target behaviour can be adopted with the available resources and opportunities (perceived behavioural control, e.g., self-efficacy) (Ajzen, 1985). Achievement goal theory posits that an individual can evaluate their competence in particular behavioural settings (e.g., engaging in PA) based on self-referencing (e.g., personal interest, effort, improvement) and normative-referencing (perception of the ability of others). The former orientation is considered as more desirable, and associated with better outcomes regarding behaviour engagement (Nicholls, 1989).

Arguably, SDT provides a more comprehensive model of the motivational processes underpinning human behaviour, compared with other theories of motivation. Certainly, SDT does not just focus on the *magnitude* (quantity) of motivation as other theories do, but posits that the *type* and *orientation* (quality) of 'why' a person chooses to engage (or disengage) in a behaviour, also holds important implications for levels of engagement (Deci & Ryan, 1987, 2000, 2008a, 2008b; Ryan & Deci, 2000). Specifically, central to SDT is that an individual's motivation may vary in its degree of relative autonomy, with more autonomous reasons for engagement (e.g., behaviour is enjoyable and personally important) linked to an increased likelihood of adopting and persisting with a behaviour (e.g., reducing sedentary time and increasing LPA). In contrast, more controlled reasons for participation (e.g., other people's approval, feeling guilty) are linked to a lesser chance of sustaining behaviour (Deci & Ryan, 1987, 2000, 2008a, 2008b; Ryan & Deci, 2000). The following sections provide an overview

of SDT, and introduces extant research that has employed SDT to understand the motivational processes underpinning change in sedentary behaviour and PA.

Self-determination theory

The development of SDT by renowned researchers, Edward L. Deci and Richard M. Ryan, commenced approximately 50 years ago (Deci & Ryan, 2008b). In 1985, 'Intrinsic Motivation and Self-Determination in Human Behaviour' (Deci & Ryan, 1985) was published to provide the first comprehensive overview of SDT, and its applications and implications in the real world. Since then, this theory of motivation has expanded and been cited widely in research seeking to understand the multitude of processes underpinning the adoption and adherence of behaviour, including in the context of PA (Deci & Ryan, 1987, 2000, 2008a, 2008b; Ryan & Deci, 2000).

According to Ryan and Deci (2000), "motivation produces". That is, motivation is a highly valued determinant of behaviour in research, scoping from healthcare to sports coaching, hypothesised by SDT to vary in both quantity *and* quality. As such, the degree of motivation ('what'), as well as the *variability* in the reasons attributed to engagement in behaviour ('why?'), has an impact on whether an individual initially takes up a behaviour, and subsequently continues to engage in the behaviour long-term (Deci & Ryan, 2000). Importantly, the quality of an individual's motivation is more highly-regarded as a predictor of long-term behaviour and important outcomes (e.g., psychological well-being) than the amount (quantity) of motivation an individual possesses (Deci & Ryan, 2008a, 2008b).

SDT posits that behavioural engagement can be regulated by more self-determined (originating from within self) or externally derived reasons. Specifically, SDT positions 6 different 'qualities' of motivation regulation on a continuum (Figure 1.6), ranging from 'non-regulation' (non-self-determined) to 'intrinsic regulation' (self-determined) (Ryan & Deci,

2000). Organismic integration theory (Deci & Ryan, 1985), a sub-theory of SDT, postulates that ‘extrinsic motivation’ (behaviour motivated by external forces or regulations) convenes between the extreme constructs of ‘amotivation’ (entirely lacking volition or desire to engage in behaviour) and ‘intrinsic motivation’ (behaviour motivated by internal reasons, motivation is completely from the self). Amotivation, comprised of ‘non-regulation’, is characterised by indifference and apathy towards behaviour. Extrinsic motivation encompasses ‘external regulation’, ‘introjected regulation’, ‘identified regulation’ and ‘integrated regulation’, becoming increasingly more self-determined from first listed, to last.

Sources of external regulation to engage in behaviour include extrinsic monetary reward or pressure from others. Introjected regulation occurs when behaviour is controlled by ‘intrapersonal’ factors, such as to avoid feelings of guilt, or to retain pride. Identified regulation is viewed as relatively more self-determined than the former, with reasons for the adoption and maintenance of behaviour attributed to the identification of personally valued benefits of engagement. Similarly, integrated regulation for behaviour occurs when identified regulations for behaviour emanate wholly from the self and correspond to the individual’s ambitions and principles. Finally, intrinsic motivation, encapsulating ‘intrinsic regulation’, has been advocated as exclusively, the construct representing “the positive potential of human nature”, where an individual purposely seeks out behaviour due to the enjoyment and challenges it presents (Ryan & Deci, 2000).

Behaviour	Non-self-determined					Self-determined
Type of motivation	Amotivation	Extrinsic motivation				Intrinsic motivation
Type of regulation	Non-regulation	External regulation	Introjected regulation	Identified regulation	Integrated regulation	Intrinsic regulation

Figure 1.6 The self-determination continuum (Deci & Ryan, 2000)

Identified, integrated and intrinsic regulation, and external and introjected regulation, represent internal and external loci of causality, respectively. Combining these regulations to result in composite constructs, is a frequent occurrence in SDT-based research seeking to examine relationships between more autonomous vs. more controlled motivation regulations for behaviour, with health behaviours (e.g., PA). Specifically, identified, integrated and intrinsic regulation are combined to form '*autonomous motivation*'[2], and external and introjected regulation are combined to form '*controlled motivation*' (Deci & Ryan, 2008a, 2008b). Therefore, behaviour driven by autonomous motivation is characterised by personal choice and volition, and aligns completely with the individual's personal values (Deci & Ryan, 2008a, 2008b). Contrastingly, behaviour determined by controlled motivation is associated with extrinsic rewards and pressure, as well as to avoid guilt or for pride (Deci & Ryan, 2008a, 2008b). It has been postulated that autonomous motivation links to more adaptive outcomes (e.g., adoption and maintenance of the target behaviour) and more controlled motivation relates to lack of uptake and non-adherence (Deci & Ryan, 2008a, 2008b).

[2] Integrated regulation was not assessed as part of this thesis, as this construct has not been shown to a great degree, as independent from identified regulation (Lonsdale, Hodge, & Rose, 2008). In addition, the Behavioural Regulation in Exercise Questionnaire-2 (Markland & Tobin, 2004), employed in this thesis does not encompass integrated regulation in its calculation of autonomous motivation. Thus, identified regulation and intrinsic motivation were joined to compute autonomous motivation in this thesis.

Self-determination theory – sedentary behaviour and physical activity research

SDT has provided a theoretical framework in previous research that attempts to understand the role of quality of motivation in the adoption and maintenance of PA among non-clinical and clinical populations (Duda et al., 2014; Fasczewski, Gill, & Rothberger, 2018; Fortier, Duda, Guerin, & Teixeira, 2012; Milne, Wallman, Guilfoyle, Gordon, & Corneya, 2008; Teixeira et al., 2012), including RA (Fenton et al., 2018c; Hurkmans et al., 2010; Yu et al., 2015a).

Research conducted by Hurkmans et al. (2010), was the first study to examine the role of autonomous and controlled motivation as determinants of PA in a large sample of RA patients. Findings revealed that higher autonomous regulation style in these individuals was related to higher levels of self-reported PA (ß = .33). However, this study had limitations. First, it employed a cross-sectional design and therefore only provided a 'snapshot' of patients' quality of motivation and PA levels at one moment in time, which may not be fully representative. Further, cross-sectional studies do not provide any insight into causality, and must be followed up with more rigorous study designs (longitudinal and experimental studies). Second, the Short Questionnaire to Assess Health-Enhancing Physical Activity (Wendel-Vos, Schuit, Saris, & Kromhout, 2003) assessed PA, which potentially succumbed to the disadvantages of self-report (e.g., social desirability bias, inaccurate participant recall).

Extending this initial study by Hurkmans et al. (2010), Yu et al. (2015a) investigated autonomous regulation for engagement in PA, with levels of self-reported PA and subjective vitality among people with RA. Autonomous motivation was measured employing the Behavioural Regulation in Exercise Questionnaire-2 (BREQ-2) (Markland & Tobin, 2004), levels of PA were self-reported using the Godin-Shepard Leisure Time Physical Activity Questionnaire (Godin & Shephard, 1985) and subjective vitality was captured via the SVS.

Structural equation modelling in this study revealed that autonomous motivation to engage in PA was positively associated with PA (ß = .30) and subjective vitality (ß = .40). Similarly to the study by Hurkmans et al. (2010), this study had a large sample size, but employed a cross-sectional design and self-reported measures of PA.

Few studies have used an SDT perspective to assess quality of motivation in the context of sedentary behaviour, with extant research taking place in non-RA groups (Babic et al., 2016; De Cocker, De Bourdeaudhuij, Cardon, & Vandelanotte, 2015; Quartiroli & Maeda, 2014; Smith et al., 2017). A cross-sectional study by Quartiroli and Maeda (2014) used an SDT lens to examine the associations between quality of motivation to engage in PA (using the BREQ-2) with self-reported sedentary time (employing the IPAQ), in individuals aged between 17-30 years old. Intrinsic and identified regulations for PA were negatively linked with self-reported sedentary time (ρ = -.11 and ρ = -.07, respectively), however, again, the cross-sectional nature of this study reduces the extent to which we can understand any causal associations. In addition, sedentary time was self-reported using a single item included in the IPAQ, reducing the accuracy of sedentary time estimates (Dall et al., 2017). Finally, the BREQ-2 was not adapted to measure quality of motivation to reduce sedentary behaviour, retaining its original form which assesses quality of motivation to engage in PA. Given that sedentary behaviour is a distinct construct from PA, potentially entailing different motives for engagement, such questionnaires should be adapted to assess specifically, quality of motivation to engage/disengage in sedentary behaviour. For example, the Motivation to Limit Screen-time Questionnaire developed in adolescents (Lubans et al., 2013).

Against this backdrop, Chapter 5 of this thesis builds on Chapter 4, to examine the role of autonomous and controlled motivation to reduce sedentary behaviour in RA, through

examining longitudinal associations with objectively-assessed sedentary time and LPA in these patients.

Contribution of this thesis

Following 'Phase 1' and 'Phase 2' of the BEF (Sallis et al., 2000), 'Phase 3' informed Chapter 5 and 6 of this thesis (Figure 1.7).

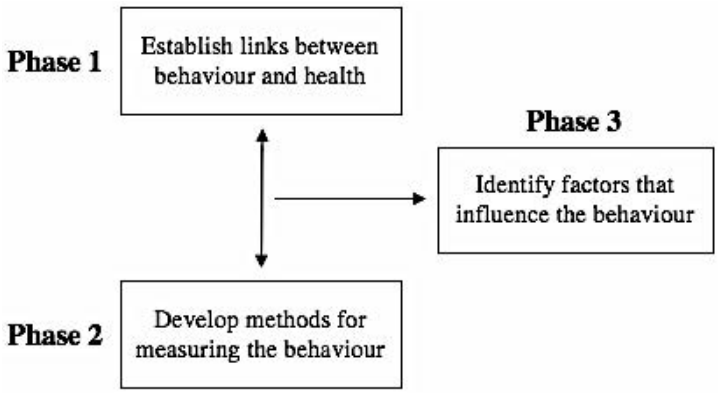

Figure 1.7 'Phase 1', 'Phase 2' and 'Phase 3' of the Behavioural Epidemiology Framework (Sallis et al., 2000), informing Chapters 2-6 of this thesis.

'Phase 3 – Identify factors that influence the behaviour'. The relationships between hypothesised determinants of behaviour (e.g., quality of motivation to reduce sedentary behaviour) and behaviour (e.g., sedentary time) should be analysed using validated measures, informed by theories of behaviour change (e.g., SDT). This investigation will then establish modifiable targets for intervention.

How does this thesis address 'Phase 3' of the Behavioural Epidemiology Framework? Identifying the modifiable determinants of sedentary time and LPA in RA, is essential in order to design interventions that have the potential to support people with RA to reduce their sedentary time (e.g., by increasing LPA). In the sections above, the relevance of SDT as a framework to identify malleable psychosocial correlates of sedentary time and PA in different

populations, including RA, has been outlined (Hurkmans et al., 2010; Quartiroli & Maeda, 2014; Yu et al., 2015a). Thus, the longitudinal study comprising Chapters 5 and 6 of this thesis is grounded in SDT, and extends findings from previous RA studies, to examine how quality of motivation to reduce sedentary behaviour may influence levels of objectively-assessed sedentary time in this patient group. Specifically, Chapter 5 presents new evidence regarding longitudinal relationships between change in autonomous and controlled motivation to reduce sedentary behaviour, using the BREQ-2 (adapted for measuring quality of motivation to reduce sedentary behaviour), with change in objectively-assessed sedentary time and LPA, in RA. Chapter 6 of this thesis builds on Chapter 5, and brings in information from Chapter 4, to test models of sedentary behaviour change and pertinent aspects of RA health, using an SDT perspective. Specifically, Chapter 6 examines how the quality of motivation to reduce sedentary behaviour possessed by an individual with RA, relates to their engagement in sedentary time and LPA, and in turn, holds implications for variability in RA health. Device-based measures of sedentary time and PA validated in Chapter 2 of this thesis, were employed in the longitudinal studies comprising Chapter 5 and 6. Akin to our overarching hypothesis that interventions to reduce sedentary time (and increase LPA) may be relevant in RA, health variables demonstrating bi-directional associations with sedentary time and LPA in Chapter 4 of this thesis (emerging as 'predictors' *and* 'outcomes' of sedentary time and LPA), were stipulated as 'outcomes' in Chapter 6, testing models of sedentary behaviour change.

Thesis aims

This thesis investigates the health-related and psychosocial correlates of objectively-assessed sedentary time and LPA in people with RA. Chapter 2 validates 2 device-based measures of sedentary time and PA, which are subsequently employed in the longitudinal studies comprising Chapters 4-6. The study in Chapter 4 specifically examines bi-directional

relationships between pertinent aspects of health in RA, with objectively-assessed sedentary time and LPA in these patients. Then, grounded in SDT, Chapter 5 studies the associations between autonomous and controlled motivation to reduce sedentary behaviour with objectively-assessed sedentary time and LPA in RA. Finally, Chapter 6 persists with an SDT perspective to test models of sedentary behaviour change, which hypothesise sequential relationships between autonomous and controlled motivation to reduce sedentary behaviour with objectively-assessed sedentary time and LPA (specifically, standing), and in turn, health outcomes in RA. The aims of this thesis are:

Aim 1: Validation of device-based assessments of sedentary time and PA in RA **(Chapter 2). a)** To develop RA-specific triaxial accelerometer cut-points (criterion standard = indirect calorimetry) for sedentary time, LPA and MPA measurement. Also, to validate the activPAL3$^{\mu TM}$ (criterion standard = direct observation) for measurement of sedentary, standing and stepping time *(laboratory validation)*. Then, using these data; **b)** to compare the validity of the new RA-specific triaxial sedentary time accelerometer cut-point vs. the widely-used non-RA uniaxial sedentary time accelerometer cut-point (<100 counts/min) for measurement of free-living sedentary time in RA, against the gold standard (activPAL3$^{\mu TM}$). To also compare within-person estimates of free-living sedentary time, LPA and MPA, quantified using the new RA-specific triaxial accelerometer cut-points vs. widely-used non-RA uniaxial accelerometer cut-points *(field validation).*

Aim 2: To assess longitudinal associations between pertinent aspects of RA health with objectively-assessed sedentary time and PA in RA, and investigate if these associations may be bi-directional **(Chapters 4 and 6).**

Aim 3: Using an SDT lens, to assess longitudinal associations between quality of motivation to reduce sedentary behaviour with objectively-assessed sedentary time and PA in RA **(Chapters 5 and 6).**

Aim 4. Informed by Chapters 4 and 5, to examine sequential associations between quality of motivation to reduce sedentary behaviour with objectively-assessed sedentary time and PA, and in turn, RA outcomes **(Chapter 6).**

Overview of participants recruited to all studies of this thesis

All data analysed in this thesis originated from 1 sample of n = 104 RA patients, recruited from Russells Hall Hospital, Dudley. All participants recruited underwent the methodology outlined in Chapter 3 of this thesis. In addition, n = 22 of these participants gave their consent to participate in an 'additional' laboratory validation study, comprising Chapter 2 of this thesis. Figure 1.8 illustrates how the data collected by employing these 2 protocols were used to answer the questions posed by this thesis.

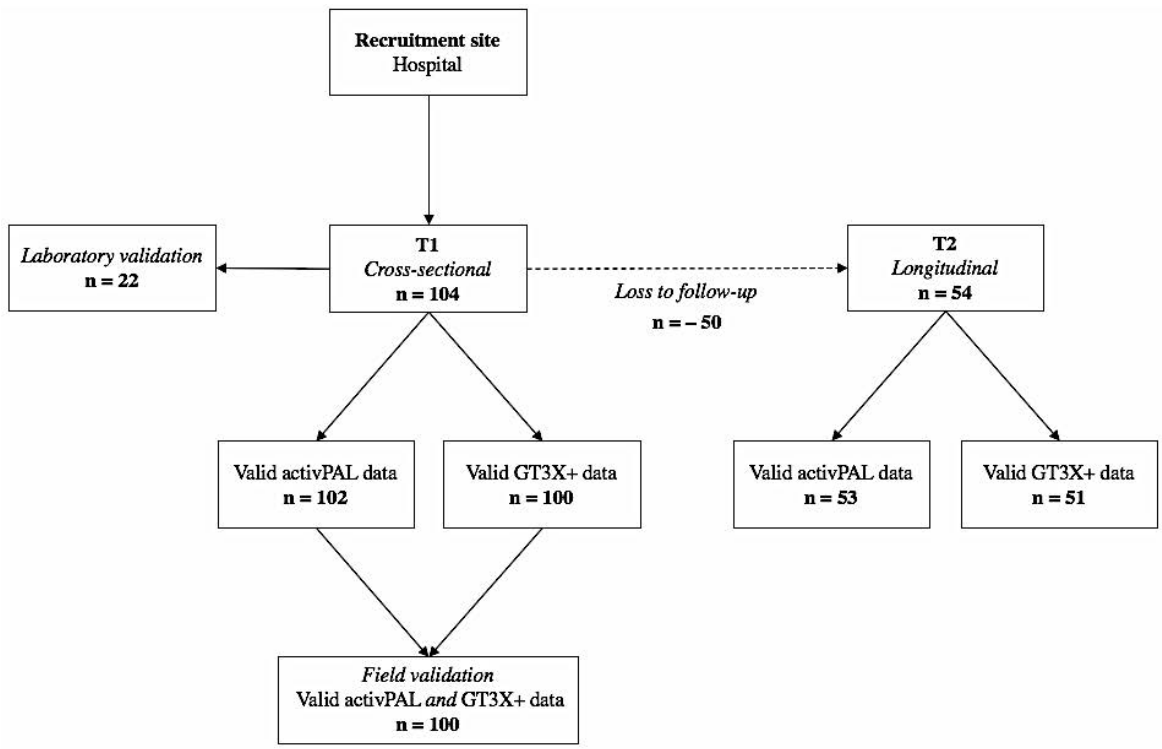

Figure 1.8 Overview of participants recruited to all studies comprising chapters of this thesis. T1, Time Point 1; T2, Time Point 2; n, number of participants

Note: ⟶ Participants recruited from the same hospital in Dudley, England

- - - - - - ▸ 6-month period between T1 and T2 (no intervention)

Loss to follow-up, due to: planed termination of data collection (n = 47), lack of time (n = 3)

CHAPTER 2

OBJECTIVE MEASUREMENT OF SEDENTARY TIME AND PHYSICAL ACTIVITY IN PEOPLE WITH RHEUMATOID ARTHRITIS: AN ACCELEROMETER AND ACTIVPAL™ VALIDATION STUDY

This manuscript is 'under review' in *Arthritis & Rheumatology*

The protocol for this study has been published in *Mediterranean Journal of Rheumatology*

Abstract

Aim: The accurate measurement of sedentary time and physical activity (PA) is essential to establish relationships between these behaviours with pertinent Rheumatoid Arthritis (RA) outcomes. A laboratory-based and free-living protocol was conducted to determine: 1a) RA-specific triaxial accelerometer cut-points for sedentary time, light-intensity PA (LPA) and moderate-intensity PA (MPA) (*criterion*, indirect calorimetry); 1b) validity of the activPAL3$^{\mu TM}$ for measurement of sedentary, standing and stepping time (*criterion*, direct observation); 2) accuracy of the (new) RA-specific vs. non-RA cut-points for measuring free-living sedentary time (*criterion*, activPAL3$^{\mu TM}$). **Methods:** *Laboratory-based:* RA patients (n = 22) were fitted with a GT3X+ accelerometer, activPAL3$^{\mu TM}$ posture sensor and indirect calorimeter. Whilst video-recorded, participants undertook 11 activities representing different intensities. *Field-based:* RA patients (n = 100) wore a GT3X+ and activPAL3$^{\mu TM}$ for 7 days. **Results:** *Laboratory-based:* ROC curve generated RA-specific cut-points (counts/min) were: sedentary time = ≤244; LPA = 245–2501; MPA = ≥2502. Bland-Altman plots revealed good agreement between activPAL3$^{\mu TM}$-assessed vs. directly observed behaviours (mins). 95% limits of agreement (LOA [lower–upper]) = 0.1–0.2 sedentary; -0.7–1.1 standing; -1.2–0.6 stepping. *Field-based:* Bland-Altman plots showed narrower 95% LOA for sedentary time (min/day) estimated by the RA-specific cut-point (≤244 counts/min = -42.6–318.0) vs. the non-RA cut-point (<100 counts/min = -19.6–432.0), compared to the activPAL3$^{\mu TM}$. **Conclusion:** The activPAL3$^{\mu TM}$ is a valid measure of sedentary time in RA. Novel RA-specific accelerometer cut-points were sensitive and specific for measuring sedentary time, LPA and MPA in these patients, and demonstrated superior agreement with the activPAL3$^{\mu TM}$ for measurement of sedentary time, compared to the non-RA cut-point.

Introduction

Research evidence supports the benefits of physical activity (PA) for improving health-related outcomes among people with Rheumatoid Arthritis (RA). More recently, studies also suggest sedentary behaviour (waking behaviour ≤1.5 metabolic equivalents (METs), whilst in a sitting/reclining/lying posture) (SBRN, 2012; Tremblay et al., 2017) is adversely associated with RA outcomes (Fenton et al., 2018b). However, most evidence regarding the role of both sedentary time and PA in RA is based on studies employing self-report methods to quantify engagement in these behaviours (Fenton et al., 2018b; Verhoeven et al., 2016).

Device-based assessments of sedentary time and PA offer a more objective measure of behaviour, and have demonstrated superior validity and reliability relative to self-report instruments (Atkin et al., 2012; Chastin et al., 2018; Edwardson et al., 2017; Healy et al., 2011a; Sylvia et al., 2014). Consequently, such devices are being more readily used to measure sedentary time and PA in different populations, including in RA (Fenton et al., 2018b; Semanik et al., 2010). Currently, accelerometers (e.g., ActiGraph [ActiGraph, LLC., Pensacola, Florida, USA]) are the most commonly-employed device in RA studies, owing to their ability to estimate the frequency, intensity and duration of free-living behaviour. The accelerometer generates sedentary time and PA estimates based on the number of accelerations (‘activity counts’) accumulated, via application of researcher-selected ‘accelerometer cut-points’. These cut-points specify whether the activity undertaken is sedentary, or PA of a light (LPA), moderate (MPA) or vigorous (VPA) intensity. However, whilst the advantages of accelerometry to measure sedentary time and PA are being increasingly recognised by RA researchers, several limitations exist regarding their application in this patient group.

First, few accelerometers have been specifically validated in people with RA. Consequently, existing RA studies employing accelerometers have relied upon validation

studies conducted among non-RA populations, to inform their analytical approach. For example, RA studies to date have largely employed uniaxial (Y-axis) accelerometer cut-points (Matthews et al., 2008; Troiano et al., 2008) developed in validation studies of healthy participants, to quantify sedentary time and PA among people with RA. Consequently, the validity of extant sedentary time and PA estimates may be affected and should be interpreted with caution, as RA patients differ markedly to people without RA in terms of their physiology, physical function and associated activity patterns. For example, RA patients demand a relatively higher basal metabolic rate compared to the general population (Metsios et al., 2008), underlying the limitation of applying accelerometer cut-points developed based on the energy requirements of behaviours in non-RA populations. Also important to highlight, is that commonly-employed cut-points are typically uniaxial, and generate sedentary time and PA estimates using data captured by a single axis (Y-axis) of movement. Technological advancements are such that triaxial accelerometers are now common place, and are able to capture data across the Y-axis (vertical), X-axis (horizontal right-left) and Z-axis (horizontal front-back), to provide a more valid assessment of behaviour (Choi, Ward, Schnelle, & Buchowski, 2012; Evenson et al., 2015). Thus, it is critical that RA-specific triaxial accelerometer cut-points are developed and validated for measurement of sedentary time and PA in RA.

Still, a key limitation of accelerometers is their inability to characterise posture – a key characteristic of sedentary behaviour (SBRN, 2012; Tremblay et al., 2017). Specifically, accelerometers work on the basis that all movements registered below a 'sedentary time cut-point' are by default, classed as sedentary (Heesch, Hill, Aguilar-Farias, van Uffelen, & Pavey, 2018). However, low-movement behaviours may occur in a sitting *or* standing posture, but both may record accelerations that register below the 'sedentary time cut-point'. Thus,

accelerometers may lead to an overestimation of sedentary time by misclassifying low-movement standing behaviours as sitting (sedentary). The activPAL™ (PAL Technologies Ltd., Glasgow, UK) is a combined posture sensor and accelerometer that addresses this limitation, and is able to accurately classify behaviours as sitting/lying (sedentary), standing or stepping. To date, studies in both clinical and non-clinical populations have demonstrated high validity of the activPAL™ for measuring these behaviours when compared to direct observation (Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016). As such, it is considered the 'gold standard' for measurement of free-living sedentary time (Chastin & Granat, 2010; Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016). Still, the activPAL™ primarily offers a measure of sedentary behaviour, rather than frequency, intensity and duration of PA. Consequently, few RA studies have employed the activPAL™ to assess sedentary time as well as PA, with extant research employing this device focusing specifically on the role of sedentary behaviour in RA (Thomsen et al., 2017).

Considering exponential growth in research centred on the role of sedentary behaviour and PA for improving RA disease outcomes, it is critical that objective devices are properly validated for use in this population. Therefore, the overarching aim of the current study was to validate a commonly employed accelerometer (ActiGraph GT3X+) and the activPAL3$^{\mu TM}$, for measurement of sedentary time and PA in RA. This validation study used a laboratory *and* field-based approach. Specific objectives were to; 1a) validate the GT3X+ against indirect calorimetry to generate RA-specific triaxial (vector magnitude [VM]) accelerometer cut-points for sedentary time, LPA and MPA, and 1b) validate the activPAL3$^{\mu TM}$ against direct observation for measurement of sedentary, standing and stepping time (*laboratory validation).* Then, using these data; 2) compare the validity of the new RA-specific triaxial sedentary time cut-point vs. the widely-used non-RA uniaxial sedentary time accelerometer cut-point (<100

counts/min) (Matthews et al., 2008; Troiano et al., 2008) for measurement of free-living sedentary time in RA, against the gold standard (activPAL3$^{\mu TM}$), and 3) compare within-person estimates of free-living sedentary time, LPA and MPA, quantified using the new RA-specific vs. commonly used non-RA accelerometer cut-points (Matthews et al., 2008; Troiano et al., 2008) (*field validation*).

Method

Participants and recruitment

Participants were recruited from outpatient clinics at Russells Hall Hospital (The Dudley Group NHS Foundation Trust). *Eligibility criteria:* a clinical diagnosis of RA (Aletaha et al., 2010) and aged ≥18 years old. For Objective 1, patients were required to be able to ambulate independently. For Objectives 2 and 3, patients were eligible if they could ambulate independently, or with an assistive device. All participants provided written informed consent. This study was approved by the local National Health Service Research Ethics Committee (16/WM/0371).

Protocol

The protocol for this study has been previously published, detailing the methodologies and analytical approaches employed (O'Brien et al., 2019), but are briefly described herein.

Objective 1: Laboratory-based validation

Participants (n = 22) reported to the laboratory, having fasted (12h prior) and refrained from exercise (48h prior). Upon arrival, participants completed physical assessments (e.g., body-mass index, Disease Activity Score-28) (Prevoo et al., 1995), and completed the Health Assessment Questionnaire (Fries et al., 1980). Participants were then fitted with the

activPAL3$^{\mu TM}$, GT3X+, heart rate monitor (Polar Electro Oy Ltd., Kempele, Finland) and Cortex Metalyzer® 3B (indirect calorimeter [Cortex Biophysik, Leipzig, Germany]) for the duration of the laboratory validation (approximately 2h). For direct observation, a video camera (Everio, JVC Ltd., USA) was set up overlooking the laboratory. All equipment was time-synchronised to facilitate accurate comparison between time-stamped raw data collected by the activPAL3$^{\mu TM}$, GT3X+ and criterions (*indirect calorimetry* = VO_2 [ml•kg•min] and METs; *direct observation* = video camera recordings).

Participants undertook 11 activities, comprising 6 standardised activities and 5 activities of daily living (ADLs [randomised]). Laboratory testing component activities ranged from 1.3-3.5 METs and were 6-min in duration (Copeland & Esliger, 2009). Five-min rest periods separated ADLs, to allow heart rate and VO_2 to return to resting levels (Copeland & Esliger, 2009; Evenson et al., 2015; Santos-Lozano et al., 2013).

Objectives 2 and 3: Field-based validation

Participants (n = 104) attended the laboratory to complete physical assessments, as per Objective 1. They then wore the activPAL3$^{\mu TM}$ and GT3X+ for 7 days, to assess free-living sedentary time and PA (O'Brien et al., 2018).

Measures

GT3X+. The GT3X+ (19g; 4.6cm x 3.3cm x 1.5cm) is a triaxial accelerometer that records accelerations on 3 axes (vertical [Y], horizontal right-left [X] and horizontal front-back [Z]), over researcher-defined time periods (epochs). These data are used to compute vector magnitude ($VM = \sqrt{(axisY^2 + axisX^2 + axisZ^2)}$), which is the outcome employed to quantify sedentary time and PA. For this study, accelerometers were set to sample movement in 1-s epochs at a rate of 30 Hertz. Participants wore the GT3X+ attached to an elastic belt on their

right hip (Aguilar-Farias et al., 2014; Pfister et al., 2017; Santos-Lozano et al., 2013; Troiano et al., 2008). For Objective 1, the device was worn for the whole laboratory validation protocol. For Objectives 2 and 3, participants wore the device for 7-days during all waking hours, removing only for water-based activities.

ActivPAL3$^{\mu TM}$. The activPAL3$^{\mu TM}$ (9g; 2.35cm x 4.3cm x 0.5cm) is a combined posture sensor and accelerometer that measures free-living behaviour over consecutive 24-h periods. Participants wore the activPAL3$^{\mu TM}$ in a mid-anterior position on the right thigh, attached with a waterproof adhesive dressing (Edwardson et al., 2017). For Objective 1, the activPAL3$^{\mu TM}$ was worn for the duration of the laboratory-based protocol. For Objectives 2 and 3, participants wore the device for 7 days, 24h/day.

Indirect calorimetry. Indirect calorimetry (Cortex Metalyzer® 3B) was the criterion standard for validating the accelerometer. The Cortex Metalyzer® 3B uses a breath-by-breath system to directly measure an individual's concentration of inspired oxygen (O_2) and expired carbon dioxide (CO_2). These data are used to calculate VO_2 (ml•kg•min) and METs, using MetaSoft® (Cortex Biophysik, Leipzig, Germany).

Direct observation. Direct observation was the criterion standard for validating the activPAL3$^{\mu TM}$. A video camera was set up on a tripod overlooking the laboratory.

Data reduction and statistical analysis

Objective 1: Laboratory-based validation

GT3X+ and indirect calorimetry. The manufacturer's software (Actilife [ActiGraph, LLC., Pensacola, Florida, USA]) was used to download time-stamped GT3X+ data in the

format of triaxial (VM) activity counts. Data were downloaded in counts/s, and converted to counts/min for analysis.

Metasoft® was used to download and export breath-by-breath VO_2 data from the Cortex Metalyzer® 3B. In Microsoft Excel, second-by-second VO_2 data were averaged across each min to compute the average VO_2 (ml•kg•min) for each min of activity. These data were then graphed to identify mins in which steady state VO_2 was achieved within each laboratory testing component (steady state = variation within ± .50 ml•kg•min). Steady state was identified as occurring in the final 2 min of each activity (min 4-6).

VO_2 (ml•kg•min) and GT3X+ data (counts/min) were therefore averaged across min 4-6 of each laboratory testing component, to provide 'steady state' VO_2 and GT3X data for each activity. These data were exported into SPSS (Chicago, USA) for statistical analysis. Where participants did not reach steady state VO_2 during an activity, their data recorded for that particular activity were excluded.

Statistical analysis: First, average (steady state) VO_2 data were converted into METs (1 MET = 3.5 ml•kg•min) and then classified as sedentary (≤1.5 METs), LPA (1.6-2.9 METs) or MPA (≥3 METs). Using these classifications, data were recoded to create binary variables for use in Receiver Operating Characteristic (ROC) curve analysis, to define RA-specific triaxial (VM) accelerometer cut-points for sedentary time, LPA and MPA. Specifically, data were recoded as sedentary/not sedentary, or MPA/not MPA using binary indicators (1/0). ROC curves identified the VM activity count maximising sensitivity (*y*-axis) and specificity (*x*-axis) for correctly classifying behaviour as sedentary or MPA. The area under the curve (AUC) value was also calculated (AUC criteria: 0.90-1.00 = excellent; 0.80-0.89 = good; 0.70-0.79 = fair; 0.60-0.69 = poor; <0.60 = failure).

ActivPAL3$^{\mu TM}$ and direct observation. PAL Connect (PAL Technologies, Ltd., Glasgow, UK) was used to download and export activPAL3$^{\mu TM}$ time-stamped data to Microsoft Excel. Time spent sedentary, standing and stepping, as well as number of steps and sit-stand transitions, were displayed every 15s. For direct observation, the researcher observed all video camera recordings, recording engagement in sitting/lying (sedentary), standing or stepping, as well as counting steps and sit-stand transitions, every 15s for the 6-min duration of each activity.

Statistical analysis: Means (M) and standard deviations (SD) were calculated for activPAL3$^{\mu TM}$-assessed and directly observed time spent sedentary, standing and stepping (min), and number of steps and sit-stand transitions. Bland-Altman analysis calculated 95% limits of agreement (LOA [lower–upper]) between activPAL3$^{\mu TM}$-assessed vs. directly observed behaviours, using the M and SD of the differences (min) between the 2 measures (M ± (SD x 1.96)) (Bland & Altman, 1986; Giavarina, 2015). Further, percentage accuracy for activPAL3$^{\mu TM}$-assessment vs. direct observation of behaviours was computed (% accuracy = (activPAL value/direct observation value) x 100).

Objectives 2 and 3: Field-based validation

Actilife was used to download 7-day GT3X+ data (1-s epochs) and check non-wear (criteria = ≥60 min of consecutive zero counts, spike tolerance of 2 min) (Semanik et al., 2010; Troiano et al., 2008). Participants' data were retained for inclusion in statistical analysis where accelerometers were worn for ≥10h/day on ≥4 days (including ≥1 weekend day) (Semanik et al., 2010; Troiano et al., 2008). The RA-specific triaxial (VM) accelerometer cut-points (developed in Objective 1) and non-RA uniaxial (Y-axis) accelerometer cut-points (Troiano et al., 2008: sedentary time = <100 counts/min; LPA = 100-2019 counts/min; MPA = 2020-5998

counts/min) (Matthews et al., 2008; Troiano et al., 2008), were then applied to 7-day GT3X+ data to derive estimates of free-living sedentary time, LPA and MPA (min/day).

For the activPAL3$^{\mu TM}$, PAL Connect was used to download and export daily movement data (15-s epochs) that corresponded to valid days measured via the GT3X+. Sleep time was manually removed from activPAL3$^{\mu TM}$ data using wear-time logbooks, self-reported waking and sleeping time, and sleep-periods identified from GT3X+ data analysis. Estimates of free-living activPAL3$^{\mu TM}$-assessed sedentary time (min/day) were then calculated using PAL Connect proprietary algorithms.

Statistical analysis: For Objective 2, Bland-Altman analysis calculated 95% LOA (lower–upper) between GT3X+- and activPAL3$^{\mu TM}$-assessed free-living sedentary time, for both RA-specific and non-RA accelerometer cut-points. LOA were calculated using the M and SD of the differences (min/day) between estimates of GT3X+- (RA-specific and non-RA cut-points) and activPAL3$^{\mu TM}$-assessed sedentary time (M ± (SD x 1.96)). For Objective 3, paired samples *t*-tests compared sedentary time, LPA and MPA estimates (min/day), derived from RA-specific vs. non-RA accelerometer cut-points.

Results

Objective 1: Laboratory-based validation

Twenty-two people with RA, (86% female, n = 19), participated in the laboratory protocol. Descriptive statistics are reported in Table 2.1.

Table 2.1 Objectives 1, 2 and 3: Participant characteristics

	Objective 1	**Objectives 2 and 3**
Age (years)	53.7 ± 12.5	58.5 ± 12.1
BMI (kg/m^2)	27.4 ± 5.7	28.9 ± 6.1
Height (m)	1.7 ± 0.1	1.6 ± 0.1
Weight (kg)	74.9 ± 18.0	80.0 ± 20.5
Body fat (%)	34.6 ± 9.3	35.6 ± 8.5
RA duration (years)	6.7 ± 6.3	10.6 ± 10.5
DAS-28	3.2 ± 1.7	4.0 ± 1.5
HAQ	0.8 ± 0.7	1.3 ± 0.8

BMI, body-mass index; RA, Rheumatoid Arthritis; DAS-28, Disease Activity Score-28; HAQ, Health Assessment Questionnaire

Note: M ± SD shown for age, BMI, height, weight, body fat percentage, RA duration, DAS-28 and HAQ score. DAS-28 was calculated using Erythrocyte Sedimentation Rate, 28 swollen-and-tender joint count and visual analogue scale (overall health from 0 [very good] – 100 [very poor]). HAQ scores were defined as, ability to undertake activities of daily living (0 = without any difficulty, 1 = with some difficulty, 2 = with much difficulty, 3 = unable to do).

GT3X+ and indirect calorimetry. Table 2.2 reports the M ± SD for GT3X+ activity counts and METs during steady state VO_2. Activity intensities (METs) achieved included sedentary (e.g., 0.8 ± 0.2, reading a newspaper), LPA (e.g., 1.9 ± 0.3, ironing and folding clothes) and MPA (e.g., 3.4 ± 0.4, walking at 4.8km/h). Table 2.3 reports results of ROC curve analysis and the RA-specific accelerometer cut-points maximising sensitivity and specificity.

The AUC demonstrated ‘excellent’ fit for RA-specific sedentary time (AUC = 1.00) and MPA (AUC = 0.94) cut-points.

Table 2.2 Objective 1: Descriptive statistics for laboratory validation of the ActiGraph GT3X+ accelerometer

Activity (MET values – Compendium of Physical Activities)	**n**	**ActiGraph GT3X+ (VM activity counts/min)**	**Energy Expenditure (METs)**
Standardised testing component 1			
Lying (1.3 METs)	20	0 ± 0	0.6 ± 0.2
Sitting (1.3 METs)	22	0 ± 0	0.7 ± 0.2
Standing (1.3 METs)	18	141 ± 45	0.8 ± 0.2
Activities of daily living			
Reading a newspaper (1.3 METs)	19	7 ± 13	0.8 ± 0.2
Washing and drying dishes (1.8 METs)	15	518 ± 315	1.8 ± 0.3
Ironing and folding clothes (2.0 METs)	12	549 ± 279	1.9 ± 0.3
Placing bed linens on pillows and duvet (2.5 METs)	18	1051 ± 526	2.3 ± 0.5
Sweeping the floor (3.3 METs)	17	1675 ± 502	2.3 ± 0.6
Standardised testing component 2			
Walking at 3.2 km/h (2.8 METs)	19	2148 ± 571	2.7 ± 0.7
Walking at 4 km/h (3.0 METs)	20	3120 ± 637	3.2 ± 0.8
Walking at 4.8 km/h (3.5 METs)	18	3944 ± 882	3.4 ± 0.4

VM, vector magnitude; METs, metabolic equivalents

Note: MET values according to the Compendium of Physical Activities (Ainsworth et al., 2011) are specified next to each activity of the laboratory protocol. M ± SD are shown for ActiGraph GT3X+ accelerometer activity counts (VM) and METs, averaged across min 4-6 of each activity. Number of participants (n) included in analysis are shown per activity. Participants who did not reach steady state VO_2 (± 0.5 ml•min•kg) during min 4-6 were excluded from that particular activity.

Table 2.3 Objective 1: ROC curve generated RA-specific triaxial (VM) accelerometer cut-points

Epoch (1-min)	RA-specific accelerometer cut-points (VM activity counts/min)	Sensitivity	Specificity	AUC
Sedentary time	≤ 244	0.99	0.03	1.00
LPA	> 244 – < 2502	X	X	X
MPA	≥ 2502	0.87	0.11	0.94

RA, Rheumatoid Arthritis; VM, vector magnitude; LPA, light-intensity physical activity; MPA, moderate-intensity physical activity; AUC, area under the curve; X, does not apply

Note: RA-specific triaxial accelerometer cut-points were developed for measurement of sedentary time, LPA and MPA, based on average VM activity counts/min and energy expenditure (METs) during steady state VO_2 (± 0.5 ml•min•kg) during min 4-6 of each activity. LPA accelerometer cut-points were defined using the upper cut-point threshold of sedentary time, and the lower cut-point threshold of MPA. The AUC represented the accuracy of the RA-specific accelerometer cut-points (0.90-1.00 = excellent; 0.80-0.89 = good; 0.70-0.79 = fair; 0.60-0.69 = poor; <0.60 = failure).

ActivPAL3$^{\mu TM}$ and direct observation. Table 2.4 reports the M ± SD for activPAL3$^{\mu TM}$-assessed and directly observed behaviours during the laboratory testing procedure. When compared to direct observation, the activPAL3$^{\mu TM}$ accurately classified duration of sedentary, standing and stepping behaviours, as well as step number, >98% of the time. For number of sit-stand transitions, classification accuracy was 72%.

Mean differences for activPAL3$^{\mu TM}$-assessed vs. directly observed behaviours were computed (sedentary time, 0.1 ± 0.1 min; standing, 0.2 ± 0.5 min; stepping, -0.3 ± 0.5 min; steps, -30 ± 44; sit-stand transitions, 2 ± 1). Bland-Altman analysis (Figure 2.1) demonstrated

narrow 95% LOA (lower–upper), for sedentary (-0.1–0.2), standing (-0.7–1.1) and stepping (-1.2–0.6) time (min). For number of steps, 95% LOA were wider (-116–57). As only M = 5 ± 1 and M = 7 ± 0 sit-to-stand transitions were recorded by the activPAL3$^{\mu TM}$ and direct observation, respectively, Bland-Altman plots could not be produced for this outcome.

Table 2.4 Objective 1: Descriptive statistics for laboratory validation of the activPAL3$^{\mu TM}$

	ActivPAL3$^{\mu TM}$	**Direct observation**	**Accuracy (%)**
Sedentary (total min)	18.1 ± 0.1	18.0 ± 0.0	99.6
Standing (total min)	29.2 ± 0.8	28.9 ± 0.6	99.2
Stepping (total min)	18.8 ± 0.8	19.1 ± 0.6	98.4
Steps (total number)	2044 ± 122	2074 ± 144	98.6
Sit-stand transitions (total number)	5 ± 1	7 ± 0	72.1

Note: M ± SD are shown for total activPAL3$^{\mu TM}$-assessed and directly observed time spent sitting/lying (sedentary), standing and stepping (total min), and number of steps and sit-stand transitions during each activity of the laboratory protocol. The percentage accuracy for activPAL3$^{\mu TM}$-assessment vs. direct observation of each behaviour is also shown (% accuracy = (activPAL3$^{\mu TM}$ value/direct observation value) x 100).

Objectives 2 and 3: Field-based validation

A total n = 100 participants provided valid 7-day GT3X+ and corresponding activPAL3$^{\mu TM}$ data (96% of n = 104). Descriptive statistics for the sample are reported in Table 2.1. Accelerometer-derived behaviour estimates (min/day) were; sedentary time = 686.1 ± 72.4 (RA-specific accelerometer cut-points) and 754.7 ± 62.5 (non-RA accelerometer cut-points), LPA = 112.6 ± 36.1 (RA-specific accelerometer cut-points) and 86.8 ± 26.2 (non-RA

accelerometer cut-points), and MPA = 84.6 ± 34.5 (RA-specific accelerometer cut-points) and 32.6 ± 19.4 (non-RA accelerometer cut-points).

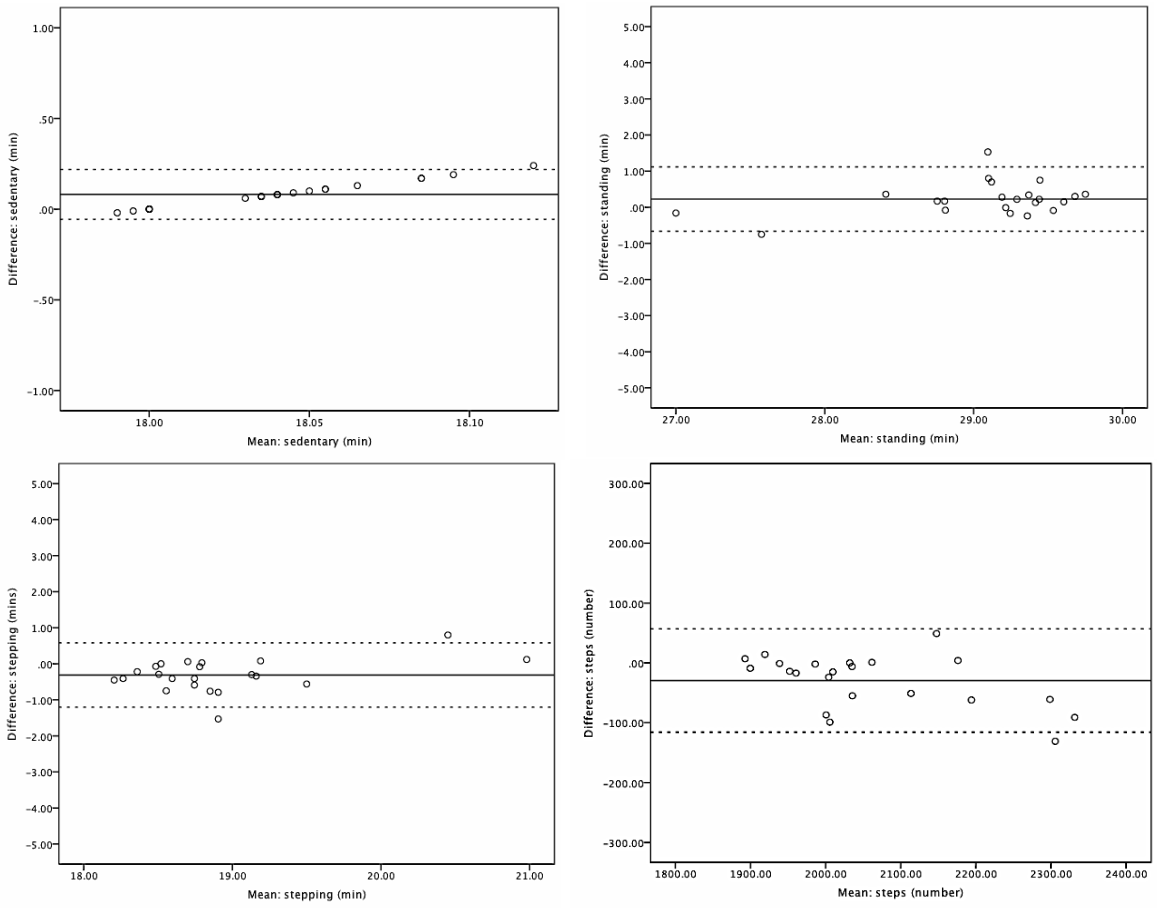

Figure 2.1 Objective 1: Bland-Altman plots showing agreement (mean difference and 95% limits of agreement [LOA]) for time spent sitting/lying (sedentary), standing, and stepping, as well as number of steps, between the activPAL3$^{\mu TM}$ vs. direct observation.

Key:

Mean difference

Lower and upper LOA (95%)

Objective 2: For the RA-specific cut-point (≤244 counts/min, VM) vs. the activPAL3$^{\mu TM}$, Bland-Altman analysis revealed a mean difference of 137.7 ± 92.0, with 95% LOA (lower–upper) = (-42.6–318.0), for sedentary time (min/day) (Figure 2.2). The majority of data points were positioned above zero and followed a downward trend, whereby a lower mean difference between measures was observed at higher levels of sedentary time.

Compared to the RA-specific cut-point, the non-RA cut-point (<100 counts/min, Y-axis) demonstrated a greater mean difference (206.2 ± 115.2) and wider 95% LOA (lower–upper) = (-19.6–432.0) vs. the activPAL3$^{\mu TM}$ for sedentary time (min/day). Bland-Altman analysis for the non-RA cut-point revealed most data points were scattered above zero, and a downward trend was observed (lower mean difference between measures at higher levels of sedentary time).

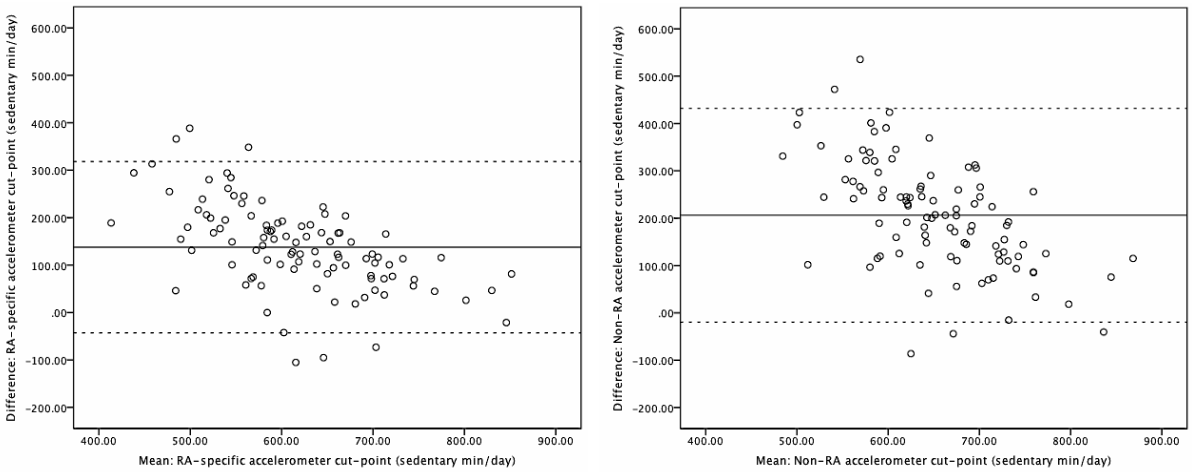

Figure 2.2 Objective 2: Bland-Altman plots showing agreement (mean difference and limits of agreement [LOA]) between accelerometer-assessed vs. activPAL3$^{\mu TM}$-assessed sedentary time. Accelerometer cut-points applied were; RA-specific (VM) accelerometer cut-points (derived from Objective 1 of this study), and non-RA (Y-axis) accelerometer cut-points.

Key:

Mean difference

Lower and upper LOA (95%)

Objective 3: Paired samples *t*-tests demonstrated significant differences ($p<.05$) between sedentary time, LPA and MPA estimates (min/day) from RA-specific vs. non-RA specific accelerometer cut-points.

Discussion

The accurate assessment of sedentary behaviour and PA in RA is essential to determine population prevalence of these behaviours, establish dose-response relationships between sedentary behaviour and PA with pertinent disease outcomes, and examine the efficacy of interventions supporting sedentary and PA behaviour change in this patient group. The current study validated the ActiGraph accelerometer and activPAL3$^{\mu TM}$ – 2 devices readily used in sedentary behaviour and PA research – for objective measurement of sedentary time and PA in people with RA.

To date, RA studies employing accelerometers have largely relied on the application of non-RA cut-points to quantify free-living sedentary time and PA in this population (Fenton et al., 2017; Fenton et al., 2018c). However, exponential growth in research focused on understanding the role of sedentary time and PA for health in different populations, has underlined a critical need for the development of population-specific accelerometer cut-points, which consider the unique physiology and associated movement patterns of the target population (Aguilar-Farias et al., 2014; Copeland & Esliger, 2009; Motl et al., 2009; Santos-Lozano et al., 2013). In response, this is the first study to calibrate the commonly-employed ActiGraph accelerometer and define RA-specific triaxial (VM) accelerometer cut-points, for valid measurement of sedentary time, LPA and MPA in RA. In our sample of n = 100 RA patients, daily sedentary time, LPA and MPA estimates significantly differed when applying RA-specific vs. non-RA cut-points to free-living accelerometer data. Given that our RA-

specific cut-points were derived according to energy requirements of behaviour among people with RA, we argue that the sedentary time and PA estimates generated by application of our novel cut-points are likely to provide more valid assessments of behaviour. We therefore recommend using the RA-specific cut-points proposed herein, in future studies employing accelerometry to quantify free-living sedentary time, LPA and MPA in RA.

Still, whilst the development RA-specific cut-points is an important step forward for research in this domain, a key drawback of accelerometers is their inability to differentiate between low-movement behaviours, undertaken in sitting vs. standing postures. Thus, this study also assessed the accuracy of the activPAL3$^{\mu TM}$ for measurement of sedentary, standing and stepping time in RA. Only one study has previously examined the ability of the activPAL to validly assess posture in RA (Larkin et al., 2016). Larkin et al. (2016) employed regression analysis to report strong associations between activPAL^{TM}-assessed sitting/lying, standing and stepping time with directly observed behaviour. However, it would be surprising to find a non-significant relationship between 2 methods that are designed to measure the same variable. Advancing the study by Larkin and colleagues (2016), we employed Bland-Altman analysis and reported high levels of agreement between activPAL3$^{\mu TM}$-assessed vs. directly observed behaviours (Bland & Altman, 1986; Dogan, 2018), and observed high classification accuracy (>98% for sedentary, standing and stepping time). This is in line with past research in non-RA populations (Edwardson et al., 2017; Sellers et al., 2016) and further supports the recommendation that the activPAL^{TM} be considered the gold standard assessment of free-living sedentary time (Chastin & Granat, 2010; Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016), including among people with RA.

On the basis of this recommendation, we examined the validity of the RA-specific sedentary time cut-point for assessment of free-living sedentary time in RA, using the

activPAL3$^{\mu TM}$ as the criterion standard. Comparing sedentary time quantified using the RA-specific cut-point vs. the activPAL3$^{\mu TM}$, results revealed a mean difference of 2.3h/day. Bland-Altman plots demonstrated most data points to fall above zero, suggesting overestimation of sedentary time using the RA-specific cut-point. Still, 95% LOA for sedentary time estimates reported herein, were not dissimilar to other validation studies comparing agreement between accelerometers and the activPAL3$^{\mu TM}$ for assessment of sedentary time in other populations (e.g., -1.9–3.6 (Aguilar-Farias et al., 2014) and -3.3–4.2 (Pfister et al., 2017) h/day). In addition, compared to the activPAL3$^{\mu TM}$, our RA-specific cut-points produced a smaller mean difference, and narrower 95% LOA, relative to the non-RA cut-point (<100 counts/min) commonly used in studies of sedentary time (Matthews et al., 2008; Troiano et al., 2008). Thus, it is possible that the observed global lack of agreement between accelerometer and activPAL^{TM}-assessed sedentary time reflects an overall reduced proficiency of accelerometers to accurately measure sedentary time, rather than relatively compromised validity of the RA cut-points described herein.

The difference between sedentary time estimates derived from the RA-specific cut-point vs. activPAL3$^{\mu TM}$ in this study (and others) (Aguilar-Farias et al., 2014; Pfister et al., 2017) could be attributed to an inability of accelerometers to differentiate between low-movement behaviours undertaken in a sitting vs. standing posture. Our data supports this as a plausible explanation for 2 reasons. First, participants' average MET values during 'standing' in the laboratory protocol was ≤1.5 METs (0.8 ± 0.2 METs), which is the energy requirement used to define sedentary behaviour. Second, the downward trend observed in Bland-Altman plots suggests agreement between accelerometer- and activPAL3$^{\mu TM}$-assessed sedentary time improves at higher levels of sedentary time where lower levels of PA (including standing) are likely to occur. That is, for people with high levels of sedentary time, standing may occupy less

of daily waking behaviour and therefore there is less opportunity to misclassify standing time. In a recent study comparing accelerometer and activPAL™-assessed sedentary time, Aguilar-Farias et al. (2014) demonstrated that their population-specific sedentary time VM cut-points (e.g., <60 counts/min) were better able to detect combined activPAL3μTM-assessed sedentary *and* standing time (AUC = 0.82), compared to activPAL3μTM-assessed sedentary time alone (AUC = 0.73).

In summary, results suggest that where possible, future studies should employ the activPAL3μTM to gain more valid estimates of sedentary time in people with RA. When this is not an option, the RA-specific cut-point represents a more valid alternative compared to the non-RA cut-point of <100 counts/min (Matthews et al., 2008; Troiano et al., 2008) for the assessment of sedentary time in this population. However, these recommendations should be considered in the context of study limitations. First, the nature of the laboratory validation meant that a free-living environment could not be wholly achieved, only replicated. Still, the laboratory protocol was informed by similar validation studies conducted in RA and non-RA populations, and included several activities typically undertaken in a free-living environment (Copeland & Esliger, 2009; Kim & Welk, 2015b; Larkin et al., 2016). Second, our laboratory protocol was not designed to investigate interruptions in sedentary time, as measured by the activPAL3μTM, and this should be addressed in future research. Third, only 1 individual undertook direct observation procedures (e.g., viewing videos, documenting time spent sedentary) during laboratory validation of the activPAL3μTM. Although our findings are supported by those of Larkin et al. (2016), future studies employing 2 independent coders of direct observation data will enable inter- and intra-observer reliability to be established, and further support the validity of these results. Finally, participants included in both laboratory-based and field-based protocols were mostly female with moderate RA disease activity. Thus,

whilst the proportion of females participating in this study is representative of the RA population (Wasserman, 2018), findings may be less generalisable to male RA patients, and those with more/less active disease. Future research should therefore confirm the validity of the newly-developed RA-specific accelerometer cut-points and activPAL3$^{\mu TM}$ in a different population of RA patients (e.g., males, more/less obese, higher/lower disease activity). Such findings might point to the development of accelerometer cut-points specific to different groups of RA patients (e.g., males, more/less obese, higher/lower disease activity).

Conclusion

The current study confirms the activPAL3$^{\mu TM}$ can be considered the gold standard for measurement of free-living sedentary time in RA. Further, RA-specific triaxial accelerometer cut-points presented herein, are sensitive and specific for measurement of sedentary time, LPA and MPA, and permit more accurate assessment of free-living sedentary time compared to commonly-employed non-RA cut-points (Matthews et al., 2008; Troiano et al., 2008). Thus, in the absence of the activPAL3$^{\mu TM}$, our data supports use of the RA-specific cut-point for assessment of sedentary time.

CHAPTER 3

LONGITUDINAL STUDY: GENERAL METHODS AND PARTICIPANT CHARACTERISTICS

The protocol for this study has been published in *Mediterranean Journal of Rheumatology*

Overview

This chapter details the methodology employed for a longitudinal study, comprising Chapters 4, 5 and 6 of this thesis[1]. In brief, n = 104 people with Rheumatoid Arthritis (RA) attended the hospital for data collection at baseline (Time Point 1 [T1] and 6-months later (Time Point 2 [T2]). The same protocol was employed at both time points. Data collected pertaining to health-related correlates and psychosocial determinants of sedentary behaviour are reported in Chapters 4 and 5, respectively. In Chapter 6, data are combined to test models relevant to promoting sedentary behaviour change in this population. Specific chapter titles and corresponding aims are:

Chapter 4. ***The bi-directional associations of health with sedentary time and physical activity in Rheumatoid Arthritis:*** To assess longitudinal associations between pertinent aspects of Rheumatoid Arthritis (RA) health with objectively-assessed sedentary time and physical activity (PA) in RA, and investigate if these associations may be bi-directional.

Chapter 5. ***The psychosocial determinants of sedentary time and physical activity in Rheumatoid Arthritis: a self-determination theory perspective*****:** Using a self-determination theory (SDT) lens, to assess longitudinal associations between quality of motivation to reduce sedentary behaviour with objectively-assessed sedentary time and PA in RA.

Chapter 6. ***Exploring the role of autonomous motivation to reduce sedentary behaviour and improve Rheumatoid Arthritis outcomes: testing models of sedentary behaviour change*****:** Informed by Chapters 4 and 5, to examine sequential associations between quality of motivation to reduce sedentary behaviour with objectively-assessed behaviours, and in turn, RA outcomes.

[1] The protocol for this longitudinal study has previously been published, (O'Brien et al., 2018) outlining all measures undertaken by participants. For the purposes of this thesis, the content of the published chapter has been amended to reflect current aims (details the methodologies and analysis directly relevant to thesis Chapters 4, 5 and 6).

Method

Participants and recruitment

Participants were recruited from Rheumatology outpatient clinics at Russells Hall Hospital in Dudley, England. *Inclusion criteria*: a clinical diagnosis of RA according to the American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) criteria (Aletaha et al., 2010) and aged ≥18 years old. *Exclusion criteria*: wheelchair users and those unable to ambulate independently with the use of an assistive device.

Eligible patients were approached about the study during Rheumatology outpatient clinics. Patients were provided with information about study procedures and given the opportunity to ask the researcher any questions. Willing patients provided informed consent to participate in the study. This study was approved by the local National Health Service Research Ethics Committee (West Midlands – Black Country Research Ethics Committee 16/WM/0371).

Protocol

This study adopted a longitudinal design. Participants were asked to visit the hospital at 2 time points; baseline (T1) and 6-month follow-up (T2). At each time point, participants were asked to undertake 2 visits (‘Visit 1’ and ‘Visit 2’) separated by a 7-day period. Specific protocols employed are described below and illustrated in Figure 3.1.

Visit 1. Participants visited the hospital to undertake physical assessments and complete questionnaires. At the end of Visit 1, participants were fitted with an activPAL3$^{\mu TM}$ (PAL Technologies Ltd., Glasgow, UK) and ActiGraph GT3X+ accelerometer (ActiGraph, LLC., Pensacola, Florida, USA) to wear for the subsequent 7 days, in order to measure habitual (daily) time spent sedentary, standing and stepping, and engaged in LPA and MPA. The researcher

gave verbal and written instructions, plus a demonstration, regarding how to wear each device. Participants were also provided with wear time logbooks to report device removal/replacement.

Visit 2. After 7 days, participants retuned to the hospital to provide a fasting blood sample, and undergo assessment of their RA disease activity (Disease Activity Score-28 [DAS-28]) During this visit, participants also completed questionnaires to report their experiences of pain and fatigue over the previous 7 days. The activPAL3$^{\mu TM}$, ActiGraph GT3X+ and wear time logbooks were also returned.

Measures

Visit 1

Participant characteristics. Information was recorded pertaining to participants' biological sex, age, ethnicity, marital status, date of diagnosis, existing chronic conditions (e.g., heart disease, diabetes, depression), current medical treatment and smoking status.

Anthropometrics and resting blood pressure. Taken in duplicate, height, weight and body composition were measured with participants bare-foot, whilst wearing light and loose-fitting clothing. Height was measured to the nearest 0.1cm using a stadiometer (SECA, Leicester Height Measure). Weight was measured to the nearest 0.1kg using Tanita body composition scales (Tanita BC-418 MA P). Body-mass index (BMI) was calculated as weight (kg)/height (m)^2. Body fat (%) was measured using Tanita scales via bioelectrical impedance analysis. For each measure, a third assessment was conducted if the 2 measures differed by ± 0.5, and an average computed (average value = (value 1 + value 2 + value 3)/3).

Resting blood pressure (BP [systolic and diastolic]) was taken in duplicate with an automatic BP machine (Mindray Accutorr PLUS). The BP cuff was placed over the brachial

artery as standard, after the participant had rested in a supine position for 5 min (Panoulas et al., 2007).

Questionnaires. Validated questionnaires were administered to the participant to assess health-related and psychosocial correlates of sedentary behaviour and PA. At Visit 1, questionnaires assessed physical function, quality of life, subjective vitality, depressive symptoms and quality of motivation to reduce sedentary behaviour. Questionnaires are detailed below and shown in Table 3.1.

Health Assessment Questionnaire. The Health Assessment Questionnaire (HAQ) is the most valid measure of functional disability in RA (Fries et al., 1980), used routinely in clinical practice as a marker of RA disease severity (Fenton et al., 2017; Khoja et al., 2016; Kirwan & Reeback, 1986; Ramey, Raynauld, & Fries, 1992; Rouse et al., 2014). The HAQ assesses participants' ability to undertake activities of daily living (ADLs) referring to the preceding 2 weeks. ADLs are categorised into the following 8 sections: 'dressing and grooming', 'rising', 'eating' 'walking' 'hygiene', 'reach', 'grip' and 'activities'. Participants were asked to rate their difficulty in undertaking specific tasks associated with each ADL, using the scale: 0 = without any difficulty; 1 = with some difficulty; 2 = with much difficulty; 3 = unable to do. For example, under the 'rising' section, participants were asked, "are you able to get in and out of bed?". Average HAQ scores were computed to indicate 'functional disability', where higher scores indicate poorer functional disability (minimum score = 0; maximum score = 3). The HAQ demonstrated high internal reliability in this study (α = .91).

Dartmouth Cooperative Functional Assessment Charts. Dartmouth Cooperative (DCOOP) Functional Assessment Charts were used to assess 'general functional status' as a more holistic indicator of physical function. The DCOOP has been validated and employed in previous research with clinical and non-clinical populations in this regard (Nelson, Landgraf,

Hays, Wasson, & Kirk, 1990). Similarly to the HAQ, participants' self-reported ability to carry out ADLs over the previous 2 weeks was recorded using the DCOOP. However, the DCOOP offers a much broader assessment of physical function relative to the HAQ, asking participants to respond to 6 items relating to their 'physical fitness' [redacted] General functional status was computed as the sum of all subscales, where higher scores relate to poorer general functional status (minimum score = 1; maximum score = 30). High internal reliability was shown by the DCOOP in this study (α = .84).

World Health Organisation Quality of Life Questionnaire. The World Health Organisation Quality of Life Questionnaire (short form [WHOQOL-BREF]) (WHO, 1998) has been recommended for assessing quality of life in RA patients (Taylor, Myers, Simpson,

McPherson, & Weatherall, 2004). In this study, participants responded to 7 items, relating to the ‘physical health’ domain of quality of life. Participants responded to items (e.g., “how well are you able to get around?”) on a 5-point scale, pertaining to perceived physical health over the previous 2 weeks. These items were summed and used in statistical analysis. Higher scores were associated with better perceived quality of life with regard to patients’ physical health (minimum score = 1; maximum score = 35). Internal reliability for the ‘physical health’ domain was low in this study (α = .22). This could be due to isolation of the ‘physical health’ domain from the WHOQOL-BREF (lessening items in the scale), and was not due to poor correlation between items with the total domain score (Tavakol & Dennick, 2011).

Subjective Vitality Scale. The Subjective Vitality Scale (SVS) was used to assess participants’ positive peak psychological functioning (Ryan & Frederick, 1997). Following the stem, “during the previous 2 weeks”, participants responded to 6 statements (e.g., “I have been feeling alive and vital”, “I have had energy and spirit”) on a 7-point scale (1 = not true at all to 7 = very true). The SVS has been validated in RA (Rouse et al., 2015), and employed in studies examining associations between PA and psychological well-being in these patients (Fenton et al., 2018c). Average scores were computed, with higher scores representing greater subjective vitality (minimum score = 1; maximum score = 7), for use in statistical analysis. In the current study, the SVS exhibited high internal reliability (α = .96).

Hospital Anxiety and Depression Scale. The prevalence of depressive symptoms was measured via the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). This scale comprises 7 items to assess depressive symptoms, and has been previously validated in RA (Treharne, Lyons, Booth, & Kitas, 2007). Following the stem, “how have you been feeling generally over the past 2 weeks”, participants were asked to rate their agreement with each of the 7 items (e.g., “I feel as if I am slowed down”) on a 4-point scale. Scores across the

7 items were summed to represent prevalence of depressive symptoms (minimum score = 0; maximum score = 21). High internal reliability was demonstrated by the HADS in this study (α = .80).

Behavioural Regulation in Exercise Questionaire-2 (adapted for reducing sedentary behaviour). Based on Self-Determination Theory (SDT) (Deci & Ryan, 1985), the Behavioural Regulation in Exercise Questionaire-2 (BREQ-2) (Markland & Tobin, 2004) measures a person's quality of motivation to engage in PA by assessing their external, introjected, identified and intrinsic regulations, as well as amotivation. This questionnaire has been validated for use in populations with chronic musculoskeletal pain (Brooks et al., 2018) and employed in RA studies examining the associations between quality of motivation for PA with levels of PA engagement (Rouse et al., 2014; Yu et al., 2015a). For this study, the BREQ-2 was adapted to measure 'quality of motivation for reducing sedentary behaviour'. Specifically, the stem, "I take part in physical activity" was adapted to read, "I aim to reduce my sedentary behaviour". Participants were asked to respond to 19 items assessing intrinsic regulation (4 items; e.g., "because I enjoy doing this"), identified regulation (4 items; e.g., "because I value the benefits of doing this"), introjected regulation (3 items; e.g., "because I feel guilty when I am not doing this"), external regulation (4 items; e.g., "because my friends and family say I should") and amotivation (4 items; e.g., "but I think doing this is a waste of time"). Participants were asked to rate their agreement with each statement on a 5-point scale (1 = strongly disagree; 2 = disagree; 3 = neutral; 4 = agree; 5 = strongly agree) in reference to their motivation to reduce sedentary behaviour over the previous 4 weeks. Previous research has developed or adapted questionnaires to assess quality of motivation to reduce sedentary behaviour using an SDT lens (Lubans et al., 2013).

To avoid any misinterpretation of the concept of ‘reducing sedentary behaviour’ by participants, the questionnaire opened with a definition of ‘reducing sedentary behaviour’ which read, “reducing sedentary behaviour refers to your overall attempts to spend less time sitting or lying down, *not* just your attempts to more frequently interrupt periods of sitting with physical activity or standing”. Participants were also provided with examples to illustrate ways people might reduce their sedentary behaviour, including, “getting off the bus at a station before the station nearest to your destination, so that you have to walk further and sit for less time”. This provided participants with context regarding ‘reducing sedentary behaviour’ prior to completing the questionnaire. Participants’ understanding was also checked by the researcher before they completed the questionnaire.

For this study, average scores for each subscale were computed, and used to produce composite scores for autonomous motivation (identified regulation + intrinsic regulation) and controlled motivation (external regulation + introjected regulation) (minimum score = 2; maximum score = 10). In this way, an initial understanding would be gained regarding the role of autonomous and controlled motivation to reduce sedentary behaviour in sedentary time and PA in RA. This ‘first step’ would provide a basis for future research in this patient group, which could extend to investigating the independent roles of external, introjected, identified and intrinsic regulations in sedentary behaviour and PA engagement. Additionally, computation of autonomous and controlled motivation to reduce sedentary behaviour increased the statistical power of regression models by reducing the number of variables in analysis. This method is also consistent with other studies using the BREQ-2 to measure quality of motivation to engage in PA in RA (Yu et al., 2015a) and non-RA (Vancampfort et al., 2013) populations.

High internal reliability was demonstrated by the adapted BREQ-2 used in this study for autonomous (α = .87) and controlled motivation (α = .81) to reduce sedentary behaviour.

Sedentary behaviour and physical activity.

ActivPAL3$^{\mu TM}$. The activPAL3$^{\mu TM}$ is a small, lightweight device (9g; 2.35cm x 4.3cm x 0.5cm) typically worn in a mid-anterior position on the right thigh, and affords the ability to measure free-living behaviour over consecutive 24-h periods. Specifically, the activPAL3$^{\mu TM}$ classifies free-living behaviour based on posture and acceleration. The activPAL3$^{\mu TM}$ is considered the gold standard measure of sedentary time (Chastin & Granat, 2010; Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016) and in this thesis, we have validated this device as a measure of sedentary, standing and stepping time in RA (Chapter 2) (O'Brien et al., 2019). From here on, the activPAL3$^{\mu TM}$ will be referred to more broadly, as the 'activPAL'.

PAL Connect (PAL Technologies Ltd., Glasgow, UK) was used to set up the activPAL for recording, and to download and analyse data. The activPAL was set to record data in 15-s epochs. The researcher attached the device via an adhesive, waterproof dressing (Tegaderm) to the mid-anterior position of the participant's right thigh (Edwardson et al., 2017). Participants were asked to wear the activPAL for 24h/day to enable assessment of habitual time spent sitting/lying (sedentary), standing and stepping, as well as number of steps and sit-stand transitions. If the participant removed the activPAL for any reason, they were asked to record this in wear time logbooks provided.

Participants' data were downloaded from the device (using PAL Connect) to a Microsoft Excel (Microsoft Corporation, Redmond, USA) format for analysis. Sleep time was determined using self-reported information from wear time logbooks, in conjunction with sleep periods identified via ActiGraph GT3X+ accelerometer data. The ActiGraph GT3X+ accelerometer protocol requested participants to wear the device only during waking hours, and to remove the device upon going to bed. Thus, enabling sleep time to be identified by

periods of accelerometer non-wear, registered during typical sleep (bedtime-waking) hours (e.g., 22:00-6:00). Sleep time identified by ActiGraph GT3X+ accelerometer data was checked against self-reported sleep (bedtime-waking) hours recorded in wear time logbooks.

Participants were required to have worn the activPAL for ≥10h/day on ≥4 days, including ≥1 weekend day, to be included in subsequent statistical analysis (Edwardson et al., 2017). The average daily waking time spent sedentary, standing and stepping (min/day), as well as the average daily percentage of time spent in these behaviours (activPAL-assessed behaviour per day [%] = (activPAL-assessed behaviour [min/day]/total activPAL wear time [min/day]) x 100), were calculated for use in subsequent statistical analysis. On this basis, n = 2 and n = 1 were excluded from cross-sectional and longitudinal analysis, respectively. Participants were required to have valid activPAL data at T1 *and* T2 to be included in longitudinal analysis (included: n = 53).

ActiGraph GT3X+ accelerometer. The ActiGraph GT3X+ triaxial accelerometer (19g; 4.6cm x 3.3cm x 1.5cm) records accelerations over researcher-selected time periods ('epochs') on the vertical (Y), horizontal right-left (X) and horizontal front-back (Z) axes. Data on these axes are then used to calculate the vector magnitude (VM) using the equation, $VM = \sqrt{(axisY^2 + axisX^2 + axisZ^2)}$. From here on, the ActiGraph GT3X+ accelerometer will be referred to more simply as the 'GT3X+'.

In the current study, the GT3X+ was initialised to record accelerations in 1-s epochs. The device was attached to an adjustable elastic belt and worn on the participant's right hip in a vertical position (Aadland & Ylvisaker, 2015; Matthews et al., 2012; Troiano et al., 2008). Participants were asked to remove the device only for sleeping and water-based activities (e.g., swimming, bathing), and to record all removal/replacement in wear time logbooks provided.

Following 7-day GT3X+-assessment of sedentary time and PA, data were downloaded using Actilife (ActiGraph, LLC., Pensacola, Florida, USA). Non-wear criteria applied to accelerometer data were; ≥60 min of consecutive '0' counts, with a spike tolerance of 2 min (Troiano et al., 2008). For accelerometer data to be considered valid, participants were required to have worn the accelerometer for ≥10h/day on ≥4 week days, including ≥1 weekend day, to be included in subsequent statistical analysis (Semanik et al., 2010; Troiano et al., 2008). On this basis, n = 4 participants were excluded from cross-sectional data analysis and n = 3 excluded from longitudinal data analysis. Participants were required to have valid GT3X+ data at T1 *and* T2 to be included in longitudinal analysis (included: n = 51).

Sedentary time, light-intensity PA (LPA) and moderate-intensity PA (MPA) were assessed by applying RA-specific triaxial (VM) accelerometer cut-points (VM counts/min: sedentary time = ≤244; LPA = 245-2501; MPA = ≥2502) to these data, as defined and validated in Chapter 2 of this thesis (O'Brien et al., 2019). The average daily time spent sedentary, and in LPA and MPA (min/day), as well as the average daily proportion of time spent in these behaviours (GT3X+-assessed behaviour per day [%] = (GT3X+-assessed behaviour [min/day]/total GT3X+ wear time [min/day]) x 100), were computed for use in subsequent statistical analysis.

Visit 2

Fasting blood sample. After a ≥12-h fast, blood was taken from the inside of the participant's arm and collected in appropriate vacutainers. Samples were used to measure serum biomarkers of inflammation (high-sensitivity C-reactive protein [hsCRP], erythrocyte sedimentation rate [ESR]). Levels of ESR were determined using standard laboratory procedures and hsCRP was quantified using Enzyme-Linked Immunosorbent Assays (ELISAs [MP Biomedicals, UK]).

Disease Activity Score-28. The DAS-28 is an established and validated measure of RA disease activity, and used routinely in clinical practice. The DAS-28 enables clinicians to make important decisions regarding RA patients' course of treatment, and is underscored as a key clinically important outcome by the EULAR (Prevoo et al., 1995; Smolen et al., 2016b; van Gestel et al., 1998; Weinblatt et al., 2006).

The DAS-28 comprises assessment of joint swelling and tenderness, in conjunction with a marker of systemic inflammation and patients' self-reported overall health. For measurement of DAS-28, the number of swollen and tender joints in 28 synovial joints of the body (hands, wrists, elbows, shoulders, knees) was examined by the researcher. The degree of swelling was visually assessed and self-reported by the researcher. Tenderness was assessed via participants' self-report when light pressure was applied to the joint by the researcher. The number of swollen and tender joints was used in conjunction with patients' ESR (mm/h) and a self-reported degree of overall health (Visual Analogue Scale, ranging from 0 [very good] to 100 [very poor]), to determine participants' DAS-28 via a clinical calculator. Criteria used by clinicians for interpretation of DAS-28 scores is: ≤3.2 = low disease activity, >3.2 – ≤5.1 = moderate disease activity and >5.1 = high disease activity (Makinen et al., 2007).

Questionnaires. Validated questionnaires were administered to the participant on Visit 2 to assess RA-related pain and fatigue during the 7-day study week (Table 3.1). This was because pain and fatigue are highly variable day-to-day, and so this research sought to capture data that aligned with objectively-assessed sedentary time and PA over the same 7 days.

McGill Pain Questionnaire. The McGill Pain Questionnaire (MPQ) has been developed and validated to evaluate pain in RA (Hawker, Mian, Kendzerska, & French, 2011; Sokka, 2005). The MPQ measures total pain (15 items), representing the sum of sensory (sum of 11

items [e.g., “throbbing”, “sharp”, “hot-burning”]) and affective (sum of 4 items [e.g., “tiring-exhausting”, “sickening”, “cruel-punishing”]) dimensions of pain (Melzack, 1987). Participants responded to each item by rating to what degree they identified with the descriptor (0 = none; 1 = mild; 2 = moderate; 3 = severe) over the previous 7 days. Total pain (total pain [15 items] = sensory pain [11 items] + affective pain [4 items]) was used in statistical analysis (minimum score = 0; maximum score = 45). Higher pain scores indicated higher degree of pain. High internal reliability was demonstrated by the MPQ in this study (α = .93).

Multidimensional Assessment of Fatigue. The Multidimensional Assessment of Fatigue (MAF) is a 15-item measure of global fatigue, developed and validated for use in RA (Hewlett, Hehir, & Kirwan, 2007). This scale has been extensively employed in previous studies of fatigue in RA (Belza, 1995; Vlietstra et al., 2019). For each item, the MAF requires participants to rate their degree of fatigue, and what extent fatigue interfered with their ability to carry out specific activities (e.g., “household chores”, “bathe or wash”, “cook”) over the previous 7 days, on a scale from 1 = not at all to 10 = a great deal. A global fatigue index was calculated (minimum score = 0; maximum score = 50). Higher global fatigue scores related to poorer fatigue outcomes. In this study, the MAF showed high internal reliability (α = .98).

Power calculation. Power calculations were conducted with G*Power (version 3.1.9.3) using data from the Physical Activity in Rheumatoid Arthritis (PARA) randomised controlled trial (Trial Number: ISRCTN04121489). In the PARA study, GT3X accelerometers measured sedentary time, LPA and MVPA in a subsample of RA participants, and hsCRP was measured as a biomarker of systemic inflammation. Cross-sectional accelerometer data were available for n = 61 participants. A priori power calculation indicated that a sample size of n = 125 would be sufficient to detect statistically significant relationships (power = 0.80, α error of probability = .05) between daily sedentary time and LPA with hsCRP. To ensure the

robustness of our calculations for detecting significant changes in broader RA outcomes, we also conducted power calculations for other RA outcomes assessed in the PARA study. For this, cross-sectional GT3X data, HAQ (physical function, n = 61), QRISK-2 (cardiovascular risk, n = 61) and subjective vitality (subjective vitality, n = 59) scores were used. A priori power calculation confirmed minimum sample sizes of n = 82 (physical function) and n = 114 (subjective vitality), would ensure adequate statistical power (power = 0.80, α error of probability = .05) to detect hypothesised associations.

Note: Recruitment, data collection and statistical analysis were conducted by Ciara O'Brien. Ciara completed Good Clinical Practice, phlebotomy and DAS-28 training during the period of PhD study. Ciara assisted the biomedical scientists at Russells Hall Hospital, Jacqueline Smith and Janet Imeson-Wood, to spin and pipette blood samples. Jacqueline and Janet analysed blood samples using Enzyme-Linked Immunosorbent Assays, to measure hsCRP. Standard laboratory procedures in Russells Hall Hospital measured ESR.

Table 3.1 Questionnaires administered to participants at T1 and T2

Variable	Questionnaire	Description
	Visit 1	
Functional disability	Health Assessment Questionnaire (HAQ)	Participants respond to 8 sections according to their ability to undertake activities over the previous 2 weeks.
General functional status	Dartmouth Cooperative Functional Assessment Charts (DCOOP)	Participants respond to 6 items with pictorial representations, according to their general functional status over the previous 2 weeks.
Quality of life	World Health Organisation Quality of Life (WHOQOL-BREF)	Participants respond to 7 items according to their physical health over the previous 2 weeks.
Subjective vitality	Subjective Vitality Scale (SVS)	Participants respond to 6 items according to their perceptions of aliveness and energy, over the previous 2 weeks.
Depressive symptoms	Hospital Anxiety and Depression Scale (HADS)	Participants respond to 7 items according to their experiences of depressive symptoms over the previous 2 weeks.
Quality of motivation to reduce sedentary behaviour	Behavioural Regulation in Exercise Questionnaire-2 (BREQ-2)	Participants respond to 19 items according to their motivation to reduce their sedentary behaviour over the previous 4 weeks.
	Visit 2	
Pain	McGill Pain Questionnaire (MPQ)	Participants respond to 11 ‘sensory descriptors’ and 4 ‘affective descriptors’ according to their degree of pain over the previous 7 days.
Fatigue	Multidimensional Assessment of Fatigue (MAF)	Participants respond to 15 items according to their degree of fatigue, and how it has interfered with ability to undertake activities, over the previous 7 days.

Note: The BREQ-2 was adapted to assess quality of motivation to ‘reduce sedentary behaviour’. Physical function measured by the HAQ and DCOOP, were labelled ‘functional disability’ and ‘general functional status’, respectively.

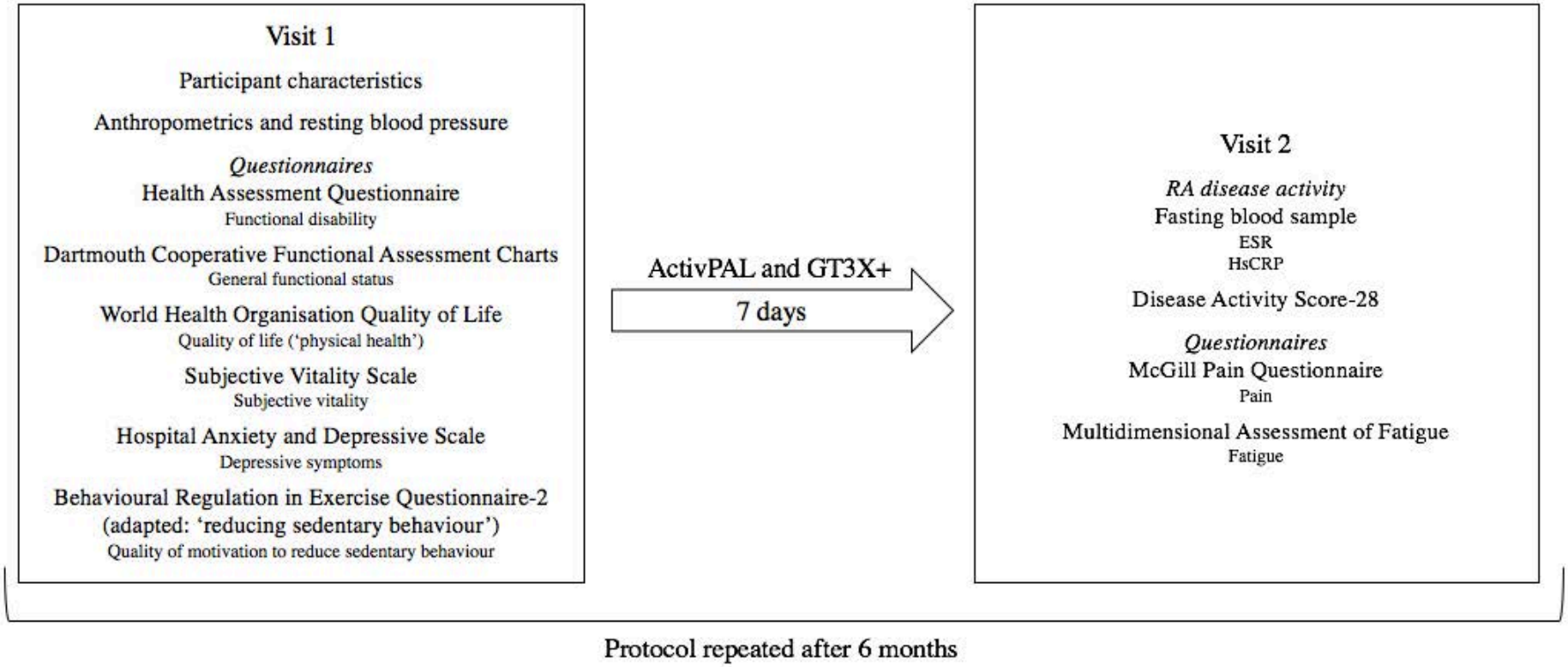

Figure 3.1 Protocol for the longitudinal studies comprising this thesis. This figure will be repeated in Chapters 4-6 and relevant measures employed in those specific chapters will be in **bold.** ESR, erythrocyte sedimentation rate; HsCRP, high-sensitivity C-reactive protein

Overview of participants recruited to studies in Chapters 4-6 of this thesis

In total, n = 104 people living with RA were recruited to this longitudinal study and underwent the protocols detailed above at baseline. These participants comprise the study samples for Chapters 4, 5 and 6 of this thesis.

Figure 3.2 displays the flow of participants through the study, and details the number of participants lost due to follow-up and invalid activPAL or GT3X+ data.

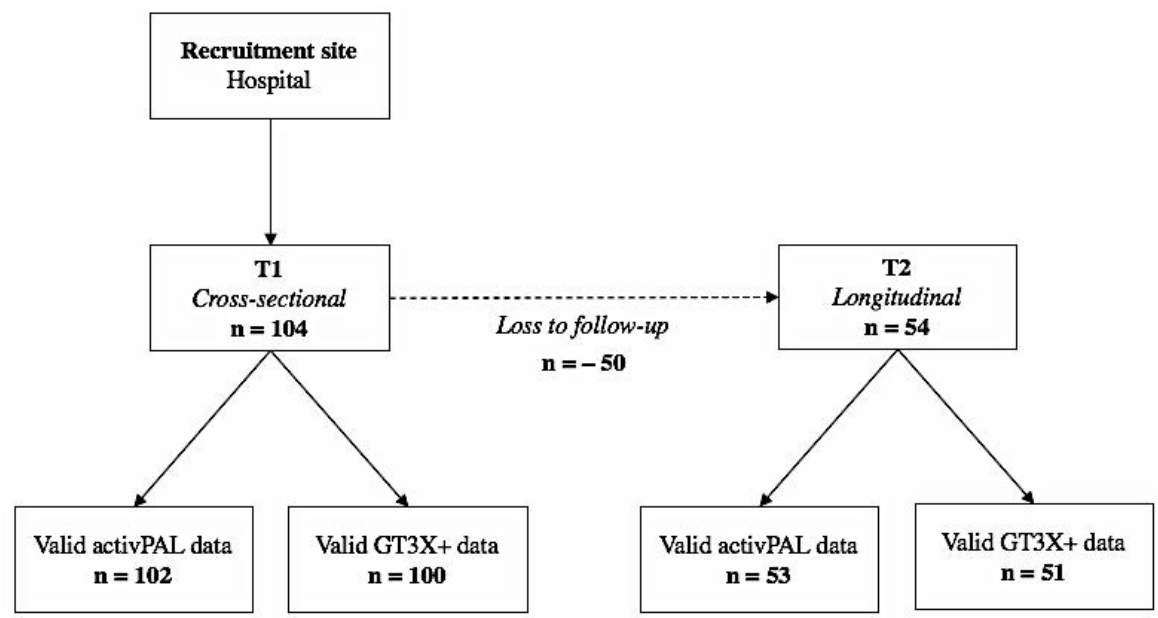

Figure 3.2 Overview of recruited participants in the longitudinal studies of Chapters 4-6. T1, Time Point 1; T2, Time Point 2; n, number of participants

Note: ⟶ Participants recruited from the same hospital in Dudley, England

- - - - - - ▸ 6-month period between T1 and T2 (no intervention)

Cross-sectional data (T1): activPAL (n = 102), GT3X+ (n = 100)
Loss to follow-up, due to: planned termination of data collection (n = 47), lack of time (n = 3)
Longitudinal data (T2): activPAL (n = 53), GT3X+ (n = 51)

Participant characteristics

Table 3.2 provides an overview of participant characteristics for RA patients recruited to this longitudinal study. Below, the demographics of the sample, as well as important features of their RA disease, physical health and levels of sedentary time and PA, are described at T1 and T2. The results of statistical tests employed to examine any differences in these variables at T2, which may occur due to participants lost to follow-up or invalid activPAL or GT3X+ data, are reported.

Demographics. At T1, 71% of the sample were female. This is representative of the RA population, in which the proportion of females is higher than males (Deane et al., 2017; Wasserman, 2018). Participants were also largely Caucasian (n = 99), with the remainder of the sample Asian-Indian (n = 2), Black Caribbean (n = 2) or Arab (n = 1). The majority of participants reported their marital status as 'married' (n = 67), with others reporting that they were 'single' (n = 12), 'divorced' (n = 12), 'widowed' (n = 11) or 'with a partner' (n = 2). On average, participants were 58 years old, with n = 34 participants (33%) ≥65 years old (considered 'older adults') (Sparling, Howard, Dunstan, & Owen, 2015).

RA disease and treatment regimen. At T1, on average, participants had moderate RA disease activity (DAS-28 >3.2 – ≤5.1) (Makinen et al., 2007) and moderate-severe disease severity (average HAQ score ranged between 1-2) (Bruce & Fries, 2003). Average disease duration was approximately 10 years. Overall, 90% of participants were on disease-modifying anti-rheumatic drugs (DMARDs), 14% were on anti-tumour necrosis factor (anti-TNF) treatment and 18% reported taking non-steroidal anti-inflammatory drugs (NSAIDs).

Physical health. According to RA-specific BMI criteria (Stavropoulos-Kalinoglou et al., 2007), on average, participants in this study were classed as 'obese' (>28kg/m^2), with

35.78% body fat, at T1. Twenty-nine participants were taking blood pressure medication to treat high BP, and comorbidities included depression (n = 14), asthma (n = 9), type 2 diabetes (n = 4), underactive thyroid (n = 4), CVD (angina, ischemic heart disease [n = 3]), chronic obstructive pulmonary disease (n = 2), glaucoma (n = 1), hyperthyroidism (n=2), type 1 diabetes (n = 1), anxiety (n = 1), post-traumatic stress disorder (n = 1) and breast cancer (n = 1). Participants' BP was higher than normal range, according to the 'normotension' BP phenotype (clinically measured systolic BP <120 mmHg; clinically measured diastolic BP <80 mmHg) (Blood Pressure UK, 2008), and BP values were comparable to other studies in RA (Yu et al., 2018).

Sedentary time and physical activity. At T1, average daily sedentary time estimates were 9h/day and 11h/day for the activPAL and GT3X+, respectively. A larger proportion of the day was spent in activPAL-assessed standing (4h/day) compared to stepping (2h/day). Similarly, participants spent greater time in GT3X+-assessed LPA (2h/day) compared to MPA (1h/day).

Independent samples *t*-test and chi-square analysis demonstrated no significant differences between participants included at T2 (n = 54), and those lost between time points (lost to follow-up, n = 50), regarding all measured variables (all $p>.05$): demographic factors (biological sex, ethnicity, marital status and age), RA disease (RA duration, disease activity [DAS-28] and disease severity [HAQ functional disability]), treatment regimen (DMARDs, anti-TNF treatment and NSAIDs), physical health (BMI [kg/m^2], body fat [%] number of comorbidities, BP) and objectively-assessed behaviour (% activPAL- and GT3X+-assessed behaviour per day).

Table 3.2 Descriptive statistics for the total sample at T1 and T2

	n	T1	n	T2	*p* value
Demographics					
Biological sex (% female)	74	71%	38	70%	.86
Age (years)	104	57.93 ± 12.55	54	58.81 ± 12.06	.75
Ethnicity (% Caucasian)	99	95%	52	96%	.38
Marital status (% married)	67	64%	38	70%	.70
RA disease and treatment regimen					
RA duration (years)	104	10.28 ± 10.42	54	9.56 ± 9.04	.45
DAS-28	104	3.97 ± 1.51	54	4.00 ± 1.45	.22
HAQ functional disability	104	1.25 ± 0.81	54	1.14 ± 0.86	.59
DMARDs (%)	94	90%	47	87%	.43
Anti-TNF (%)	15	14%	11	20%	.32
NSAIDs (%)	19	18%	11	20%	.28
Physical health					
Height (m)	104	1.65 ± 0.10	54	1.65 ± 0.10	.80
Weight (kg)	104	80.49 ± 20.49	54	81.36 ± 21.94	.80
BMI (kg/m^2)	104	29.28 ± 6.23	54	29.61 ± 6.62	.92
Body fat (%)	103	35.78 ± 8.49	53	35.72 ± 9.57	.55
Systolic BP (mmHG)	104	130 ± 15	54	131 ± 13	.48
Diastolic BP (mmHG)	104	77 ± 10	54	77 ± 8	.08

ActivPAL					
Valid wear time (min/day)	102	913.02 ± 56.74	53	941.34 ± 60.39	.13
Sedentary (min/day)	102	546.05 ± 116.59	53	574.82 ± 98.81	.49
Standing (min/day)	102	267.51 ± 101.00	53	266.63 ± 92.72	.26
Stepping (min/day)	102	99.44 ± 37.39	53	99.91 ± 40.34	.16
Sedentary (%)	102	59.98 ± 12.91	53	61.39 ± 11.63	.33
Standing (%)	102	29.16 ± 10.47	53	28.07 ± 8.92	.41
Stepping (%)	102	10.87 ± 3.96	53	10.54 ± 4.04	.30
GT3X+ (VM)					
Valid wear time (min/day)	100	881.66 ± 64.91	53	890.57 ± 70.65	.05
Sedentary (min/day)	100	682.74 ± 72.52	53	690.65 ± 67.54	.44
LPA (min/day)	100	113.42 ± 35.41	53	113.97 ± 35.48	.45
MPA (min/day)	100	85.48 ± 34.59	53	86.00 ± 37.37	.21
Sedentary (%)	100	77.48 ± 6.41	53	77.69 ± 6.74	.59
LPA (%)	100	12.86 ± 3.92	53	12.77 ± 3.90	.88
MPA (%)	100	9.70 ± 3.70	53	9.55 ± 3.74	.43

n, number of participants; T1, Time Point 1; T2, Time Point 2; RA, Rheumatoid Arthritis; DAS-28, Disease Activity Score-28; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; DMARDs, disease-modifying anti-rheumatic drugs; Anti-TNF, anti-tumour necrosis factor; NSAIDs, non-steroidal anti-inflammatory drugs; BMI, body-mass index; BP, blood pressure; CVD, cardiovascular disease; LPA, light-intensity physical activity; MPA, moderate-intensity physical activity

Note: Values are percentages (%) or mean ± standard deviation. Due to functional disability, 1 person could not access the Tanita scales for measurement of body fat (%) at both time points. Collectively 92% and 94% of participants were on some form of treatment to control their disease activity at T1 and T2, respectively (DMARDs, anti-TNF treatment, NSAIDs). *p* values are reported, and * $p < .05$ and ** $p < .01$ represent any significant differences in variables between participants included at T2, and those lost to follow-up. Additional information relevant to Chapters 4, 5 and 6 will be presented within each chapter.

CHAPTER 4

THE BI-DIRECTIONAL ASSOCIATIONS OF HEALTH WITH SEDENTARY TIME AND PHYSICAL ACTIVITY IN RHEUMATOID ARTHRITIS

Abstract

Aim: This study examined longitudinal associations between pertinent aspects of RA health with device-assessed sedentary time and physical activity (PA) in Rheumatoid Arthritis (RA). The presence of bi-directional associations was also tested. **Method:** RA patients completed physical assessments and questionnaires to measure pain, fatigue, physical function, quality of life and psychological well-being. A fasting blood sample determined high-sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate. Disease Activity Score-28 (DAS-28) was assessed. Participants wore an activPAL and GT3X+ to measure free-living 7-day sedentary time and PA. This protocol was repeated after 6 months. *Statistical analysis:* In regressions, health variables were modelled as 'predictors' of sedentary time and PA. Bi-directional path analysis were conducted to determine whether RA health could be a cause *and* consequence of sedentary time and PA. **Results:** Longitudinal regression analysis revealed that change in health outcomes were associated with change in activPAL-assessed sedentary time (hsCRP [ß = .45], pain [ß = .28], fatigue [ß = .29], general functional status [ß = .42], quality of life [ß = -.38], subjective vitality [ß = -.40]), and associated with activPAL-assessed standing (hsCRP [ß = -.40], pain [ß = -.30], fatigue [ß = -.32], general functional status [ß = -.44], quality of life [ß = .41], subjective vitality [ß = .37]) and stepping time (depressive symptoms [ß = -.23]). Most relationships were shown to be bi-directional. **Conclusion:** ActivPAL-assessed behaviours showed a multitude of associations with RA health. Several of these relationships were bi-directional in nature – pertinent aspects of health in RA, might be a cause *and* consequence of sedentary time and PA in this patient group. This provides scope for intervention targeting sedentary behaviour change in order to improve important clinically- and patient-important outcomes in people with RA.

Introduction

Rheumatoid Arthritis (RA) is a chronic autoimmune condition (Angelotti et al., 2017) affecting 0.5-1% of adults worldwide (Uhlig et al., 2014; Wasserman, 2018). High-grade systemic inflammation that is characteristic of RA, causes musculoskeletal deterioration which contributes to joint pain and functional disability in these patients (Smolen et al., 2016a; Uhlig et al., 2014). People with RA may also experience high levels of fatigue and depression (Katz, 2017a, 2017b; Matcham et al., 2013). These disease manifestations can adversely impact the patient's quality of life (Matcham et al., 2014; Rosa-Goncalves et al., 2018; Senra et al., 2017).

RA is typically treated with pharmacological treatment, which has considerably improved over the last 3 decades. A strategy termed 'treat-to-target' involves early intervention with traditional disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate, and the more recently introduced biologic DMARDs, such as anti-tumour necrosis factor (anti-TNF) treatments, aiming to tightly control RA inflammatory disease activity, which is usually monitored with the Disease Activity Score-28 (DAS-28) (Prevoo et al., 1995; Smolen et al., 2017; van Gestel et al., 1998; Versteeg et al., 2018). However, treat-to-target approaches to RA management are occasionally ineffective at controlling disease activity, while many patients who achieve well-controlled disease activity still report symptoms such as pain, fatigue, functional disability and compromised psychological well-being (Santos et al., 2019; Taylor et al., 2016). Additionally, advances in treatment has incurred a 300% increase in direct healthcare costs (Chaudhari, 2008). Thus, non-pharmacological management of RA and a shift towards more 'holistic' methods, has attracted considerable research interest among healthcare professionals, academics and patients (Metsios & Kitas, 2018; Santos et al., 2019; Scott, Machin, Mallen, & Hider, 2018; Summers et al., 2019). A combination of pharmacological and non-pharmacological methods has been suggested for the treatment of RA (Scott et al.,

2018). While advancements in pharmaceutical intervention has dramatically improved clinically- and patient-important outcomes, non-pharmacological methods can offer self-management of RA, and potentially alleviate the impact of disease that 'treat-to-target' approaches do not directly address (e.g., subjective experiences of pain and fatigue) (Santos et al., 2019; Scott et al., 2018; Taylor et al., 2016).

Physical activity (PA) has been advocated as a non-pharmacological approach for managing disease among people with RA, with specific recommendations for participation endorsed by leading organisations worldwide (e.g., European League Against Rheumatism [EULAR] and American College of Rheumatology) for research into the management of RA (Rausch Osthoff et al., 2018; Santos et al., 2019). Certainly, the benefits of moderate-to-vigorous-intensity PA (MVPA, ≥3 metabolic equivalents [METs]) for improving disease outcomes in people with RA has been extensively documented. For example, studies indicate higher levels of MVPA are beneficially associated with systemic inflammation, disease activity, physical function, pain, fatigue and psychological well-being in this patient group (Cooney et al., 2011; de Jong et al., 2003; Loppenthin et al., 2015; Metsios & Kitas, 2018; Metsios et al., 2015; Plasqui, 2008; Rahnama & Mazloum, 2012; Rongen-van Dartel et al., 2015; Verhoeven et al., 2016). However, debilitating symptoms of RA, such as pain, fatigue and compromised physical function, may prevent a patient engaging in MVPA (Tan et al., 2019; Veldhuijzen van Zanten et al., 2015). People with RA may therefore engage in low levels of MVPA (Tierney et al., 2012) and spend long periods of the day engaged in sedentary behaviour (Fenton et al., 2018b).

Sedentary behaviour is defined as any waking activity expending energy ≤1.5 METs whilst in a sitting/reclining/lying posture (SBRN, 2012; Tremblay et al., 2017). It is distinct from 'physical inactivity' which is more precisely operationalised as lack of engagement in

recommended levels of MVPA (Owen et al., 2010; van der Ploeg & Hillsdon, 2017). Sedentary behaviour is regarded as hazardous for health, with increasing evidence linking it with elevated inflammation in clinical and non-clinical populations (Carson et al., 2014; Carter et al., 2017; Falconer et al., 2014; Ford & Caspersen, 2012; Healy et al., 2011b; Henson et al., 2013). Adverse associations between sedentarity with pain, fatigue, physical function and depression have also been documented in older adults (Balboa-Castillo et al., 2011; Dogra & Stathokostas, 2012; Okely et al., 2019; Park et al., 2018; Rosenberg et al., 2016; Santos et al., 2012; Sardinha et al., 2015; Seguin et al., 2012; van der Berg et al., 2014).

Fenton et al. (2018b) reported that people with RA typically spend 9h/day engaged in sedentary behaviour. The high accrual of sedentary time in this patient group, may perpetuate negative health outcomes already prevalent in RA, but few studies have examined these relationships. For example, sedentary time has been related to both clinically- and patient-important outcomes among people with RA (e.g., disease activity and physical function) (Fenton et al., 2018b; Summers et al., 2019; Thomsen et al., 2017). In a recent qualitative study, there was a call for interventions to reduce sedentary time in the RA population (Thomsen et al., 2015). However, prior to their development, it is critical that high-quality evidence is generated to establish the relationships between sedentariness with health in RA. In addition, we must consider that by reducing sedentary time, naturally, upright behaviours requiring >1.5 METs (PA) will constitute an increased proportion of their day. Interestingly, ‘non-exercise’ behaviours, encompassing sedentary behaviour and light-intensity PA (LPA, 1.6-2.9 METs), have been reported to comprise most of the waking day in RA (Hammam et al., 2019; Summers et al., 2019). Thus, it is of value to investigate the role of LPA, as well as sedentary behaviour, for health in RA.

Participation in LPA has been associated with health outcomes in non-RA populations. For example, LPA has been linked with improved physical function in older adults (Buman et al., 2010; Ekwall et al., 2009; Marques et al., 2014) and people with osteoarthritis (White et al., 2017). RA studies are in their infancy, but have revealed associations between engagement in LPA with lower disease activity, better physical function and enhanced psychological well-being (Fenton et al., 2018c; Khoja et al., 2016; Summers et al., 2019). LPA also shows a strong inverse correlation with sedentary time among people with RA (Fenton et al., 2017), suggesting that replacing sedentary time with LPA is a viable approach to sedentary behaviour change in this patient group. Thus, LPA might be a vehicle for increasing levels of PA and possibly reduce the burden of disease in this patient group, particularly where pain, fatigue and functional disability might preclude engagement in MVPA (Tan et al., 2019; Veldhuijzen van Zanten et al., 2015).

The notably low quantity and quality of studies investigating important relationships between sedentary behaviour and LPA with health indicators in RA, has been highlighted by EULAR (Rausch Osthoff et al., 2018) and several researchers (Fenton et al., 2018b; O'Brien et al., 2018). Certainly, most evidence elucidating relationships between sedentary behaviour and LPA with pertinent RA outcomes is based on cross-sectional studies, which reduces the predictive value of the role of sedentary time and LPA with health in this patient group (Carlson & Morrison, 2009; Solem, 2015). For example, important RA symptomology, such as pain and fatigue, could be determinants of higher sedentarity and lower levels of LPA, and/or consequences of these behaviours. Indeed, some cross-sectional studies propose health variables as outcomes of sedentary time and LPA (Fenton et al., 2018c; Khoja et al., 2016), whilst others suggest health variables are predictors of these behaviours in RA (Summers et al., 2019). It is important to discover if these relationships are reciprocal by nature, in order to

confirm scope to intervene and subsequently improve health outcomes in this patient group (van der Ploeg & Hillsdon, 2017). Research which moves beyond cross-sectional design is therefore required to gain a deeper understanding about the potential bi-directionality of these associations. For example, longitudinal studies analyse data beyond a single moment in time and provide some insight into direction of change (Carlson & Morrison, 2009; Solem, 2015).

Further, a number of extant cross-sectional studies rely on patients to accurately self-report their sedentary time and PA accumulated throughout the day, which may introduce social desirability bias and errors in recall (Atkin et al., 2012; Healy et al., 2011a; Sylvia et al., 2014). Device-based measurement methods, such as accelerometers and posture sensors, offer a more objective measure of free-living behaviour, with superior validity and reliability compared to self-report (Healy et al., 2011a; Sylvia et al., 2014). Accelerometers enable the frequency, intensity and duration of movement behaviour to be quantified, based on accelerations of human movement. However, the ability of accelerometers to detect posture (sitting/reclining/lying vs. standing) – a fundamental element of the definition of sedentary behaviour (SBRN, 2012; Tremblay et al., 2017) – is limited (An et al., 2017; Kozey-Keadle et al., 2011). The activPAL (PAL Technologies Ltd., Glasgow, UK) is a posture sensor that can distinguish between sitting and standing postures with high accuracy (Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016). However, whilst the activPAL is considered the gold standard measure of free-living sedentary time (Chastin & Granat, 2010; Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016), very few RA studies have employed this device to examine the role of sedentary time in RA (Thomsen et al., 2017).

In the present study, device-based measures were employed to assess free-living sedentary time and PA, to; 1) determine associations between clinically- and patient-important

RA outcomes, with objectively-assessed sedentary time and PA, and 2) test the presence of bi-directional relationships in these associations in people with RA.

Method

The methodology for the current study is described in Chapter 3 of this thesis. Figure 4.1 illustrates the specific measures employed[1].

Statistical analysis

Preliminary analysis: Statistical analysis was conducted using SPSS and AMOS software (IBM Corporation, Armonk, NY [version 24]). Descriptive statistics were computed for all measured variables at Time Point 1 (T1) and Time Point 2 (T2), and change scores (change = T2 – T1). Kolmogorov-Smirnov tests of normality were conducted to check normality of data, in addition to formal inspection of graphs (histograms, Q-Q plots). Non-normally data were log-transformed to try and achieve normal distribution of data. However, despite applying suitable transformations (e.g., log transformation), normal distribution was not attained for several variables. Consequently, bootstrapping – a non-parametric resampling procedure – was employed in all subsequent regression analysis to account for non-normal distribution of the data.

[1] For the remainder of Chapter 4, questionnaires will be referred to in acronym form. Specifically, Health Assessment Questionnaire = HAQ, Dartmouth Cooperative Functional Assessment Charts = DCOOP, World Health Organisation Quality of Life = WHOQOL-BREF, Subjective Vitality Scale = SVS, and Hospital Anxiety and Depression Scale = HADS.

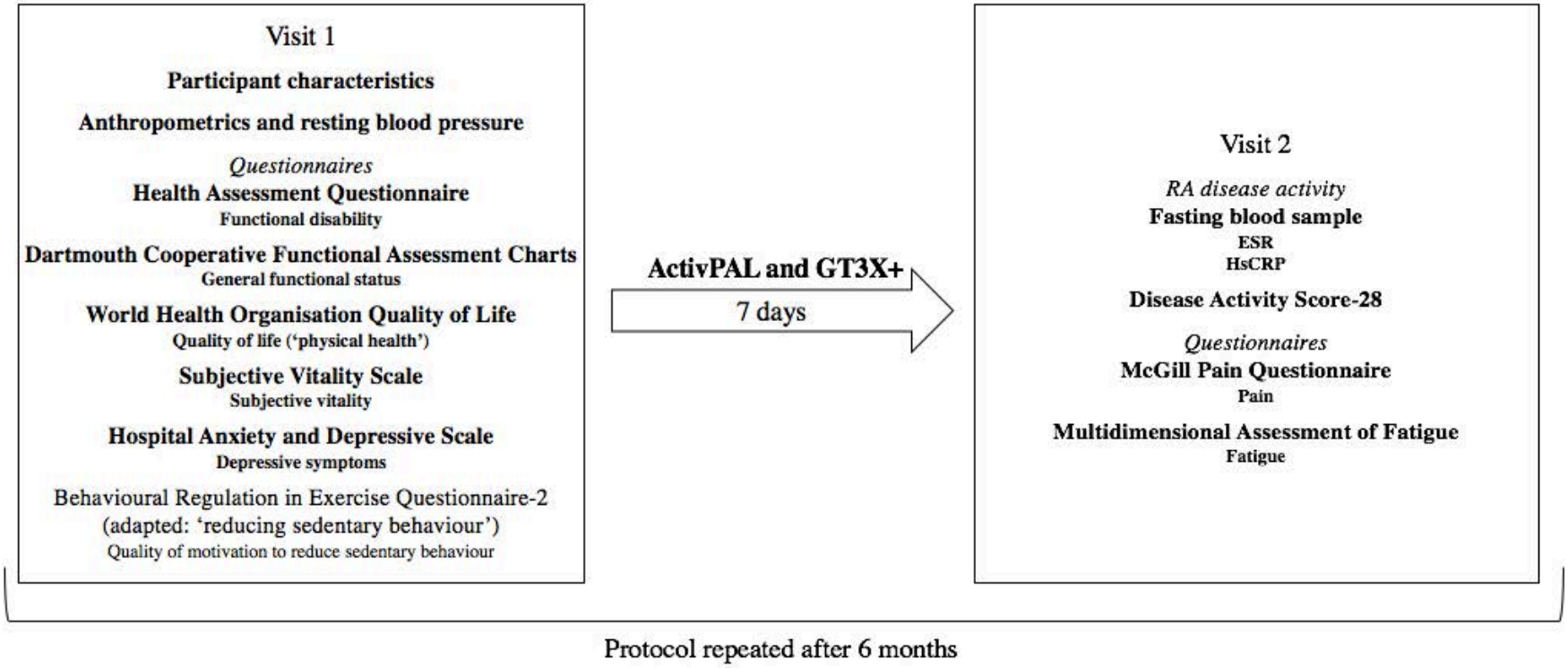

Figure 4.1 Protocol for Chapter 4 of this thesis. Measures specific to this chapter are in **bold.** ESR, erythrocyte sedimentation rate; HsCRP, high-sensitivity C-reactive protein. This study employed a longitudinal design. Participants visited the hospital for data collection at 2 time points ('Time Point 1' [T1] and 6-month follow-up 'Time Point 2' [T2]). At T1 and T2, the same protocols were employed. At T1 and T2, participants attended the hospital for 'Visit 1' and 'Visit 2', separated by 7 days.

Bootstrapping discards parametric statistical assumptions and robustly calculates 95% confidence intervals (CI) by resampling data (typically x ≥1000 samples) from the original sample (Efron, 1987; Efron & Tibshirani, 1986; Efron & Tibshirani, 1994; Hopkins, Marshall, Batterham, & Hanin, 2009; Puth, Neuhauser, & Ruxton, 2015). Bootstrapping has been recommended to deal with non-normal distribution of data, and has been applied in regression analysis (Wright, London, & Field, 2011) examining associations between health and behaviour (Fenton, Duda, Appleton, & Barrett, 2017). It has been argued that bootstrapping holds advantages over and above conventional statistical tests. For example, this resampling procedure is simple to undertake, avoids the challenges of assumption violation and simulates obtaining data from a large sample, which is ideal for research with small sample sizes (Scharkow, 2017; Wood, 2004). It has also been suggested that bootstrapping will be universally applied to sample data in future research, over and above selection of conventional parametric tests (Howell, 2007; Wright et al., 2011).

Bootstrapping is employed in research following consideration of; 1) whether the sample in the study represents the population in question, and 2) the sample size (Scharkow, 2017). In this study, 'bias-corrected and accelerated' bootstrapping was applied to all data in regression and bi-directional path analysis, using 1000 samples with 95% CI (Efron & Tibshirani, 1986; Kruisdijk et al., 2017; Puth et al., 2015; Wright et al., 2011). Bias-corrected and accelerated bootstrapping (Efron, 1987) is a commonly-used method, and is recommended for application in small sample sizes, although a sample size of at least n = 20 for generating 95% CI, and n = 50 for generating 99% CI, has been advocated (Chernick & LaBudde, 2011; Puth et al., 2015; Scharkow, 2017). Descriptive data in Chapter 3 indicated that our sample (longitudinal data set, n = 54) was predominantly female participants, with an average age of 58 years old. This is representative of the RA population, as there are more females and disease

onset typically occurs beyond 30 years old (Wasserman, 2018). Additionally, participant characteristics of height, weight, BMI, body fat percentage, DAS-28, disease severity (HAQ) and disease duration were similar to other RA studies (Metsios et al., 2009; Sokka et al., 2008; Stavropoulos-Kalinoglou et al., 2013).

Main analysis: Data analysis was conducted in 3 phases; 1) correlation and regression analysis examined cross-sectional relationships between health variables with objectively-assessed sedentary time and PA at T1, 2) change scores were computed and used to examine longitudinal relationships between health variables with objectively-assessed sedentary time and PA, via correlation and regression analysis, and 3) results from regression analysis informed the final phase of investigation, testing bi-directional associations via path models.

1) Cross-sectional analysis (T1)

Pearson's correlations were conducted using T1 data, to examine the cross-sectional bivariate associations between health (DAS-28, high-sensitivity C-reactive protein [hsCRP], pain, fatigue, HAQ functional disability, DCOOP general functional status, quality of life, subjective vitality and depressive symptoms) with activPAL-assessed sedentary, standing and stepping time, and GT3X+-assessed sedentary time, LPA and MPA (% waking behaviour per day). Following this, multivariate regression analysis explored cross-sectional associations between the aforementioned health variables with objectively-assessed behaviour, adjusting for age and biological sex. These co-variates were determined owing to the fact that that previous research suggests age and biological sex are associated with health parameters and free-living behaviour in RA (Fenton et al., 2017; Fenton et al., 2018c).

The ultimate aim of this study is to produce findings that are relevant, and can be applied in clinical practice. With this in mind, regression models were constructed to align with a 'clinical perspective', in which RA disease is first hypothesised to influence lifestyle

behaviours (such as sedentary time and PA) (Hernandez-Hernandez, Ferraz-Amaro, & Diaz-Gonzalez, 2014; Iversen et al., 2017). Therefore, health variables were entered into regression models as independent variables ('predictors') and activPAL- and GT3X+-assessed behaviours (% waking behaviour per day) were entered as dependent variables ('outcomes')[2].

Unstandardised bootstrapped coefficients (B) and 95% CI were computed to determine the direction and statistical significance of associations. Significant relationships were confirmed where bootstrapped 95% CIs did not cross zero. Standardised non-bootstrapped coefficients (ß) were also reported to aid interpretation of the strength of observed relationships (small = .1; medium = .3; large = .5) (Cohen, 1992). R^2 values were interpreted as the unique variance in objectively-assessed sedentary time or PA explained by the health variable, age and biological sex.

2) Longitudinal analysis (change from T1-T2)

As per cross-sectional analysis, regression models examined whether change in health variables (T1-T2) significantly predicted change in activPAL- and GT3X+-assessed sedentary time and PA (T1-T2), adjusting for age and biological sex. Regression analysis were interpreted in the same manner as cross-sectional regression models.

[2]ActivPAL- and GT3X+-assessed behaviours were entered into regression models expressed as percentages of device wear time (% behaviour per day = (device-assessed behaviour [min/day]/total device wear time [min/day]) x 100) in cross-sectional and longitudinal analysis to reduce the number of variables in each model, thus increasing statistical power.

3) Bi-directional analysis

Results from longitudinal analysis were used to inform bi-directional analysis. Specifically, where health variables were significantly 'predicting' activPAL- and GT3X+-assessed sedentary time and PA in longitudinal regression analysis (according to bootstrapped data), these associations were tested in path analysis to test bi-directionality.

If significant associations observed in longitudinal regression analysis for non-bootstrapped data were between *known* normally distributed variables (tested with Kolmogorov-Smirnov tests), these were included in bi-directional analysis. Additionally, we also considered that the smaller sample size for longitudinal analysis may have reduced the statistical power of regression models, relative to cross-sectional analysis. Therefore, any significant associations reported in cross-sectional models which demonstrated comparable effect sizes to longitudinal models (± ß = .1), were also tested with bi-directional path models.

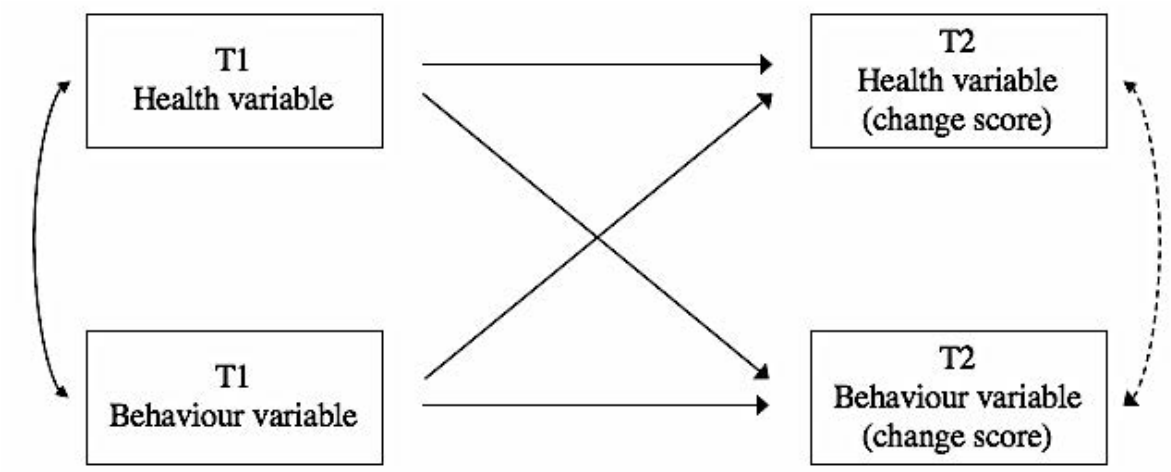

Figure 4.2 Example path model used to test for bi-directional associations
T1, Time Point 1; T2, Time Point 2; 'Health variable', RA health variable; 'Behaviour variable', activPAL-assessed behaviour (sedentary, standing or stepping time)

Note: ⟶ Path specified between variables

⟷ Bi-directional association tested

Figure 4.2 illustrates the model employed to investigate bi-directional associations between health variables with objectively-assessed sedentary time and PA. Owing to; 1) the small sample size (not permitting a full measurement model), and 2) several of the variables were 'directly measured' (DAS-28, hsCRP, activPAL- and GT3X-assessed behaviours), all variables were modelled as observed variables (Byrne, 2010).

To explicate Figure 4.2, the 'T2 health variable' and 'T2 behaviour variable' represent change in the variable from T1 to T2. Thus, T2 variables in the model represent 'change scores' (since T1 variables are controlled for), and by correlating these T2 variables, we can test whether the changes of these variables are associated. A significant association observed between T2 variables specified in the model (changes in these 2 variables from T1 to T2 are correlated), indicates a bi-directional association. In this study, bootstrapped 95% CI were used to determine statistical significance – significant bi-directional associations were identified where the 95% CI did not cross zero.

Good fit between the hypothesised bi-directional model and the data must also be confirmed in order to trust the parameters specified. Therefore, model fit was assessed using the chi-square statistic (χ^2), comparative fit index (CFI), Tucker Lewis Index (TLI) and root mean square error of approximation (RMSEA, 90% CI). This selection of model fit indices is suited to small sample sizes (Schermelleh-Engel & Moosbrugger, 2003). Model fit criteria were; non-significant χ^2 (p >.05), CFI and TLI values ≥.95, and RMSEA <.06 with 90% CI (lower boundary) containing 0, suggesting an excellent fit between the model and the data. Good model fit criteria were; non-significant χ^2 (p >.05), CFI and TLI values ≥.90, and RMSEA <.08 with 90% CI (lower boundary) <.05 (Schermelleh-Engel & Moosbrugger, 2003; Schreiber, Nora, Stage, Barlow, & King, 2006).

It should also be noted, that diagonal arrows specified in the hypothesised model allow investigation of whether the ‘T1 health variable’ predicts change in the ‘T2 behaviour variable’, and vice versa (associations tested in prior regression models within this chapter). However, owing to the small sample size, we were unable to examine these associations via path models due to low statistical power.

Results

Key characteristics of the study sample have been previously reported in Chapter 3 (Table 3.2) of this thesis. Table 4.1 presents the descriptive statistics for specific variables included in the current thesis chapter. Loss of participants between T1 and T2 (n = 50) was predominantly due to planned termination of data collection (n = 47) and lack of time (n = 3).

Table 4.1 Descriptive statistics for the total sample at T1 and T2, and change between T1 and T2 (change = T2 – T1)

	n	T1	n	T2	n	Change
Biological sex (% female)	74	71%	38	70%	X	X
Age (years)	104	57.93 ± 12.55	54	58.81 ± 12.06	54	0.50 ± 0.50
RA outcomes as 'predictors'						
DAS-28	104	3.97 ± 1.51	54	4.00 ± 1.45	54	0.20 ± 1.27
hsCRP (mg/l)	102	6.07 ± 7.64	52	6.18 ± 8.25	52	0.90 ± 8.34
Pain	104	12.72 ± 10.94	54	13.37 ± 10.87	54	2.24 ± 11.53
Fatigue	104	24.89 ± 13.06	54	23.81 ± 13.21	54	-1.54 ± 8.65
HAQ functional disability	104	1.25 ± 0.81	54	1.14 ± 0.86	54	-.07 ± 0.44
DCOOP general functional status	104	17.42 ± 4.75	54	17.22 ± 4.60	54	0.28 ± 3.41
Quality of life (physical health)	104	21.17 ± 5.76	54	22.17 ± 6.22	54	0.76 ± 3.46
Subjective vitality	104	3.33 ± 1.65	54	3.40 ± 1.69	54	0.14 ± 1.24
Depressive symptoms	104	5.41 ± 3.64	54	5.48 ± 4.50	54	0.20 ± 2.86
ActivPAL						
Valid wear time (min/day)	102	913.02 ± 56.74	53	941.34 ± 60.39	53	20.49 ± 54.16
Sedentary (min/day)	102	546.05 ± 116.59	53	574.82 ± 98.81	53	37.92 ± 65.31
Standing (min/day)	102	267.51 ± 101.00	53	266.63 ± 92.72	53	-13.10 ± 59.86
Stepping (min/day)	102	99.44 ± 37.39	53	99.91 ± 40.34	53	-4.29 ± 19.83
Sedentary (%)	102	59.98 ± 12.91	53	61.39 ± 11.63	53	2.76 ± 6.82
Standing (%)	102	29.16 ± 10.47	53	28.07 ± 8.92	53	-2.06 ± 5.93
Stepping (%)	102	10.87 ± 3.96	53	10.54 ± 4.04	53	-0.70 ± 2.15

GT3X+ (VM)						
Valid wear time (min/day)	100	881.66 ± 64.91	53	890.57 ± 70.65	51	-5.68 ± 58.24
Sedentary (min/day)	100	682.74 ± 72.52	53	690.65 ± 67.54	51	-2.08 ± 53.79
LPA (min/day)	100	113.42 ± 35.41	53	113.97 ± 35.48	51	-0.47 ± 19.84
MPA (min/day)	100	85.48 ± 34.59	53	86.00 ± 37.37	51	-3.08 ± 20.23
Sedentary (%)	100	77.48 ± 6.41	53	77.69 ± 6.74	51	0.25 ± 3.56
LPA (%)	100	12.86 ± 3.92	53	12.77 ± 3.90	51	0.06 ± 2.19
MPA (%)	100	9.70 ± 3.70	53	9.55 ± 3.74	51	-0.31 ± 2.07

n, number of participants; T1, Time Point 1; T2, Time Point 2; DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein; HAQ, Health Assessment Questionnaire; DCOOP, Dartmouth Cooperative Functional Assessment Charts; LPA, light-intensity physical activity; MPA, moderate-intensity physical activity; X, not applicable

Note: Values are percentages (%) or mean ± standard deviation. Only change scores required for longitudinal correlation and regression analysis were computed. The HAQ and DCOOP were measured as indicators of physical function, but labelled as functional disability and general functional status, respectively. HsCRP results were unavailable for 2 participants during analysis with Enzyme-Linked Immunosorbent Assays. At T1, 92% of participants were on some form of medication to control their disease activity (disease-modifying anti-rheumatic drugs [90%], anti-tumour necrosis factor treatment [14%], non-steroidal anti-inflammatory drugs [18%]). Thus, medication was not a factor adjusted for in cross-sectional and longitudinal regression analysis.

Cross-sectional analysis (T1)

Table 4.2 reports results from cross-sectional bivariate correlation analysis carried out at T1. Table 4.3 and Table 4.4 report results from cross-sectional regression analysis with activPAL-assessed and GT3X+-assessed behaviours, respectively.

Regression analysis (adjusted Model 2): For activPAL-assessed behaviours, significant positive relationships were observed between DAS-28, pain, HAQ functional disability and DCOOP general functional status with sedentary time. Significant negative associations were found between quality of life with sedentary time. The inverse significant associations were found with standing time, except for pain. DAS-28, pain, fatigue, HAQ functional disability and DCOOP general functional status were significantly negatively related to stepping time, and quality of life was significantly positively linked to stepping time.

For GT3X+-assessed behaviours, DAS-28, pain, HAQ functional disability and DCOOP general functional status were significantly positively associated with sedentary time. Quality of life was significantly negatively associated with sedentary time. No RA health outcomes were associated with LPA. Significant negative associations were observed between DAS-28, hsCRP, pain, fatigue, HAQ functional disability and DCOOP general functional status with MPA, and significant positive relationships were shown between quality of life with MPA.

Table 4.2 Bivariate correlations between health-related correlates with activPAL- and GT3X+-assessed sedentary time and PA (T1)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1 Age															
2 Sedentary (activPAL)	.05														
3 Standing (activPAL)	.01	-.96**													
4 Stepping (activPAL)	-.18	-.71**	.50**												
5 Sedentary (GT3X+)	.18	82**	-.69**	-.86**											
6 LPA (GT3X+)	.00	-.78**	.72**	.66**	-.85**										
7 MPA (GT3X+)	-.31**	-.60**	.43**	.80**	-.83**	.42**									
8 DAS-28	.12	.29**	-.24*	-.31**	.29**	-.13	-.38**								
9 hsCRP (mg/l)	.08	.18	-.15	-.19	.20*	-.08	-.27**	.34**							
10 Pain	-.04	.21*	-.16	-.26**	.20	-.09	-.25*	.55**	.15						
11 Fatigue	-.17	.19	-.15	-.23*	.13	-.06	-.16	.53**	.22*	.72**					
12 HAQ functional disability	.15	.25*	-.20*	-.28**	.22*	-.11	-.26**	.64**	.08	.57**	.58**				
13 DCOOP general functional status	.00	.29**	-.25*	-.30**	.24*	-.14	-.28**	.62**	.21*	.61**	.76**	.69**			
14 Quality of life (physical health)	-.01	-.33**	.28**	.33**	-.27**	.18	.28**	-.66**	-.28**	-.64**	-.74**	-.76**	-.85**		
15 Subjective vitality	.03	-.19	.16	.17	-.13	.09	.13	-.51**	-.15	-.42**	-.65**	-.57**	-.71**	.68*	
16 Depressive symptoms	-.00	.13	-.11	-.15	.12	-.05	-.17	.60**	.24*	.56**	.68**	.54**	.73**	-.70*	-.70**

LPA, light-intensity physical activity; MPA, moderate-intensity physical activity; DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein; HAQ, Health Assessment Questionnaire; DCOOP, Dartmouth Cooperative Functional Assessment Charts

Note: * $p < .05$; ** $p < .01$. Bivariate correlations were adjusted for activPAL and GT3X+ wear time. Time in sedentary, standing, stepping, LPA and MPA, were calculated as percentages of activPAL and GT3X+wear time, for use in bivariate correlations. All variables are non-transformed.

Table 4.3 Linear regressions between health-related correlates with activPAL-assessed sedentary, standing and stepping time (T1)

	Sedentary				Standing				Stepping			
	B	**95% CI (lower – upper)**	**R^2**	**ß**	**B**	**95% CI (lower – upper)**	**R^2**	**ß**	**B**	**95% CI (lower – upper)**	**R^2**	**ß**
***1* DAS-28**	2.48**	.94 – 4.01	.09	.29**	-1.68*	-2.84 – -.47	.06	-.24*	-.80**	-1.26 – -.34	.10	-.31**
2 DAS-28	2.55**	.95 – 4.05		.30**	-1.77**	-3.00 – -.56		-.26**	-.78**	-1.27 – -.31		-.30**
Age	.01	-.20 – .24	.00	.01	.03	-.15 – .22	.00	.04	-.05	-.10 – .00	.02	-.15
Biological sex	6.76*	1.08 – 12.24	.06	.24*	-5.14*	-9.56 – -.26	.05	-.23*	-1.61*	-3.01 – -.06	.04	-.19*
***1* hsCRP**	.30	-.07 – .80	.03	.18	-.20	-.51 – .05	.02	-.15	-.10*	-.20 – -.01	.03	-.19
2 hsCRP	.23	-.15 – .75		.14	-.16	-.49 – .11		-.12	-.08	-.17 – .01		-.15
Age	.03	-.17 – .22	.00	.03	.03	-.17 – .23	.00	.03	-.06	-.11 – .01	.03	-.17
Biological sex	5.85*	.05 – 11.75	.04	.21*	-4.62*	-8.62 – -.63	.04	-.20*	-1.23	-2.96 – .54	.02	-.14
***1* Pain**	.25*	.03 – .49	.05	.21*	-.15	-.34 – .02	.03	-.16	-.09**	-.16 – -.030	.07	-.26**
2 Pain	.23*	.01 – .49		.20*	-.14	-.31 – .03		-.15	-.09**	-.16 – -.04		-.26**
Age	.06	-.17 – .25	.00	.06	.00	-.15 – .16	.00	.01	-.06*	-.12 – -.00	.04	-.19*
Biological sex	6.02*	.23 – 12.57	.05	.21*	-4.67*	-9.04 – -.39	.04	-.20*	-1.35	-2.94 – .36	.02	-.16
***1* Fatigue**	.19*	.01 – .36	.04	.19[x]	-.12	-.26 – .02	.02	-.15	-.07*	-.13 – -.00	.05	-.23*
2 Fatigue	.19	-.01 – .37		.20*[x]	-.12	-.26 – .03		-.15	-.08*	-.14 – -.01		-.26**
Age	.08	-.14 – .30	.01	.08	-.01	-.18 – .17	.00	-.01	-.07*	-.14 – .00	.05	-.22*
Biological sex	6.17*	-.02 – 12.22	.05	.22*	-4.76*	-9.30 – -.35	.04	-.21*	-1.41	-2.94 – .20	.03	-.16
***1* HAQ functional disability**	.49**	.12 – .83	.06	.25*	-.32*	-.61 – -.04	.04	-.20*	-.17**	-.29 – -.04	.08	-.28**
2 HAQ functional disability	.47**	.11 – .79		.24*	-.32*	-.60 – -.05		-.20*	-.15*	-.27 – -.04		-.25*
Age	.02	-.18 – .23	.00	.01	.03	-.12 – .17	.00	.04	-.05	-.11 – .01	.02	-.15
Biological sex	6.12*	.72 – 11.29	.05	.22*	-4.70	-9.47 – .20	.04	-.21*	1.41	-2.97 – .41	.03	-.16

***1* DCOOP general functional status**	.79**	.31 – 1.25	.09	.29**	-.54*	-.95 – -.09	.06	-.25*	-.25**	-.39 – -.11	.09	-.30**
2 DCOOP general functional status	.76**	.29 – 1.22		.28**	-.51*	-.92 – -.08		-.23*	-.24**	-.38 – -.11		-.30**
Age	.05	-.21 – .31	.00	.05	.01	-.15 – .18	.00	.01	-.06	-.12 – .00	.04	-.18
Biological sex	5.95*	-.20 – 11.80	.04	.21*	-4.59	-9.64 – .03	.04	-.20*	-1.36	-2.93 – .09	.02	-.16
***1* Quality of life (physical health)**	-.74**	-1.15 – -.32	.11	-.33**	.51**	.18 – .87	.08	.28**	.23**	.11 – .35	.11	.33**
2 Quality of life (physical health)	-.70**	-1.09 – -.29		-.31**	.48*	.14 – .83		.26**	.22**	.10 – .35		.32**
Age	.05	-.16 – .24	.00	.05	.01	-.16 – .19	.00	.01	-.06*	-.12 – -.00	.04	-.19*
Biological sex	5.53	-.13 – 11.00	.04	.20*	-4.30*	-8.56 – -.50	.04	-.19	-1.23	-2.80 – .47	.02	-.14
***1* Subjective vitality**	-.24*	-.48 – -.01	.03	-.19[x]	.17	-.04 – .39	.03	.16	.07	-.00 – .15	.03	.17
2 Subjective vitality	-.23	-.49 – .03		-.17	.16	-.06 – .37		.15	.07	-.01 – .15		.17
Age	.06	-.14 – .26	.00	.05	.01	-.17 – .18	.00	.01	-.06	-.13 – .00	.04	-.19
Biological sex	6.09*	.30 – 11.61	.05	.22*	-4.68*	-8.70 – -.64	.04	-.21*	-1.41	-3.06 – .38	.03	-.16
***1* Depressive symptoms**	.47	-.30 – 1.16	.02	.13	-.30	-.87 – .25	.01	-.11	-.17	-.35 – .04	.02	-.15
2 Depressive symptoms	.42	-.35 – 1.12		.12	-.26	-.83 – .34		-.09	-.16	-.35 – .06		-.14
Age	.05	-.17 – .25	.00	.05	.01	-.17 – .20	.00	.01	-.06	-.12 – .00	.03	-.18
Biological sex	6.17*	.45 – 12.84	.05	.22*	-4.75*	-9.09 – -.50	.04	-.21*	-1.41	-2.95 – .14	.03	-.16

CI, confidence intervals; DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein; HAQ, Health Assessment Questionnaire; DCOOP, Dartmouth Cooperative Functional Assessment Charts

B, unstandardised coefficient (from bootstrapped data); ß, standardised beta coefficient; R^2, variance explained in the dependent variable (sedentary, standing or stepping time) by the independent variable (health-related correlates)

Note: * $p < .05$; ** $p < .01$. Model ***'1'*** adjusted for activPAL wear time. Model ***'2'*** adjusted for activPAL wear time, age and biological sex. [x]significant/non-significant result for non-bootstrapped, standardised coefficient, was different from bootstrapped, unstandardised coefficient. Sedentary, standing and stepping time were calculated as percentages of activPAL wear time for use in regression analysis.

Table 4.4 Linear regressions between health-related correlates with GT3X+-assessed sedentary time, LPA and MPA (T1)

	Sedentary				LPA				MPA			
		95% CI				95% CI				95% CI		
	B	(lower – upper)	R^2	ß	B	(lower – upper)	R^2	ß	B	(lower – upper)	R^2	ß
***1* DAS-28**	1.23**	.49 – 2.01	.09	.29**	-.32	-.77 – .10	.02	-.13	-.91**	-1.30 – -.56	.14	-.38**
2 DAS-28	1.20**	.45 – 1.97		.29**	-.36	-.84 – .11		-.14	-.84**	-1.23 – -.45		-.35**
Age	.07	-.03 – .17	.02	.13	.01	-.06 – .08	.00	.03	-.08*	-.13 – -.03	.07	-.26**
Biological sex	2.87	-.23 – 5.85	.04	.20*	-1.81	-3.74 – .01	.04	-.21*	-1.06	-2.44 – .44	.02	-.13
***1* hsCRP**	.17*	.03 – .33	.04	.21*	-.04	-.16 – .05	.01	-.08	-.13**	-.23 – -.06	.08	-.27**
2 hsCRP	.14	-.01 – .31		.17	-.02	-.14 – .08		-.04	-.12**	-.21 – -.05		-.24*
Age	.09	-.03 – .19	.03	.17	.00	-.07 – .07	.00	.01	-.09**	-.15 – -.03	.09	-.30**
Biological sex	2.13	-.75 – 5.18	.02	.15	-1.67	-3.65 – .26	.04	-.19	-.47	-1.89 – 1.07	.00	-.06
***1* Pain**	.12*	-.00 – .22	.04	.20[x]	-.03	-.11 – .04	.01	-.09	-.09**	-.14 – -.03	.06	-.25*
2 Pain	.12*	.00 – .22		.19*	-.03	-.11 – .04		-.08	-.09**	-.14 – -.03		-.25**
Age	.09	-.02 – .21	.03	.17	.00	-.07 – .07	.00	.01	-.09**	-.15 – -.04	.10	-.31**
Biological sex	2.55	-.69 – 5.66	.03	.18	-1.72	-3.56 – .20	.04	-.20	-.84	-2.26 – .56	.01	-.10
***1* Fatigue**	.06	-.03 – .16	.02	.13	-.02	-.08 – .04	.00	-.06	-.05	-.10 – .01	.03	-.16
2 Fatigue	.08	-.03 – .18		.15	-.02	-.08 – .03		-.06	-.06*	-.11 – -.01		-.20*
Age	.10	-.00 – .22	.04	.19	.00	-.06 – .06	.00	.00	-.10	-.16 – -.04	.11	-.33**
Biological sex	2.62	-.13 – 5.56	.03	.18	-1.74	-3.64 – .04	.04	-.20*	-.89	-2.56 –.75	.01	-.11
***1* HAQ functional disability**	.21*	.02 - .40	.05	.22*	-.07	-.18 – .05	.01	-.11	-.15*	-.27 – -.03	.07	-.26**
2 HAQ functional disability	.19*	.02 – .36		.19[x]	-.067	-.18 – .05		-.11	-.12*	-.24 – -.01		-.21*
Age	.07	-.03 – .18	.02	.14	.010	-.06 – .07	.00	.03	-.08**	-.13 – -.02	.07	-.27**
Biological sex	2.58	-.25 – 5.33	.03	.18	-1.72*	-3.597 – -.13	.04	-.20*	-.86	-2.43 – .79	.01	-.11

***1* DCOOP general functional status**	.33**	.09 – .58	.06	.24*	-.12	-.28 – .04	.02	-.14	-.22**	-.37 – -.09	.08	-.28**
2 DCOOP general functional status	.32*	.08 – .58		.23*	-.11	-.26 – .02		-.13	-.21**	-.35 – -.07		-.26**
Age	.08	-.01 – .18	.03	.16	.01	-.06 – .07	.00	.02	-.09**	-.15 – -.03	.09	-.29**
Biological sex	2.59	-.22 – 5.24	.03	.18	-1.73	-3.79 – .36	.04	-.20*	-.87	-2.53 – .85	.01	-.11
***1* Quality of life (physical health)**	-.30**	-.50 – -.10	.07	-.27**	.12*	.01 – .23	.03	.18[x]	.18**	.06 – .30	.08	.28**
2 Quality of life (physical health)	-.28**	-.48 – -.08		-.25*	.13	-.01 – .23		.17	.17**	.05 – .29		.26**
Age	.08	-.02 – .19	.03	.16	.01	-.06 – .07	.00	.02	-.09**	-.15 – -.04	.09	-.30**
Biological sex	2.36	-.81 – 5.38	.03	.17	-1.64	-3.53 – .14	.04	-.19	-.74	-2.25 – .82	.01	-.09
***1* Subjective vitality**	-.08	-.20 – .04	.02	-.13	.04	-.03 – .11	.01	.09	.05	-.03 – .12	.02	.13
2 Subjective vitality	-.08	-.20 – .04		-.13	.03	-.04 – .11		.08	.05	-.02 – .12		.13
Age	.09	-.01 – .20	.03	.17	.00	-.06 – .07	.00	.01	-.09**	-.15 – -.04	.10	-.31**
Biological sex	2.56	-.49 – 5.84	.03	.18	-1.72	-3.53 – .20	.04	-.20	-.86	-2.46 – .70	.01	-.10
***1* Depressive symptoms**	.22	-.10 – .51	.02	.13	-.058	-.29 – .17	.00	-.05	-.17	-.33 – .01	.03	-.17
2 Depressive symptoms	.20	-.14 – .51		.12	-.05	-.26 – .17		-.04	-.16	-.33 – .02		-.16
Age	.09	-.02 – .21	.03	.17	.00	-.06 – .07	.00	.01	-.09**	-.14 – -.04	.10	-.31**
Biological sex	2.54	-.30 – 5.31	.03	.18	-1.72*	-3.33 – -.13	.04	-.20	-.83	2.30 – .62	.01	-.10

CI, confidence intervals; DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein; HAQ, Health Assessment Questionnaire; DCOOP, Dartmouth Cooperative Functional Assessment Charts

B, unstandardised coefficient (from bootstrapped data); ß, standardised beta coefficient; R^2, variance explained in the dependent variable (sedentary, LPA or MPA) by the independent variable (health-related correlates)

Note: * $p < .05$; ** $p < .01$. Model ***'1'*** adjusted for GT3X+ wear time. Model ***'2'*** adjusted for GT3X+ wear time, age and biological sex. [x]significant/non-significant result for non-bootstrapped, standardised coefficient, was different from bootstrapped, unstandardised coefficient. Sedentary time, LPA and MPA were calculated as percentages of GT3X+ wear time for use in regression analysis.

Longitudinal analysis

Results from bivariate correlations conducted on longitudinal data are reported in Table 4.5. Table 4.6 and Table 4.7 show results from longitudinal regression analysis employing the activPAL and GT3X+, respectively.

Regression analysis (adjusted Model 2): For activPAL-assessed behaviours, change in hsCRP, pain, fatigue (non-bootstrapped only) and DCOOP general functional status was significantly positively associated with change in sedentary time. Change in quality of life and subjective vitality was significantly negatively associated with change in sedentary time. Change in hsCRP, pain, fatigue and DCOOP general functional status was significantly negatively related to change in standing time. Change in quality of life and subjective vitality was significantly positively associated with standing time. Change in depressive symptoms was significantly negatively related to change in stepping time. No significant associations were observed between RA health outcomes with GT3X+-assessed behaviours.

Comparison of activPAL- and GT3X+-assessed sedentary time. Consistent associations between activPAL- and GT3X+-assessed sedentarity were observed for change in hsCRP, but only for non-bootstrapped regression analysis.

Table 4.5. Bivariate correlations between health-related correlates with activPAL- and GT3X+-assessed sedentary time and PA (longitudinal – T1-T2)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1 Age															
2 Sedentary (activPAL)	.03														
3 Standing (activPAL)	.03	-.95**													
4 Stepping (activPAL)	-.17	-.55*	.27												
5 Sedentary (GT3X+)	.09	.73**	-.56**	-.77**											
6 LPA (GT3X+)	-.09	-.64**	.52**	.61**	-.85**										
7 MPA (GT3X+)	-.05	-.58**	.42**	.68**	-.82**	.39**									
8 DAS-28	.10	.24	-.24	-.11	.03	-.02	-.04								
9 hsCRP (mg/l)	.00	.45**	-.40**	-.34*	.33*	-.23	-.33*	.60**							
10 Pain	-.06	.26	-.27*	-.07	.02	.11	-.16	.49**	.35*						
11 Fatigue	.00	.27	-.29*	-.05	.08	-.07	-.07	.31*	.28*	.57*					
12 HAQ functional disability	.30*	.05	-.08	.08	-.05	.04	.05	.24	-.03	.16	.05				
13 DCOOP general functional status	.14	.41**	-.41**	-.18	.15	-.10	-.15	.46**	.30*	.51**	.55**	.35**			
14 Quality of life (physical health)	-.03	-.38**	.41**	.07	-.16	.05	.22	-.25	-.15	-.44**	-.35**	-.16	-.56**		
15 Subjective vitality	-.04	-.38**	.33*	.29*	-.23	.22	.15	-.08	-.12	-.15	-.50**	-.12	-.53**	.43**	
16 Depressive symptoms	.01	.28*	-.24	-.25	.18	-.08	-.23	.00	.11	.37**	.42**	-.08	.56**	-.49**	-.52**

LPA, light-intensity physical activity; MPA, moderate-intensity physical activity; DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein; HAQ, Health Assessment Questionnaire; DCOOP, Dartmouth Cooperative Functional Assessment Charts

Note: * $p < .05$; ** $p < .01$. Bivariate correlations were adjusted for activPAL and GT3X+ wear time. All variables are non-transformed. Time in sedentary, standing, stepping, LPA and MPA, were calculated as percentages of activPAL and GT3X+ wear time, for use in bivariate correlations

Table 4.6 Linear regressions between health-related correlates with activPAL-assessed sedentary, standing and stepping time (longitudinal – T1-T2)

	Sedentary				Standing				Stepping			
		95% CI				95% CI				95% CI		
	B	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**
***1* DAS-28**	1.29	-.42 – 2.90	.06	.24	-1.11	-2.39 – .19	.06	-.24	-.19	-.61 – .25	.01	-.11
2 DAS-28	1.32	-.45 – 3.01		.25	-1.18	-2.39 – .11		-.26	-.14	-.61 – .36		-.09
Age	.13	-3.79 – 4.43	.00	.01	.59	-2.88 – 3.99	.00	.05	-.70	-1.94 – .44	.03	-.16
Biological sex	-1.20	-5.83 – 3.60	.01	-.08	1.73	-2.16 – 5.47	.02	.14	-.53	-1.82 – .67	.01	-.12
***1* hsCRP**	.36**	.08 – .53	.21	.45**	-.28**	-.42 – -.03	.16	-.40**	-.09	-.16 – .00	.12	-.34*[x]
2 hsCRP	.36**	.08 – .52		.45**	-.28**	-.43 – -.03		-.40**	-.09	-.15 – .01		-.34*[x]
Age	.89	-2.33 – 4.34	.01	.07	-.04	-2.97 – 2.93	.00	-.00	-.82	-1.87 – .21	.04	-.19
Biological sex	-.33	-4.20 – 3.49	.00	-.02	1.01	-2.63 – 4.89	.01	.08	-.69	-1.84 – .30	.02	-.15
***1* Pain**	.18*	.01 – .32	.07	.26[x]	-.16*	-.31 – -.02	.08	-.27*	-.02	-.06 – .05	.01	-.07
2 Pain	.19*	.01 – .35		.28[x]	-.18*	-.34 – -.02		-.30*	-.01	-.07 – .06		-.06
Age	.65	-2.89 – 4.46	.00	.05	.12	-2.73 – 2.78	.00	.01	-.75	-1.96 – .49	.03	-.18
Biological sex	-1.54	-5.93 – 2.08	.01	-.11	2.06	-1.61 – 5.97	.03	.16	-.52	-1.70 – .69	.01	-.11
***1* Fatigue**	.21	-.00 – .51	.07	.27	-.20*	-.42 – -.03	.09	-.29*	-.01	-.08 – .05	.00	-.05
2 Fatigue	.22	-.01 – .52		.29*[x]	-.22*	-.45 – -.03		-.32*	-.01	-.08 – .06		-.02
Age	.42	-3.42 – 4.22	.00	.03	.33	-2.65 – 3.00	.00	.03	-.73	-1.87 – .46	.03	-.17
Biological sex	-1.68	-6.53 – 2.72	.01	-.11	2.23	-.99 – 5.13	.03	.17	-.55	-1.75 – .47	.01	-.12
***1* HAQ functional disability**	.09	-.49 – .61	.00	.05	-.14	-.56 – .34	.01	-.08	.05	-.08 – .24	.01	.08
2 HAQ functional disability	.07	-.50 – .70		.03	-.15	-.65 – .33		-.09	.09	-.07 – .29		.14
Age	.32	-3.45 – 3.92	.00	.02	.63	-2.87 – 4.61	.00	.05	-.92	-2.09 – .27	.04	-.22
Biological sex	-.85	-5.55 – 4.58	.00	-.06	1.35	-2.75 – 6.03	.01	.11	-.51	-1.78 – .71	.01	-.11

***1* DCOOP general functional status**	.83**	.35 – 1.46	.17	.41**	-.72**	-1.25 – -.31	.17	-.41**	-.12	-.27 – -.00	.03	-.18
2 DCOOP general functional status	.86**	.30 – 1.47		.42**	-.77**	-1.30 – -.27		-.44**	-.09	-.26 – .06		-.15
Age	-.52	-4.20 – 3.58	.00	-.04	1.17	-2.01 – 4.31	.01	.10	-.63	-1.85 – .48	.02	-.15
Biological sex	-1.33	-5.29 – 2.32	.01	-.09	1.85	-1.27 – 5.29	.02	.14	-.52	-1.67 – .55	.01	-.11
***1* Quality of life (physical health)**	-.75**	-1.15 – -.16	.15	-.38**	.70**	.32 – .96	.17	.41**	.05	-.12 – .17	.01	.07
2 Quality of life (physical health)	-.74**	-1.17 – -.06		-.38**	.69**	.24 – .97		.41**	.05	-.12 – .17		-.08
Age	.34	-3.45 – 3.99	.00	.03	.41	-2.48 – 2.93	.00	.04	-.72	-1.80 – .27	.03	-.17
Biological sex	-.25	-4.20 – 3.03	.00	-.02	.85	-2.61 – 4.60	.00	.07	-.61	-1.80 – .50	.02	-.13
***1* Subjective vitality**	-.34*	-.61 – -.08	.14	-.38**	.26*	.03 – .50	.11	.33*	.08*	.00 – .16	.08	.29*
2 Subjective vitality	-.37*	-.64 – -.08		-.40**	.29*	.04 – .55		.37**	.08	-.01 – .15		.27
Age	.31	-3.33 – 4.20	.00	.02	.42	-2.53 – 3.49	.00	.04	-.70	-1.80 – .39	.03	-.16
Biological sex	-1.97	-6.03 – 2.18	.02	-.13	2.30	-1.11 – 5.72	.03	.18	-.34	-1.42 – .74	.01	-.07
***1* Depressive symptoms**	.67	-.04 – 1.34	.08	.28*[x]	-.49	-1.10 – .16	.06	-.24	-.19*	-.38 – -.04	.06	-.25[x]
2 Depressive symptoms	.73	-.02 – 1.41		.31*[x]	-.56	-1.26 – .11		-.27	-.17*	-.36 – -.02		-.23[x]
Age	.39	-3.27 – 3.70	.00	.03	.35	-2.67 – 3.76	.00	.03	-.71	-1.82 – .38	.03	-.17
Biological sex	-1.80	-6.12 – 2.60	.01	-.12	2.15	-1.63 – 5.66	.03	.17	-.35	-1.43 – .66	.01	-.08

CI, confidence intervals; DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein; HAQ, Health Assessment Questionnaire; DCOOP, Dartmouth Cooperative Functional Assessment Charts

B, unstandardised coefficient (from bootstrapped data); ß, standardised beta coefficient; R^2, variance explained in the dependent variable (sedentary, standing or stepping time) by the independent variable (health-related correlates)

Note: * $p < .05$; ** $p < .01$. Model ***'1'*** adjusted for activPAL wear time. Model ***'2'*** adjusted for activPAL wear time, age and biological sex. [x]significant/non-significant result for non-bootstrapped, standardised coefficient, was different from bootstrapped, unstandardised coefficient. Sedentary, standing and stepping time were calculated as percentages of activPAL wear time for use in regression analysis.

Table 4.7 Linear regressions between health-related correlates with GT3X+-assessed sedentary time, LPA and MPA (longitudinal – T1-T2)

	Sedentary				LPA				MPA			
		95% CI				95% CI				95% CI		
	B	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**
***1* DAS-28**	.08	-.72 – .82	.00	.03	-.03	-.59 – .62	.00	-.02	-.06	-.60 – .53	.00	-.04
2 DAS-28	.08	-.89 – .92		.03	-.02	-.62 – .73		-.02	-.06	-.61 – .58		-.04
Age	.66	-1.73 – 3.38	.01	.09	-.40	-1.72 – .83	.01	-.09	-.22	-1.44 – .94	.00	-.05
Biological sex	-.46	-2.98 – 2.07	.00	-.06	.13	-1.15 – 1.26	.00	.03	.32	-1.04 – 1.51	.01	.07
***1* hsCRP**	.14	-.08 – .23	.11	.33*[x]	-.06	-.12 – .08	.05	-.23	-.08	-.13 – .02	.11	-.33*
2 hsCRP	.14	-.10 – .23		.33*[x]	-.06	-.13 – .10		-.23	-.08	-.13 – .04		-.33*
Age	.83	-1.01 – 2.79	.01	.12	-.40	-1.57 – .75	.01	-.09	-.39	-1.44 – .60	.01	-.10
Biological sex	-.22	-2.24 – 2.11	.00	-.03	.18	-1.41 – 1.40	.00	.04	.03	-1.23 – 1.07	.00	.01
***1* Pain**	.01	-.11 – .08	.00	.02	.03	-.03 – .09	.01	.11	-.04	-.09 – .05	.03	-.16
2 Pain	.02	-.11 – .10		.05	.02	-.03 – .10		.10	-.04	-.10 – .05		-.19
Age	.72	-1.40 – 3.09	.01	.10	-.36	-1.64 – .83	.01	-.08	-.32	-1.32 – .57	.00	-.08
Biological sex	-.53	-2.60 – 1.50	.00	-.07	.00	-1.50 – 1.29	.00	.00	.52	-.80 – 1.92	.01	.11
***1* Fatigue**	.03	-.08 – .17	.01	.08	-.02	-.09 – .04	.00	-.07	-.02	-.10 – .04	.01	-.07
2 Fatigue	.04	-.10 – .19		.10	-.02	-.10 – .05		-.08	-.02	-.10 – .04		-.09
Age	-.69	-1.40 – 2.86	.01	.10	-.41	-1.58 – .77	.01	-.10	-.24	-1.32 – .71	.00	-.06
Biological sex	-.61	-2.60 – 1.41	.01	-.08	.21	-1.17 – 1.49	.00	.04	.39	-1.00 – 1.69	.01	.08
***1* HAQ functional disability**	-.05	-.30 – .14	.00	-.05	.03	-.10 – .17	.00	.04	.03	-.11 – .17	.00	.05
2 HAQ functional disability	-.10	-.31 – .09		-.10	.05	-.06 – .18		.08	.05	-.11 – .20		.09
Age	.90	-.95 – 2.85	.01	.13	-.52	-1.84 – .81	.01	-.12	-.35	-1.57 – .84	.01	-.09
Biological sex	-.52	-2.61 – 1.51	.00	-.07	.17	-1.16 – 1.31	.00	.03	.34	-.91 – 1.60	.01	.07

***1* DCOOP general functional status**	.16	-.13 – .46	.02	.15	-.07	-.28 – .12	.01	-.10	-.09	-.25 – .08	.02	-.15
2 DCOOP general functional status	.16	-.16 – .47		.15	-.06	-.31 – .15		-.10	-.10	-.28 – .10		-.16
Age	.53	1.66 – 2.93	.01	.08	-.35	-1.91 – .97	.01	-.08	-.14	-1.26 – .90	.00	-.04
Biological sex	-.58	-2.35 – 1.52	.01	-.07	.18	-1.22 – 1.42	.00	.04	.38	-.95 – 1.73	.01	.08
***1* Quality of life (physical health)**	-.16	-.41 – .16	.03	-.16	.03	-.19 – .19	.00	.05	.13	-.02 – .25	.05	.22
2 Quality of life (physical health)	-.16	-.41 – .19		-.16	.03	-.21 – .20		.05	.13	-.04 – .23		.21
Age	.67	-1.34 – 2.71	.01	.10	-.41	-1.62 – .71	.01	-.09	-.23	-1.40 – .83	.00	-.06
Biological sex	-.33	-2.08 – 1.40	.00	-.04	.11	-1.35 – 1.54	.00	.02	.21	-1.05 – 1.71	.00	.05
***1* Subjective vitality**	-.11	-.27 – .08	.05	-.23	.06	-.05 – .15	.05	.22	.04	-.06 – .13	.02	.15
2 Subjective vitality	-.11	-.30 – .09		-.24	.07	-.05 – .16		.23	.05	-.06 – .15		.17
Age	.65	-1.36 – 2.46	.01	.09	-.39	-1.66 – .87	.01	-.09	-.22	-1.37 – .96	.00	-.05
Biological sex	-.80	-2.51 – .94	.01	-.10	.34	-1.11 – 1.61	.01	.07	.44	-.93 – 1.72	.01	.10
***1* Depressive symptoms**	.24	-.09 – .61	.03	.18	-.06	-.30 – .16	.01	-.08	-.18	-.38 – .03	.05	-.23
2 Depressive symptoms	.27	-.06 – .63		.21	-.07	-.30 – .16		-.09	-.20	-.41 – .03		-.26
Age	.67	-1.11 – 2.57	.01	.10	-.41	-1.75 – .92	.01	-.09	-.23	-1.26 – .75	.00	-.06
Biological sex	-.81	-2.55 – .92	.01	-.10	.23	-1.04 – 1.45	.00	.05	.57	-.62 – 1.71	.01	.12

CI, confidence intervals; DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein; HAQ, Health Assessment Questionnaire; DCOOP, Dartmouth Cooperative Functional Assessment Charts

B, unstandardised coefficient (from bootstrapped data); ß, standardised beta coefficient; R^2, variance explained in the dependent variable (sedentary, LPA or MPA) by the independent variable (health-related correlates)

Note: * $p < .05$; ** $p < .01$. Model ***'1'*** adjusted for GT3X+ wear time. Model ***'2'*** adjusted for GT3X+ wear time, age and biological sex. [x]significant/non-significant result for non-bootstrapped, standardised coefficient, was different from bootstrapped, unstandardised coefficient. Sedentary time, LPA and MPA were calculated as percentages of GT3X+ wear time for use in regression analysis.

Bi-directional analysis

A total of 15 models were tested to examine possible bi-directional relationships between health variables with activPAL-assessed behaviours. Results for standardised path coefficients (ß) and model fit are reported in Figures 4.3-4.4 and Table 4.8, respectively. 95% CI (lower – upper) are reported below.

DAS-28 (.01 – .62), pain (.08 – .57) fatigue (.13 – .65) and DCOOP general functional status (.14 – .65) showed significant positive bi-directional associations with sedentary time. Quality of life (-.62 – -.05) and subjective vitality (-.72 – -.12) demonstrated significant negative bi-directional associations with sedentary time. Models demonstrated excellent fit to the data. The positive bi-directional relationship between hsCRP with sedentary time (-.09 – .66) was non-significant, but showed a medium effect size. Additionally, this model showed excellent fit to the data.

Pain (-.57 – -.11), fatigue (-.70 – -.23) and DCOOP general functional status (-.64 – -.12) showed significant negative bi-directional associations with standing time. Significant positive bi-directional relationships were observed between quality of life (.09 – .66) and subjective vitality (.12 – .70) with standing time. Models demonstrated excellent fit to the data. Negative bi-directional associations between DAS-28 (-.60 – -.05) and hsCRP (-.61 – .15) with standing time were non-significant, but with medium effect sizes. These models had excellent fit to the data.

A negative bi-directional relationship between depressive symptoms with stepping time (-.41 – .04) was non-significant, with a small effect size. Nevertheless, the model showed excellent fit to the data.

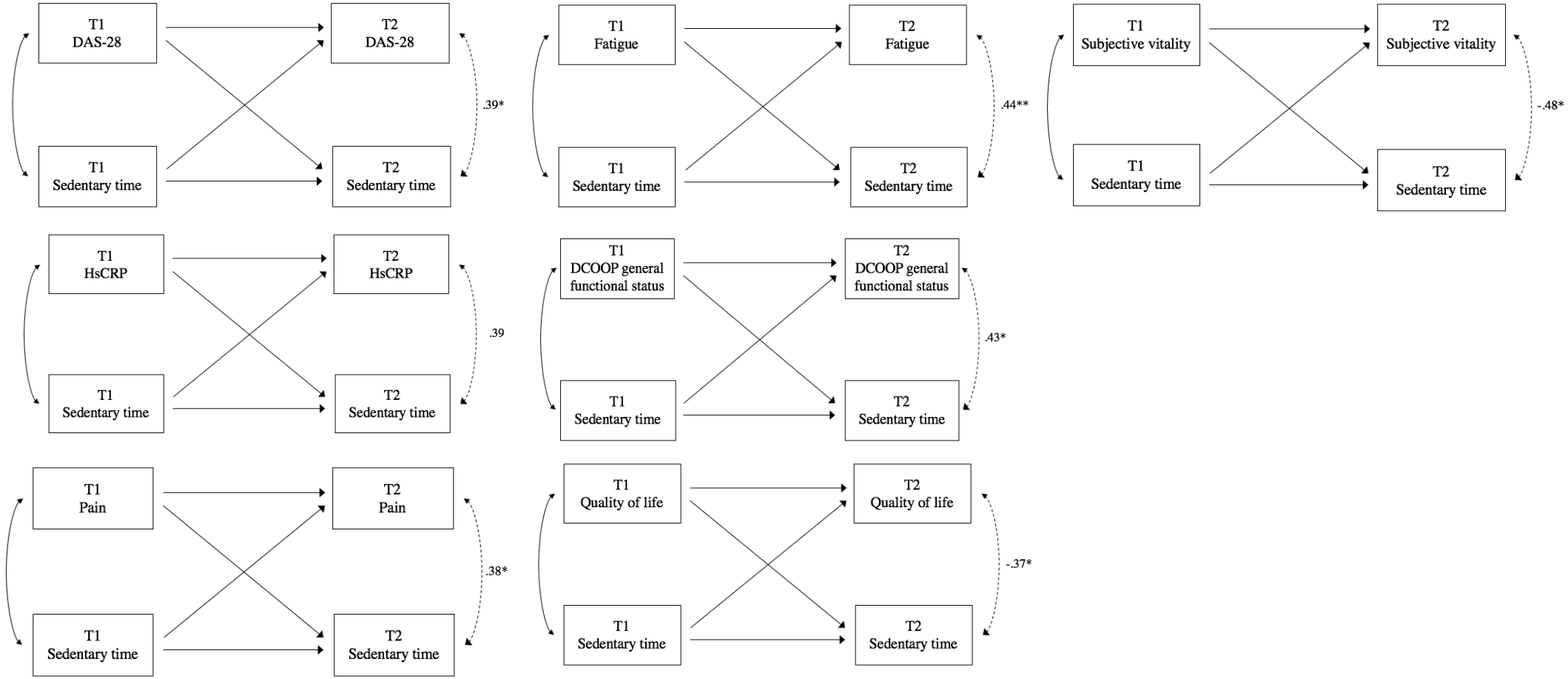

Figure 4.3 Path analysis demonstrating a bi-directional association (ß) between health with activPAL-assessed sedentary time

T1, Time Point 1; T2, Time Point 2

Note: Sedentary time was calculated as a percentage of activPAL wear time, for use in bi-directional analysis

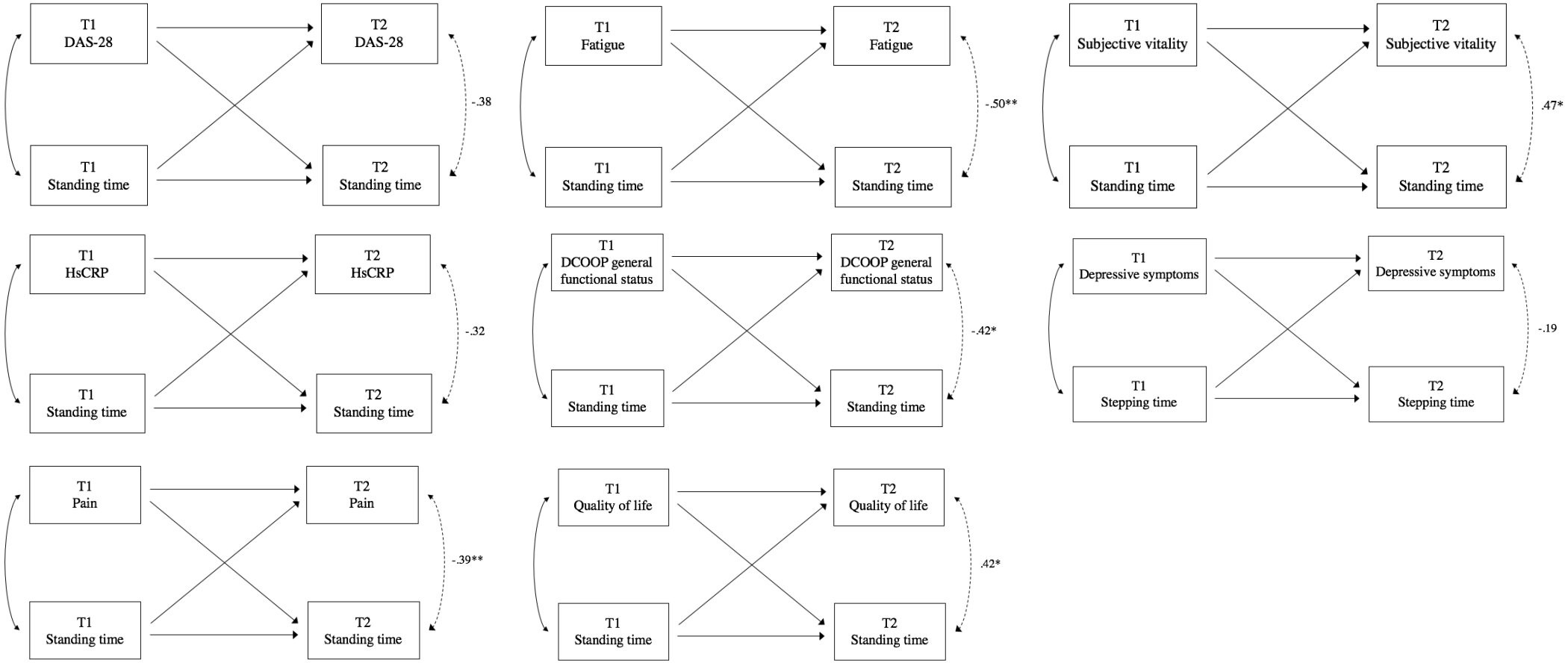

Figure 4.4 Path analysis demonstrating bi-directional associations (ß) between health with activPAL-assessed standing time and depressive symptoms with activPAL-assessed stepping time

T1, Time Point 1; T2, Time Point 2

Note: Standing and stepping time were calculated as a percentage of activPAL wear time, for use in bi-directional analysis

Table 4.8 Bi-directional associations between health variables with activPAL-assessed behaviours (longitudinal) – model fit

Health variable ◄- -► activPAL-assessed behaviour	χ^2	**CFI**	**TLI**	**RMSEA**	**90% CI (low – high)**	**PCLOSE**	**Model fit**
DAS-28 ◄- -► sedentary time*	3.95, p = .79	1.00	1.06	.00	.00 – .11	.84	Excellent
HsCRP ◄- -► sedentary time	4.55, p = .72	1.00	1.07	.00	.00 – .13	.78	Excellent
Pain ◄- -► sedentary time*	4.19, p = .76	1.00	1.06	.00	.00 - .12	.81	Excellent
Fatigue ◄- -► sedentary time**	6.91, p = .44	1.00	1.00	.00	.00 – .17	.53	Excellent
DCOOP general functional status ◄- -► sedentary time*	3.48, p = .84	1.00	1.06	.00	.00 – .10	.88	Excellent
Quality of life ◄- -► sedentary time*	3.10, p = .88	1.00	1.06	.00	.00 – .09	.91	Excellent
Subjective vitality ◄- -► sedentary time*	6.49, p = .48	1.00	1.01	.00	.00 – .16	.57	Excellent
DAS-28 ◄- -► standing time	4.46, p = .73	1.00	1.06	.00	.00 – .13	.79	Excellent
HsCRP ◄- -► standing time	4.91, p = .67	1.00	1.07	.00	.00 – .14	.74	Excellent
Pain ◄- -► standing time**	4.72, p = .69	1.00	1.06	.00	.00 – .13	.76	Excellent
Fatigue ◄- -► standing time**	6.82, p = .45	1.00	1.00	.00	.00 – .17	.54	Excellent
DCOOP general functional status ◄- -► standing time*	3.65, p = .82	1.00	1.06	.00	.00 – .10	.86	Excellent
Quality of life ◄- -► standing time*	3.39, p = .85	1.00	1.06	.00	.00 – .10	.89	Excellent
Subjective vitality ◄- -► standing time*	6.56, p = .48	1.00	1.01	.00	.00 – .16	.56	Excellent
Depressive symptoms ◄- -► stepping time	3.83, p = .80	1.00	1.06	.00	.00 – .11	.85	Excellent

DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein; DCOOP, Dartmouth Cooperative Functional Assessment Charts

χ^2, chi-square statistic; CFI, comparative fit index; TLI, Tucker Lewis index; RMSEA, root mean square error of approximation; CI, confidence intervals; PCLOSE, closeness of fit; ◄- -► Bi-directional association

Note: *p < .05; **p < .01. For χ^2, degrees of freedom were 7. RMSEA encompasses CI (90%) and PCLOSE for assessing model fit.

Discussion

This study employed validated devices to objectively-assess sedentary time and PA in people living with RA, and examined cross-sectional *and* longitudinal associations between pertinent aspects of RA health with these behaviours in this patient group. The presence of bi-directional associations was also tested.

Findings at T1 revealed that on average, RA patients spent 9h/day (activPAL) and 11h/day (GT3X+) sedentary. Reasons for higher estimates of GT3X+-assessed vs. activPAL-assessed sedentary time could be due to the inability of accelerometry to detect posture (An et al., 2017; Kozey-Keadle et al., 2011), possibly resulting in some misclassification of time spent engaged in low-energy standing as sedentary time (see Chapter 2). Still, employing the activPAL *and* GT3X+ was an advantage. Specifically, the activPAL is the gold standard measure of free-living sedentary time (Chastin & Granat, 2010; Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016) and overcame the inability of the GT3X+ accelerometer to capture posture. The GT3X+ accelerometer had potential however to generate 'valid' estimates of LPA and MPA in these participants when applying RA-specific cut-points, addressing the uncertain validity of the activPAL to capture intensity of free-living behaviour. Thus, employing both devices in this study provided interesting insight into the disparities in sedentary time estimates and associations between RA health using the activPAL and GT3X+.

Cross-sectional analysis revealed associations between several pertinent RA health outcomes (DAS-28, pain, HAQ functional disability, DCOOP general functional status [positive] and quality of life [negative]) with activPAL- *and* GT3X+-assessed sedentary time in RA. These are mostly consistent with other cross-sectional studies that have examined associations between RA health (DAS-28 and functional disability) with sedentary time (Giles et al., 2008; Greene et al., 2006; Khoja et al., 2016; Summers et al., 2019). For example, a

positive association between HAQ functional disability with self-reported and accelerometer-assessed sedentary time was revealed by Greene et al. (2006) and Khoja et al. (2016), respectively. Khoja et al. (2016) also revealed a positive association between DAS-28 with accelerometer-assessed sedentary time in RA. More recently, Summers et al. (2019) compared daily accelerometer-assessed sedentary time between female RA patients with moderate to high disease activity (DAS-28 >3.2) vs. low disease activity (DAS-28 ≤3.2). Summers and colleagues (2019) reported significant differences in sedentary time between groups, whereby patients with moderate to high disease activity engaged in 10% more sedentary time per day, compared to patients with low disease activity.

As well as investigating the links between a broader range of RA outcomes with sedentary time, the present study addressed several limitations emerging from previous work. First, the activPAL and GT3X+, validated for use in RA, were employed to quantify sedentary time, as opposed to self-report methods (Giles et al., 2008; Greene et al., 2006). Second, sedentary behaviour was defined according to the widely-accepted definition proposed by the Sedentary Behaviour Research Network (SBRN, 2012; Tremblay et al., 2017). Certainly, this was not considered by Khoja and colleagues (2016), who inaccurately defined sedentary behaviour (≤1 MET).

This is the first study to examine cross-sectional associations between clinically- and patient-important health outcomes with the current gold standard measure of free-living sedentary time, the activPAL (Chastin & Granat, 2010; Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016), among a relatively large sample of RA patients. An additional aim of the present study was to examine associations between RA health indicators with device-assessed PA, specifically activPAL-assessed standing and stepping time, and GT3X+-assessed LPA and MPA. Results revealed associations between DAS-28, HAQ functional

disability, DCOOP general functional status (negative) and quality of life (positive) with activPAL-assessed standing and stepping time, with additional associations found between pain and fatigue (negative) with stepping time. Interestingly, no cross-sectional associations were found between any health outcomes with GT3X+-assessed LPA, despite the results relating to activPAL-assessed standing time. Akin to the earlier discussion, it is possible that the GT3X+ classified low-energy standing as sedentary time, and therefore the former behaviour would have not been included in GT3X+-derived estimates of LPA. Findings suggest that the targeted RA health outcomes hold important associations with activPAL-assessed standing time, thus should be accurately measured in future work seeking to objectively-assess free-living behaviour in RA.

No previous studies have employed the activPAL to examine relationships between RA health with standing and stepping time, and few studies have examined the association between accelerometer-assessed LPA in RA. Khoja et al. (2016), demonstrated cross-sectional negative associations between DAS-28 and HAQ functional disability with accelerometer-assessed LPA. However, like with sedentary behaviour, the authors erroneously defined LPA as occurring between 1.1-2.9 METs, restricting the accuracy of their results. In their cross-sectional study, Summers et al. (2019) reported that female patients with moderate to high disease activity spent significantly less time in accelerometer-assessed LPA (18%), compared to those with low disease activity.

Contrasting to the present study, Fenton et al. (2018c) did not observe a significant association between HAQ functional disability with objectively-assessed LPA in RA patients. Although, in their cross-sectional study, HAQ functional disability to ‘rise’ and ‘walk’ were isolated for analysis, whilst the present study included all components (‘dressing and grooming’, ‘rising’, ‘eating’ ‘walking’ ‘hygiene’, ‘reach’, ‘grip’ and ‘activities’). LPA

typically encompasses activities undertaken as part of an individual's everyday life. These activities may involve the ability to 'rise' and 'walk', but may also extend to the ability to, for example, 'reach' and 'dress and groom'. Perhaps, therefore, Fenton et al. (2018c) did not capture a broad enough range of activities in the HAQ that closely represented overall levels of LPA, by solely including 'rise' and 'walk' in analysis. In addition, this cross-sectional study had a small sample size (n = 50), thus limiting its statistical power.

The overarching limitations of previous work examining the associations between RA health with engagement in sedentary behaviour and LPA, is a cross-sectional design and a reliance on accelerometers. Although a cross-sectional design allows researchers to 'quickly and easily' detect and compare associations across a large number of variables, this methodological approach only provides information relating to one single moment in time (a 'snapshot'). This means that the data collected might not be representative of longer-term health and behaviour. Thus, resulting cross-sectional associations provide no inference regarding change in one variable (e.g., RA health), predicting change in another (e.g., RA sedentary time) (Carlson & Morrison, 2009; Caruana et al., 2015; Solem, 2015). However, the progression of observational research typically entails cross-sectional associations to be recognised between variables of interest in a population, preceding a longitudinal study to gain a deeper insight into 'change predicting change', or bi-directionality (Caruana et al., 2015).

With this in mind, the present study conducted more rigorous examination of the associations between RA health with device-assessed sedentary time and PA in its subsequent analytical step – longitudinal analysis. Further, to gain more insight into whether change in RA health was a cause *and* consequence of change in sedentary time or PA, these longitudinal data were tested in bi-directional analysis. This is first study to examine both the longitudinal and

bi-directional associations between change in numerous ‘physiological’ and ‘psychological’ disease outcomes, with change in objectively-assessed sedentary time and PA in RA.

Interestingly, results from longitudinal regression analysis revealed significant associations between change in RA health with change in activPAL-assessed behaviours only, particularly for sedentary and standing time, in people with RA. It might be that the activPAL is more sensitive with regard to detecting sedentarity and standing compared to the GT3X+, with the latter potentially misclassifying standing as sedentary time. Aligned with this point, Dontje et al. (2018) examined whether the activPAL was sensitive to detect ‘real change’ in sedentary time in different study designs with older adults, including longitudinal studies at group level. In this way, sensitivity was termed ‘responsiveness to change’, and findings demonstrated that the activPAL performed admirably in this regard. Of notable interest was the finding that the activPAL was ‘most responsive’ when average estimates of sedentary time were based on one day, rather than 7 days, in this sample of older adults. Although, the authors emphasised that the optimal activPAL monitoring period is 7 days to generate more reliable sedentary behaviour estimates. This has been reiterated in a recent review by Edwardson et al. (2017). In addition, when considering people living with RA may experience fluctuating disease activity (‘flare ups’) during a short period of time, which may affect their levels of sedentary time, a 7-day measurement protocol might provide a more reliable and valid representation of average daily behavioural patterns, than just a single day. As such, RA patients in this study wore the activPAL for 7 days (at T1 and T2) in order to assess their free-living sedentary time (and standing and stepping time), and we posit that this device was highly sensitive to detecting change in these behaviours in this longitudinal study.

Findings from the present longitudinal study revealed that change in hsCRP, pain, fatigue, DCOOP general functional status (positive), quality of life and subjective vitality

(negative) were related to change in activPAL-assessed sedentary time. The inverse associations were found for standing time. Results were first interpreted as RA health 'predicting' behavioural outcomes in these patients (regression models were constructed to align with a 'clinical perspective'). Indeed, inflammatory disease activity and debilitating features of RA (e.g., pain, fatigue) have been cited as reasons for engagement/disengagement in sedentary behaviour and PA in this patient group (Hernandez-Hernandez et al., 2014; Tan et al., 2019; Thomsen et al., 2015; Veldhuijzen van Zanten et al., 2015). Our findings suggest that changes in RA health may indeed be predictive of engagement in sedentary and standing behaviour in these patients.

Past research has also underlined the possibility that sedentary behaviour and PA might be contributors to variability in RA health, as well as consequences of disease outcomes (Thomsen et al., 2015; Veldhuijzen van Zanten et al., 2015). This is the first study to examine this hypothesis, testing bi-directional associations between RA health with sedentary time and PA in these patients. This facilitated a deeper understanding regarding whether changes in these behaviours may have potential predictive value to determine changes in important RA outcomes. Results confirmed the presence of significant bi-directional associations between DAS-28, pain, fatigue, DCOOP general functional status, quality of life and subjective vitality with activPAL-assessed sedentary time. In addition, significant bi-directional associations were observed between these health outcomes (except DAS-28) with activPAL-assessed standing time.

Bi-directional associations were not statistically significant between hsCRP with activPAL-assessed sedentary or standing time. Additionally, DAS-28 was not significantly bi-directionally associated with activPAL-assessed standing time. However, the medium effect sizes indicated that with a larger sample size, these results might have emerged significant. It

is interesting to discern the clinical relevance of the present findings relating to RA disease activity. For example, a decrease in sedentary time of approximately 65 min/day, may lead to a decrease of 3.3mg/l in hsCRP or a decrease in DAS-28 of 0.5. DCOOP general functional status *did* show a significant bi-directional association with activPAL-assessed sedentary time – a decrease in sedentary time of approximately 65 min/day may decrease DCOOP general functional status score by 1 (e.g., responding to, "during the past 2 weeks, how would you rate your health in general?" with '4 = fair' from '5 = poor').

The significant longitudinal associations, and medium effect sizes demonstrated in bi-directional analysis, between hsCRP with sedentary time (positive) and standing (negative) in RA patients, are of particular interest in this study. Certainly, hsCRP is an important clinical biomarker of inflammatory RA disease activity, and elevated inflammation in this patient group has been implicated in the development of several patient-important outcomes (e.g., pain, fatigue, functional disability) (Hazes, 2003; Madsen et al., 2016; Nerurkar et al., 2019; Walsh & McWilliams, 2014). Present findings revealed that hsCRP was positively correlated with pain (ß = .35), fatigue (ß = .28) and DCOOP general functional status (ß = .30) in these RA patients. Thus, future research might consider examining whether hsCRP mediates the relationships between sedentariness and other health outcomes (such as those assessed herein). This will serve to address the 'sedentary-inflammation' hypothesis (Fenton & Kitas, 2016), which postulates a cyclical relationship between sedentary behaviour, inflammation and health outcomes in RA.

Another compelling finding from the present study was the lack of significant longitudinal and bi-directional associations between depressive symptoms with device-based assessments of sedentary time in RA patients, compared to those for 'physiological' outcomes (e.g., hsCRP, pain, physical function). This disparity could be attributed to the fact that

sedentarity encompasses both ‘mentally active’ (e.g., reading a book) and ‘passive’ (e.g., watching television) behaviours, demonstrated to have independent consequences for indicators of psychological well-being, such as depression (Hallgren et al., 2019; Hallgren et al., 2018). Specifically, a recent prospective study has demonstrated that engaging in mentally active sedentary behaviours for >3 h/day can reduce the risk of depression (Hallgren et al., 2018). Hallgren et al. (2018) also revealed non-significant relationships between engagement in passive, or combined mentally active and passive (total), sedentary behaviours with incident depression. It is possible that RA participants in the present study engaged in more passive, or a combination of mentally active and passive, sedentary behaviours throughout the day, resulting in non-significant associations with depressive symptoms. These ‘types’ of sedentary behaviour are likely to have not affected associations with more ‘physiological’ RA outcomes, which may just rely on the posture of free-living behaviour and not the context by which it occurs. However, these interpretations cannot be confirmed due to the device-based methods employed in the present study, which did not take into account specific contexts of patients’ sedentary behaviour. Future research should address this, because if psychological benefit can result from sedentary behaviours which entail people with RA to be mentally active, then we must be cautious promoting reductions in sedentary time in this patient group.

Current findings suggest sedentarity may represent both a consequence *and* cause of some clinically- and patient-important aspects of RA health (Figure 4.5). Additionally, considering the reciprocal associations with RA health, increasing standing time (concurrent to reducing sedentary time) may represent an avenue through which RA health could be improved. Indeed, the strong inverse correlation between sedentary and standing time (ß = -.95), suggests that interventions which target replacing sedentary time with standing time, may be a feasible approach for intervention in these patients. Moreover, the standardised path

coefficients representative of the bi-directional associations between health with sedentary *and* standing time in this patient group were almost identical (e.g., DCOOP general functional status with sedentary time [ß = .43] and standing time [ß = -.42]). Together, these findings substantiate the potential of lower-intensity PA, such as standing behaviour, to displace sedentary time in this patient group for health benefits ('sit less, stand more'). Experimental studies however, are required to confirm the causality of such associations.

The present investigation was marked by a number of strengths. This was the first longitudinal study, inclusive of bi-directional analysis, to examine relationships between several clinically- and patient-important health outcomes, with free-living behaviour in RA. A wide range of variables highly relevant to 'physiological' *and* 'psychological' aspects of RA health were included, and measured via validated clinical assessments (e.g., DAS-28) and questionnaires (e.g., HAQ, MAF) in this population. Additionally, device-based assessments of sedentary time and PA (activPAL and GT3X+), validated specifically in RA, were employed for measurement of free-living behaviour in these patients. Novel insight into bi-directional associations between RA outcomes with sedentary and standing time, provided evidence relevant to the development of sedentary behaviour change interventions in this patient group.

Some limitations of this study must be acknowledged. First, despite the large sample size in the cross-sectional study, the subsequent longitudinal study involved a reduced sample. However, no significant differences were found between participants included at T2, and those lost to follow-up between T1 and T2, based on measured variables. Bootstrapping was used in statistical analysis to overcome some issues relating to small sample size. Nevertheless, the sample size meant it was still not possible to test more sophisticated statistical models, including; structural equation models (full measurement models), bi-directional models which encompassed the relationships explored separately via regressions, and models that included

multiple activity behaviours (e.g., sedentary *and* standing time). However, the latter approach may not have been possible due to multicollinearity between the behaviours comprising the majority of RA patients' waking day (e.g., sedentary time and standing time and/or LPA). Further, 'excellent model fit' and consistent values for selected indices (e.g., RMSEA = .00) (Bandalos, 2018) in path analysis could be due to $\chi^2 \leq$ degrees of freedom (7) in each model.

Additionally, the sample consisted of mostly female participants with moderate disease activity and severity. Whilst a higher proportion of females is representative of the RA population (Wasserman, 2018), findings from this study are limited in their generalisability to males with RA and those with more/less active disease. Further, this study did not gauge the intensity of activPAL-assessed stepping. However, to our knowledge, only 1 study has validated the activPAL to classify PA intensity (LPA and MPA) in 'healthy adults', which is not generalisable to RA (Lyden, Keadle, Staudenmayer, & Freedson, 2017). Finally, device-assessed sedentary time and PA meant that the context of these behaviours could also not be determined – this must be addressed in future studies, particularly with regard to capturing mentally active and passive sedentary behaviours in RA.

Conclusion

Longitudinal associations between activPAL-assessed sedentary and standing time with several clinically- and patient-important RA outcomes in the present study were also bi-directional in nature. As such, results suggest that sedentary and standing time may represent causes *and* consequences of variability in RA health. Future research should employ experimental study designs to test (via interventions) whether replacing sedentary time with standing may improve relevant indicators of health in RA, from a clinical *and* patient perspective.

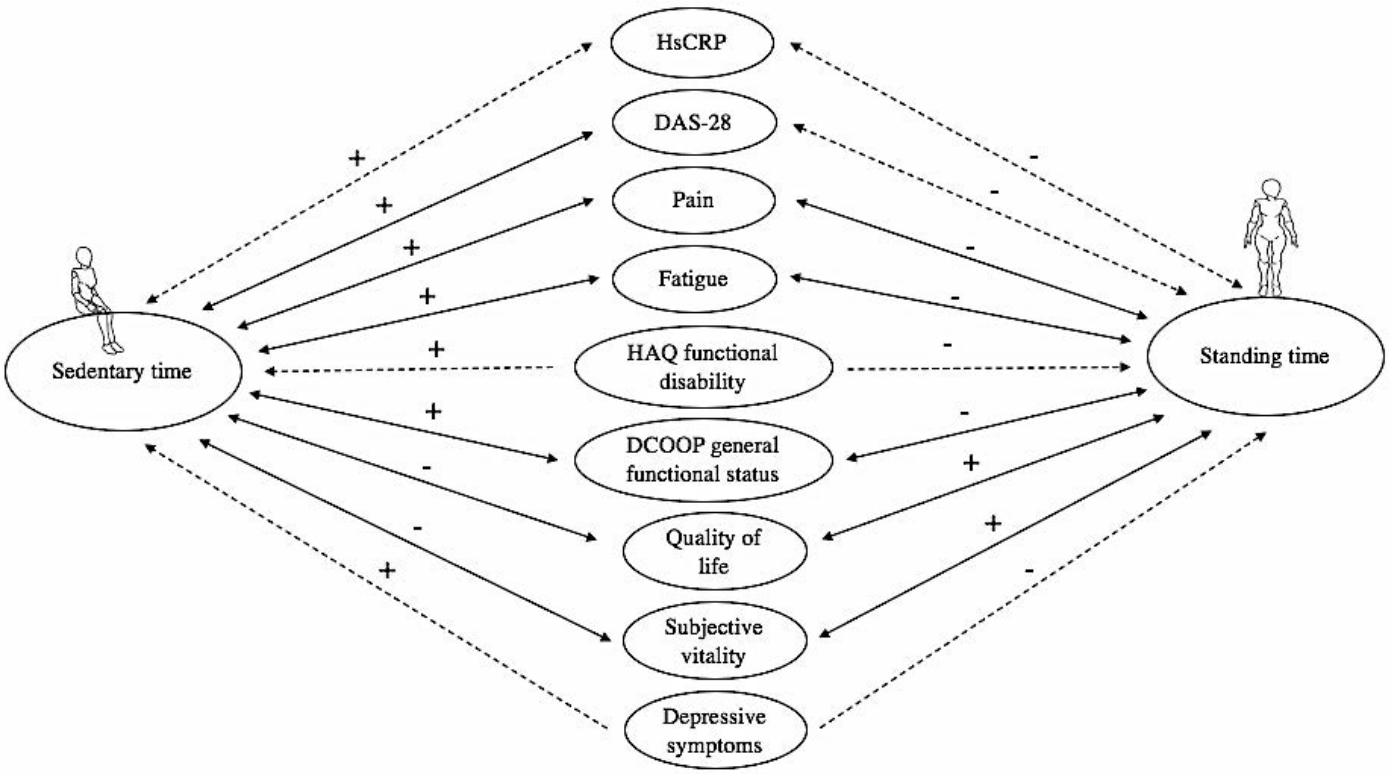

Figure 4.5 Bi-directional associations between clinically- and patient-important disease outcomes with activPAL-assessed sedentary and standing time in people with RA (all health variables are shown, even those not tested in bi-directional path analysis).

Note:

- - - - - - - ► Non-significant longitudinal association

◄———► Significant bi-directional association

◄- - - - - - ► Non-significant bi-directional association

CHAPTER 5

THE PSYCHOSOCIAL DETERMINANTS OF SEDENTARY TIME AND PHYSICAL ACTIVITY IN RHEUMATOID ARTHRITIS: A SELF-DETERMINATION THEORY PERSPECTIVE

Abstract

Aim: This study adopted a self-determination theory (Deci & Ryan, 1985) perspective, to examine longitudinal associations between autonomous and controlled motivation to reduce sedentary behaviour with levels of device-assessed sedentary time and physical activity (PA), in people with Rheumatoid Arthritis (RA). **Method:** RA patients visited the hospital for data collection at 2 time points, 6 months apart. The same protocols were undertaken at both time points, whereby participants attended the hospital for 'Visit 1' and 'Visit 2', 7 days apart. On each visit, participants undertook physical assessments to evaluate their general health and RA health. Additionally, they completed an adapted version of the Behavioural Regulation in Exercise Questionnaire-2 to assess their autonomous and controlled motivation to reduce sedentary behaviour. Participants wore an activPAL and GT3X+ for the subsequent 7 days, to measure free-living time spent sedentary (activPAL and GT3X+), standing and stepping (activPAL), and in light-intensity PA (LPA) and moderate-intensity PA (GT3X+). **Results:** Longitudinal regression analysis demonstrated that change in autonomous motivation to reduce sedentary behaviour was negatively associated with change in activPAL-assessed sedentary time (ß = -.44), and positively related to change in activPAL-assessed standing (ß = .38), and stepping (ß = .33) time. Change in autonomous motivation to reduce sedentary behaviour was negatively linked to change in GT3X+-assessed sedentary time (ß = -.36), with inverse associations observed for change in GT3X+-assessed LPA (ß = .35). Change in controlled motivation to reduce sedentary behaviour was not linked to any behaviours. **Conclusion:** Results suggest that autonomous motivation to reduce sedentary behaviour may represent a malleable psychosocial determinant of sedentary time among people with RA. Experimental research is required to establish the potential of targeting autonomous motivation to reduce sedentary behaviour for interventions promoting sedentary behaviour change in RA.

Introduction

Rheumatoid Arthritis (RA) is a chronic autoimmune disease, characterised by heightened systemic inflammation (Angelotti et al., 2017) and affecting between 0.5-1% of adults worldwide (Uhlig et al., 2014; Wasserman, 2018). RA is debilitating for the patient, with inflammation-driven joint pain, as well as functional disability and fatigue all symptomatic of this condition (Smolen et al., 2016a; Uhlig et al., 2014). People with RA may also experience compromised mental health, with approximately 66% of patients experiencing depressive symptoms (Fiest et al., 2017; Katz, 2017a, 2017b; Matcham et al., 2013).

Engagement in physical activity (PA) is recommended for the management of RA (Rausch Osthoff et al., 2018). This guidance is based on evidence which consistently demonstrates that higher levels of moderate-to-vigorous-intensity PA (MVPA, ≥3 metabolic equivalents [METs]) is associated with lower systemic inflammation and disease activity, less functional disability, pain and fatigue, and improved psychological well-being (Cooney et al., 2011; de Jong et al., 2003; Loppenthin et al., 2015; Metsios & Kitas, 2018; Metsios et al., 2015; Plasqui, 2008; Rahnama & Mazloum, 2012; Rongen-van Dartel et al., 2015; Verhoeven et al., 2016). However, despite the acknowledged health benefits, very few people living with RA undertake recommended levels of MVPA required to accrue benefits to health (Tierney et al., 2012). Reasons reported for low levels of MVPA include pain and fatigue, as well as misconceived safety fears (e.g., exacerbated joint damage) (Veldhuijzen van Zanten et al., 2015). In addition, rheumatology health professionals typically recommend MVPA in the form of scheduled, structured aerobic and/or resistance ‘exercise training’ for people with RA (Metsios & Kitas, 2018) which, considering the aforementioned patient-reported barriers to MVPA, may be perceived as too challenging for these patients.

Consequently, researchers are increasingly recognising the importance of 'non-exercise' behaviours for clinical groups, who may experience mobility limitations due to disease characteristics (Manns et al., 2012), such as people with RA. Specifically, seeking to determine the potential relevance of sedentary behaviour (≤1.5 METs) and light-intensity PA (LPA, 1.6-2.9 METs), occurring lower down the PA continuum than MVPA, for clinically- and patient-important health outcomes. Indeed, for people with RA, 'non-exercise' behaviour comprises approximately 97% of the waking day (Hammam et al., 2019; Summers et al., 2019) and should not be discounted. Addressing these 'non-exercise' behaviours may offer an alternative approach to promoting more active lifestyles among people with RA, and perceived as more feasible.

Sedentary behaviour is defined as waking behaviour requiring energy expenditure ≤1.5 METs undertaken in a sitting/reclining/lying posture (SBRN, 2012; Tremblay et al., 2017). Common sedentary behaviours include sitting whilst reading a book or travelling in a vehicle (Ainsworth et al., 2011). For people with RA, evidence from cross-sectional studies suggests that more sedentary time is linked to higher disease activity and reduced physical function (Fenton et al., 2018b; Summers et al., 2019). Studies also indicate reverse cross-sectional associations for LPA, whereby links between LPA engagement with lower disease activity, improved physical function, less depressive symptoms and higher subjective vitality have been demonstrated in this patient group (Fenton et al., 2018c; Khoja et al., 2016; Summers et al., 2019). In addition, data from this thesis (Chapter 4) has revealed longitudinal positive associations between sedentary time with high-sensitivity C-reactive protein (hsCRP), pain, fatigue and general functional status, and negative relationships with quality of life and subjective vitality. Reverse associations were found for standing time. Work presented in this thesis and others also, indicate that sedentary time and LPA are strongly inversely correlated

among people with RA (Fenton et al., 2017). This further highlights that promoting LPA may be a feasible approach to ameliorating the potential negative health consequences of sedentary time in this patient group. As such, interventions which focus on supporting people with RA to reduce their sedentary time and increase their LPA (e.g., replacing sedentary time with standing) may help to reduce the burden of disease for these individuals.

However, prior to the development of sedentary behaviour change interventions in RA, it is essential that *malleable determinants* of this behaviour are established. Current evidence in this field points to populations most at need of changing their sedentary behaviour (e.g., older adults, patient groups), but little is known about the modifiable determinants of sedentary time that can potentially form intervention targets to elicit behaviour change (Chastin et al., 2015a). A gap in knowledge regarding the determinants of sedentary behaviour 'across the life course' has been emphasised in a recent review and framework generated from an important body of work, 'Determinants of Diet and Physical Activity' (DEDIPAC) (Chastin et al., 2015a; Chastin et al., 2016). For example, Chastin et al. (2015a) emphasised the importance of confirming modifiable determinants of sedentary behaviour in older adults, who represent the 'most sedentary' age group. The authors explain that understanding the most effective intervention strategies, such as targeting motivation, is of significant research priority. Finally, Chastin and colleagues (2015a) remarked on the paucity of qualitative and longitudinal studies in the area, which could provide greater insight into the 'causes' of sedentary behaviour.

A transdisciplinary consensus framework, namely the 'Systems of Sedentary behaviours' (SOS-framework), has subsequently been developed (Chastin et al., 2016). The SOS-framework has identified groups of determinants ('clusters') that are expected to influence sedentary behaviour in youth, adults and older adults, and warrant investigation to inform behaviour change interventions. Specifically, the clusters include 'Physical Health and

Wellbeing', 'Social and Cultural Context', 'Built and Natural Environment', 'Psychology and Behaviour', 'Politics and Economics' and 'Institutional and Home Settings'. Interestingly, 'Psychology and Behaviour', relating to the motivation of an individual, received the highest consensus percentage (80%) and was highly ranked as a research priority (2nd).

With this in mind, it could be suggested that motivation may provide a focus for investigating the malleable determinants of sedentary behaviour in people with RA, who, similarly to older adults, exhibit high levels of sedentary time (Fenton et al., 2018b). Aside from the disease-related features that might contribute towards sedentarity in this patient group, *motivation* may play an additional or combined role in determining their levels of sedentary behaviour. Thomsen et al. (2015) suggested increasing patient motivation to reduce sedentary behaviour in RA, but to date, no studies have investigated motivation as a determinant of sedentary behaviour in RA.

Research seeking to examine the role of motivation in sedentary behaviour change in people with RA, should be grounded in psychological theory (Michie et al., 2008). This allows for a deeper understanding into the motivational processes underlying this behaviour, and thus more specific targets can be established for interventions. Self-determination theory (SDT) (Deci & Ryan, 1985) might offer such a theoretical perspective. SDT has been extensively applied in the context of PA promotion, to understand the role of motivation in PA behaviour (Teixeira et al., 2012). The central assumption of SDT is that an individual's *quality of motivation* is associated with the variability in engagement in the target behaviour (e.g., reducing sedentary behaviour). SDT posits that quality of motivation lies on a continuum ranging from controlled motivation (lower quality) to autonomous motivation (higher quality) (Deci & Ryan, 1985, 2008a, 2008b; Ryan & Deci, 2000). Behaviour occupies the 'self-determined' tail of this continuum when the individual possesses autonomous motivation, and

the ‘non-self-determined’ end when controlled motivation is fostered. Behaviour is considered to be guided by autonomous motivation where one experiences identified regulation (engaging in behaviour due to identifying the benefits it presents, and valuing these benefits) and/or intrinsic regulation (engaging in behaviour because of enjoyment and interest). Conversely, controlled motivation is assumed to be operating where behaviours are guided by external regulation (driven by external factors, such as monetary gain or pressure) and/or introjected regulation (behaviour is compelled by internal factors, such as the avoidance of guilt or to retain pride). In the context of behaviour change, autonomous motivation is reported to result in more optimal uptake and long-term maintenance of the target behaviour, with more controlled motivation linked to lessened likelihood of adopting and persisting with the target behaviour (Deci & Ryan, 2008a, 2008b).

Specifically considering PA behaviour change, research grounded in SDT has been conducted to understand the role of autonomous and controlled motivation towards variability in levels of PA in both clinical and non-clinical populations. Overall, results of this research suggest that where individuals experience more autonomous motivation, greater PA engagement is likely to result (Duda et al., 2014; Fasczewski et al., 2018; Fortier et al., 2012; Milne et al., 2008; Teixeira et al., 2012). To date, there are a paucity of studies using an SDT lens to examine whether RA patients’ quality of motivation predicts variability in PA in RA. This is substantiated by a recent review (Demmelmaier & Iversen, 2018), which reports that studies and interventions minimally apply any theory to investigate PA behaviour change in this patient group. Hurkmans and colleagues (2010) provided the first preliminary evidence in this area, highlighting that more autonomous motivation for PA was cross-sectionally linked with higher levels of self-reported PA in people with RA. In a later study, Yu et al. (2015a)

corroborated this finding, reporting a positive cross-sectional association between autonomous regulation style with engagement in self-reported PA in this patient group.

Few studies in *any* population have examined the role of autonomous and controlled motivation with regard to sedentary behaviour. Studies to date have examined how autonomous and controlled motivation to engage in PA is associated with sedentary behaviour engagement, and have not been conducted in clinical populations (Quartiroli & Maeda, 2014; Rollo, Gaston, & Prapavessis, 2016). For example, Quartiroli and Maeda (2014) conducted a cross-sectional study to assess relationships between quality of motivation to engage in PA (employing the Behavioural Regulation in Exercise Questionnaire-2 [BREQ-2]) (Markland & Tobin, 2004) with self-reported sedentary time (via a single item on the International Physical Activity Questionnaire) (Craig et al., 2003) in young adults. Findings demonstrated that identified and intrinsic regulations for PA were negatively associated with sedentary time. However, this study assessed participants' quality of motivation to engage in PA, rather than more specifically, autonomous and controlled motivation to reduce sedentary behaviour. Indeed, whilst sedentary time and PA are inversely associated, sedentary behaviour is an independent behaviour to PA (van der Ploeg & Hillsdon, 2017). Thus, sedentary behaviour is likely to be influenced by different determinants to those impacting engagement in PA (Chastin et al., 2015a).

More recent studies have examined the role of autonomous and controlled motivation to reduce sedentary behaviour for variability in sedentarity. Such studies have been conducted mostly in adolescents (Babic et al., 2016; Smith et al., 2017) and have investigated the effectiveness of interventions promoting autonomous motivation to limit screen-time. Further highlighting the importance of specifically measuring quality of motivation to reduce sedentary behaviour, Lubans et al. (2013) developed the Motivation to Limit Screen-time Questionnaire,

which is based on SDT and was subsequently employed in the studies by Babic et al. (2016) and Smith et al. (2017). These experimental studies revealed that increases in autonomous motivation to limit screen-time corresponded with reductions in adolescent screen-time. Similarly, a workplace intervention targeting autonomous motivation to reduce sedentary behaviour, lead to lower self-reported sedentariness in a group of adults (De Cocker et al., 2015).

These studies have provided some support for the role of autonomous motivation to reduce sedentary behaviour among these groups. However, generalising results from these studies to individuals with RA is a challenge, as these patients are likely to engage in different sedentary behaviours and for different reasons than adolescents and non-RA adults. Thus, there is a need for research examining quality of motivation to reduce sedentary behaviour, and its implications for sedentarity in RA. Therefore, the aim of this longitudinal study was to examine associations between autonomous and controlled motivation to reduce sedentary behaviour with objectively-assessed sedentary time and PA in people with RA. It is hypothesised that an increase in autonomous motivation to reduce sedentary behaviour will be associated with a decrease in device-assessed sedentary time, and an increase in device-assessed standing time, stepping time, LPA and MPA, in people living with RA. Conversely, an increase in controlled motivation to reduce sedentary behaviour is hypothesised to be related to an increase in device-assessed sedentary time, and a decrease in device-assessed standing time, stepping time, LPA and MPA, in this patient group.

Method

The methodology for this study is described in detail in Chapter 3. Figure 5.1 illustrates the specific measures employed.

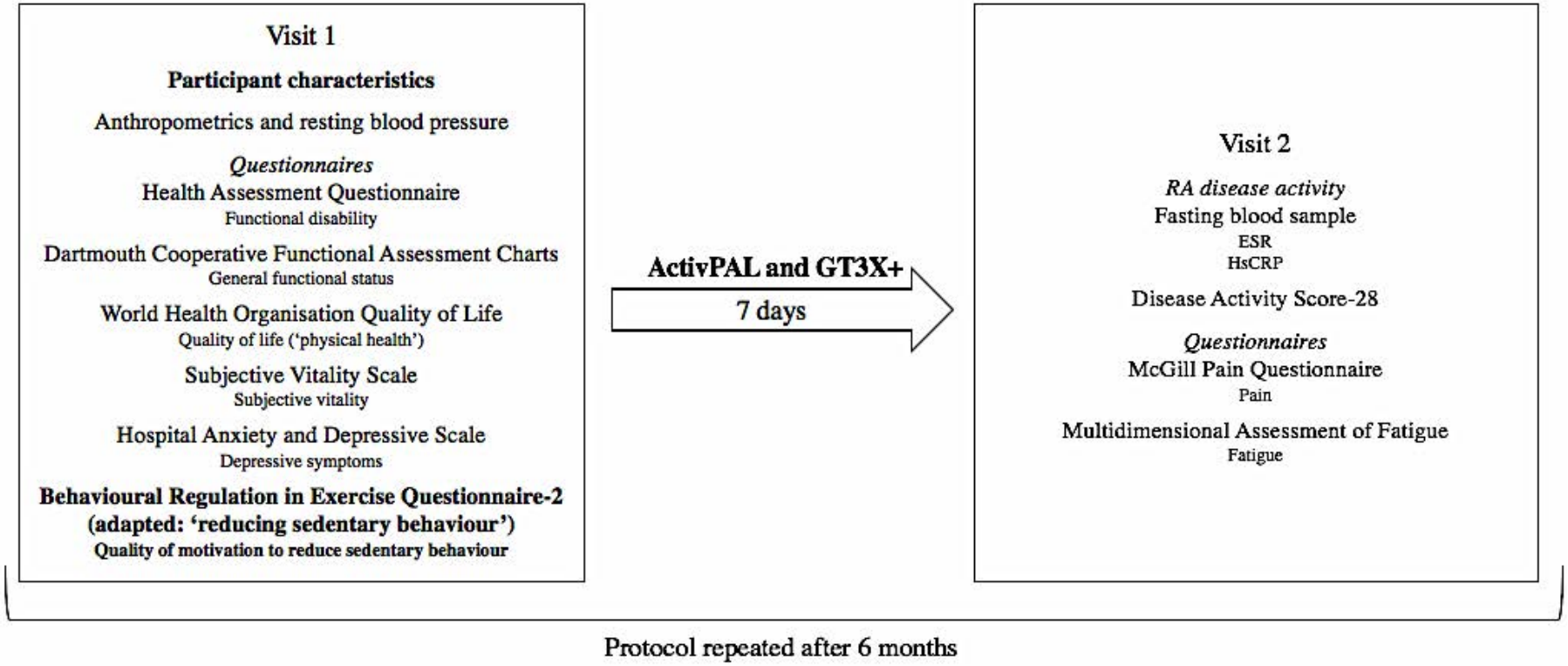

Figure 5.1 Protocol for Chapter 5 of this thesis. Measures specific to this chapter are in **bold.** This study employed a longitudinal design. Participants visited the hospital for data collection at 2 time points ('Time Point 1' [T1] and 6-month follow-up 'Time Point 2' [T2]). At T1 and T2, the same protocols were employed. At T1 and T2, participants attended the hospital for 'Visit 1' and 'Visit 2', separated by 7 days.

Statistical analysis

Preliminary analysis: All statistical analysis were conducted using SPSS (IBM Corporation, Armonk, NY [version 24]). Descriptive statistics were computed for all measured variables at Time Point 1 (T1) and Time Point 2 (T2), calculating change scores (change = T2 – T1). Kolmogorov-Smirnov tests of normality and visual inspection of graphs (histograms, Q-Q plots) were conducted. Where data were non-normally distributed, log and square root transformations were employed to try and achieve a normal distribution. However, following such transformations, normal distribution could not be achieved for several variables.

Bootstrapping is a non-parametric resampling method, whereby data is repeatedly tested from original sample data (typically x ≥1000 samples) to compute 95% confidence intervals (CI) (Efron, 1987; Efron & Tibshirani, 1986; Efron & Tibshirani, 1994; Hopkins et al., 2009; Puth et al., 2015). This procedure has been employed in previous studies conducting regression analysis with non-normally distributed data, due to evidence promoting its use over and above alternative non-parametric statistical tests (Scharkow, 2017; Wood, 2004).

It has been recommended that bootstrapping only be applied to analysis with samples representative of the population of interest and of a sufficient size (Scharkow, 2017). 'Bias-corrected and accelerated bootstrapping' (Efron, 1987) is commonly employed in smaller samples (typically n = 50) (Chernick & LaBudde, 2011; Puth et al., 2015; Scharkow, 2017). Owing to our small sample size and non-normally distributed data, we considered bias-corrected and accelerated bootstrapping an appropriate approach to cross-sectional and longitudinal regression analysis in this study (1000 samples with 95% CI) (Efron & Tibshirani, 1986; Kruisdijk et al., 2017; Puth et al., 2015; Wright et al., 2011).

Main analysis: The main statistical analysis was conducted in 2 phases; 1) cross-sectional associations (T1) between autonomous and controlled motivation to reduce sedentary

behaviour with device-assessed sedentary time and PA, were analysed using correlation and regression models, and 2) change scores were computed and employed in correlation and regression analysis to examine these associations longitudinally.

1) Cross-sectional analysis (T1)

Bivariate Pearson's correlation and regression analysis were firstly employed to examine the cross-sectional associations between autonomous or controlled motivation to reduce sedentary behaviour, with activPAL-assessed sedentary, standing and stepping time, and GT3X+-assessed sedentary time, LPA and MPA, at T1.

Autonomous and controlled motivation to reduce sedentary behaviour were entered separately into regression models as independent variables ('predictors'). Dependent variables ('outcomes') were activPAL- and GT3X+-assessed behaviours (% waking behaviour per day)[1]. All models were adjusted for age and biological sex, hypothesised as likely to affect estimates of sedentary behaviour and PA in RA (Fenton et al., 2017; Fenton et al., 2018c).

Significant associations were determined by examining 95% bootstrapped CIs and corresponding unstandardized bootstrapped coefficients (B). Significant relationships were confirmed where the bootstrapped 95% CI did not cross zero. In addition, standardised non-bootstrapped coefficients (ß) were interpreted to establish the strength of associations (small = .1; medium = .3; large = .5) (Cohen, 1992). R^2 values were reported to represent the unique variance in the dependent variable (sedentary time or PA), explained by the independent variable (autonomous or controlled motivation to reduce sedentary behaviour) and covariates (age and biological sex).

[1]ActivPAL- and GT3X+-assessed behaviours were entered into regression models expressed as percentages of device wear time (% behaviour per day = (device-assessed behaviour [min/day]/total device wear time [min/day]) x 100) in cross-sectional and longitudinal analysis to reduce the number of variables in each model, thus increasing statistical power.

2) Longitudinal analysis

Regression analysis was employed to examine longitudinal associations between change in autonomous or controlled motivation to reduce sedentary behaviour (independent variables [‘predictors’]), with change in objectively-assessed sedentary time and PA (dependent variables [‘outcomes’]). Models were constructed and reported as per cross-sectional analysis, using change scores for all measured variables.

Results

Key characteristics of the study sample are reported in Chapter 3 (Table 3.2). Table 5.1 shows descriptive statistics relevant to this chapter. Planned termination of data collection (n = 47) and lack of time (n = 3) resulted in a loss of n = 50 participants in longitudinal analysis.

Cross-sectional analysis (T1)

Table 5.2 reports cross-sectional bivariate correlations at T1. Results of cross-sectional regression analysis are reported in Tables 5.3 and 5.4.

Regression analysis (adjusted Model 2): For activPAL-assessed behaviours, results revealed autonomous motivation to reduce sedentary behaviour was significantly negatively associated with sedentary time, and significantly positively associated with standing and stepping time. Controlled motivation for reducing sedentary behaviour was negatively associated with stepping time.

For GT3X+-assessed behaviours, regression models indicated autonomous motivation to reduce sedentary behaviour was significantly negatively related to sedentary time, and significantly positively associated with LPA and MPA. Controlled motivation to reduce sedentary behaviour was significantly positively associated with sedentary time, and significantly negatively linked to MPA.

Table 5.1 Descriptive statistics for the total sample at T2, and change between T1 and T2 (change = T2 – T1)

	n	T1	n	T2	n	Change
Biological sex (% female)	74	71%	38	70%	X	X
Age (years)	104	57.93 ± 12.55	54	58.81 ± 12.06	54	0.50 ± 0.50
'Predictors'						
Autonomous motivation (to reduce sedentary behaviour)	104	7.26 ± 1.42	54	7.50 ± 1.51	54	-.04 ± 1.21
Controlled motivation to reduce sedentary behaviour)	104	4.24 ± 1.58	54	4.22 ± 1.69	54	-.05 ± 1.72
ActivPAL						
Valid wear time (min/day)	102	913.02 ± 56.74	53	941.34 ± 60.39	53	20.49 ± 54.16
Sedentary (min/day)	102	546.05 ± 116.59	53	574.82 ± 98.81	53	37.92 ± 65.31
Standing (min/day)	102	267.51 ± 101.00	53	266.63 ± 92.72	53	-13.10 ± 59.86
Stepping (min/day)	102	99.44 ± 37.39	53	99.91 ± 40.34	53	-4.29 ± 19.83
Sedentary (%)	102	59.98 ± 12.91	53	61.39 ± 11.63	53	2.76 ± 6.82
Standing (%)	102	29.16 ± 10.47	53	28.07 ± 8.92	53	-2.06 ± 5.93
Stepping (%)	102	10.87 ± 3.96	53	10.54 ± 4.04	53	-0.70 ± 2.15
GT3X+ (VM)						
Valid wear time (min/day)	100	881.66 ± 64.91	53	890.57 ± 70.65	51	-5.68 ± 58.24
Sedentary (min/day)	100	682.74 ± 72.52	53	690.65 ± 67.54	51	-2.08 ± 53.79
LPA (min/day)	100	113.42 ± 35.41	53	113.97 ± 35.48	51	-0.47 ± 19.84
MPA (min/day)	100	85.48 ± 34.59	53	86.00 ± 37.37	51	-3.08 ± 20.23
Sedentary (%)	100	77.48 ± 6.41	53	77.69 ± 6.74	51	0.25 ± 3.56
LPA (%)	100	12.86 ± 3.92	53	12.77 ± 3.90	51	0.06 ± 2.19
MPA (%)	100	9.70 ± 3.70	53	9.55 ± 3.74	51	-0.31 ± 2.07

n, number of participants; T1, Time Point 1; T2, Time Point 2; X, not applicable

Note: Values are percentages (%) or mean ± standard deviation. Only change scores required for correlation and regression analysis were computed. At T1, 92% of participants were on some form of medication to control their disease activity (disease-modifying anti-rheumatic drugs [90%], anti-tumour necrosis factor treatment [14%], non-steroidal anti-inflammatory drugs [18%]). Thus, medication was not a factor adjusted for in cross-sectional and longitudinal regression analysis.

Table 5.2 Bivariate correlations between quality of motivation to reduce sedentary behaviour with activPAL- and GT3X+-assessed sedentary time and PA (T1)

	1	2	3	4	5	6	7	8
1 Age								
2 Sedentary (activPAL)	.05							
3 Standing (activPAL)	.01	-.96**						
4 Stepping (activPAL)	-.18	-.71**	.50**					
5 Sedentary (GT3X+)	.18	.82**	-.69**	-.86**				
6 LPA (GT3X+)	.00	-.78**	.72**	.66**	-.85**			
7 MPA (GT3X+)	-.31**	-.60**	.43**	.80**	-.83**	.42**		
8 Autonomous motivation (to reduce sedentary behaviour)	.16	-.28**	.23*	.31**	-.30**	.25*	.25*	
9 Controlled motivation (to reduce sedentary behaviour)	-.05	.16	-.12	-.19	.22*	-.17	-.20*	-.22*

LPA, light-intensity physical activity; MPA, moderate-intensity physical activity

Note: * $p < .05$; ** $p < .01$. Bivariate correlations were adjusted for activPAL and GT3X+ wear time. Time in sedentary, standing, stepping, LPA and MPA, were calculated as percentages.

Table 5.3 Linear regressions between quality of motivation with activPAL-assessed sedentary, standing and stepping time (T1)

	Sedentary				Standing				Stepping			
		95% CI				**95% CI**				**95% CI**		
	B	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**
***1* Autonomous motivation**	-2.54**	-4.28 – -.86	.08	-.28**	1.68*	.15 – 3.20	.05	.23*	.86**	.25 – 1.52	.10	.31**
2 Autonomous motivation	-2.63**	-4.31 – -1.04		-.29**	1.64*	.04 – 3.09		.22*	.99**	.44 – 1.59		.35**
Age	.11	-.12 – .31	.01	.11	-.03	-.20 – .15	.00	-.04	-.08*	-.14 – -.03	.07	-.26**
Biological sex	5.84*	.95 – 11.26	.04	.21*	-4.55*	-8.98 – -.32	.04	-.20*	-1.29	-2.69 – .24	.02	-.15
***1* Controlled motivation**	1.30	-.33 – 2.80	.03	.16	-.81	-1.92 – .36	.02	-.12	-.48	-1.00 – .03	.04	-.19
2 Controlled motivation	1.15	-.36 – 2.55		.14	-.67	-1.71 – .45		-.10	-.48*	-.95 – .00		-.19
Age	.06	-.13 – .24	.00	.05	.01	-.17 – .17	.00	.01	-.06*	-.12 – .00	.04	-.19*
Biological sex	6.00*	.81 – 11.08	.04	.21*	-4.65*	-9.54 – -.24	.04	-.20*	-1.3	-2.96 – .24	.02	-.15

CI, confidence intervals

B, unstandardised coefficient (from bootstrapped data); ß, standardised beta coefficient; R^2, variance explained in the dependent variable (sedentary, standing or stepping time) by the independent variable (autonomous or controlled motivation to reduce sedentary behaviour).

Note: * $p < .05$; ** $p < .01$. Model ***'1'*** adjusted for activPAL wear time. Model ***'2'*** adjusted for activPAL wear time, age and biological sex. [x]significant/non-significant result for non-bootstrapped, standardised coefficient, was different from bootstrapped, unstandardised coefficient. Sedentary, standing and stepping time were calculated as percentages of activPAL wear time for use in regression analysis.

Table 5.4 Linear regressions between quality of motivation with GT3X+-assessed sedentary time, LPA and MPA (T1)

	Sedentary				LPA				MPA			
		95% CI				**95% CI**				**95% CI**		
	B	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**
***1* Autonomous motivation**	-1.34*	-2.30 – -.43	.09	-.30**	.69*	.19 – 1.31	.06	.25*	.65*	.07 – 1.32	.06	.25*
2 Autonomous motivation	-1.46**	-2.40 – -.54		-.32**	.67*	.16 – 1.27		.24*	.79**	.27 – 1.31		.30**
Age	.12*	.02 – .21	.06	.23*	-.01	-.07 – .05	.00	-.03	-.11**	-.16 – -.05	.13	-.36**
Biological sex	2.25	-.74 – 4.95	.03	.16	-1.57	-3.27 – .24	.03	-.18	-.69	-2.15 – .98	.01	-.08
***1* Controlled motivation**	.91*	.14 – 1.72	.05	.22*	-.42	-.88 – .09	.03	-.17	-.48*	-.92 – -.12	.04	-.20*
2 Controlled motivation	.83*	.05 – 1.59		.20*	-.38	-.82 – .12		-.15	-.45*	-.83 – -.11		-.19*
Age	.09	-.02 – .20	.03	.17	.00	-.06 – .07	.00	.01	-.09**	-.15 – -.04	.10	-.31**
Biological sex	2.33	-.59 – 5.47	.03	.16	-1.61	-3.19 – -.01	.03	-.19	-.73	-2.34 – .89	.01	-.09

CI, confidence intervals

B, unstandardised coefficient (from bootstrapped data); ß, standardised beta coefficient; R^2, variance explained in the dependent variable (sedentary, LPA or MPA) by the independent variable (autonomous or controlled motivation to reduce sedentary behaviour).

Note: * $p < .05$; ** $p < .01$. Model ***'1'*** adjusted for GT3X+ wear time. Model ***'2'*** adjusted for GT3X+ wear time, age and biological sex. [x]significant/non-significant result for non-bootstrapped, standardised coefficient, was different from bootstrapped, unstandardised coefficient. Sedentary time, LPA and MPA were calculated as percentages of GT3X+ wear time for use in regression analysis.

Longitudinal analysis

Results from bivariate correlation analysis conducted on longitudinal data, are shown in Table 5.5. Results from longitudinal regression analysis are shown in Table 5.6 and Table 5.7 for activPAL and GT3X+ behaviours, respectively.

Regression analysis (adjusted Model 2): For activPAL-assessed behaviours, change in autonomous motivation to reduce sedentary behaviour was significantly negatively associated with change in sedentary time, and significantly positively related to change in standing and stepping time. For GT3X+-assessed behaviours, change in autonomous motivation to reduce sedentary behaviour was significantly negatively linked to change in sedentary time, with the reverse significant association observed for change in LPA. No significant relationships were found between change in controlled motivation for reducing sedentary behaviour with change in any activPAL- and GT3X+-assessed behaviours.

Comparison of activPAL- and GT3X+-assessed sedentary time. Change in autonomous motivation to reduce sedentary behaviour was significantly negatively associated with change in activPAL- *and* GT3X+-assessed sedentary time.

Table 5.5 Bivariate correlations between quality of motivation to reduce sedentary behaviour with activPAL- and GT3X+-assessed sedentary time and PA (longitudinal – T1-T2)

	1	2	3	4	5	6	7	8
1 Age								
2 Sedentary (activPAL)	.03							
3 Standing (activPAL)	.03	-.95**						
4 Stepping (activPAL)	-.17	-.55**	.27					
5 Sedentary (GT3X+)	.09	.73**	-.56**	-.77**				
6 LPA (GT3X+)	-.09	-.64**	.52**	.61**	-.85**			
7 MPA (GT3X+)	-.05	-.58**	.42**	.68**	-.82**	.39**		
8 Autonomous motivation (to reduce sedentary behaviour)	.03	-.43**	.38**	.33**	-.37**	.35**	.27	
9 Controlled motivation (to reduce sedentary behaviour)	.12	.01	.03	-.10	-.05	-.10	.19	-.10

LPA, light-intensity physical activity; MPA, moderate-intensity physical activity

Note: * $p < .05$; ** $p < .01$. Bivariate correlations were adjusted for activPAL and GT3X+ wear time. Time in sedentary, standing, stepping, LPA and MPA, were calculated as percentages of activPAL and GT3X+wear time, for use in bivariate correlations. All variables are non-transformed.

Table 5.6 Linear regressions between quality of motivation with activPAL-assessed sedentary, standing and stepping time (longitudinal – T1-T2)

	Sedentary				Standing				Stepping			
		95% CI				**95% CI**				**95% CI**		
	B	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**
***1* Autonomous motivation**	-2.44**	-3.70 – -.95	.19	-.43**	1.85**	.52 – 2.88	.14	.38**	.59*	.20 – 1.15	.11	.33*
2 Autonomous motivation	-2.45**	-3.72 – -.89		-.44**	1.86**	.61 – 2.79		.38**	.59*	.18 – 1.15		.33*
Age	.55	-3.00 – 4.01	.00	.04	.23	-2.86 – 3.64	.00	.02	-.75	-1.84 – .30	.03	-.18
Biological sex	-1.02	-4.31 – 2.53	.01	-.07	1.55	-1.60 – 4.43	.02	.12	-.54	-1.71 – .61	.01	-.12
***1* Controlled motivation**	.02	-1.07 – .99	.00	.01	.10	-.92 – 1.35	.00	.03	-.12	-.53 – .29	.01	-.10
2 Controlled motivation	.02	-1.13 – 1.06		.01	.07	-1.02 – 1.35		.02	-.09	-.49 – .33		-.07
Age	.46	-3.20 – 4.45	.00	.03	.26	-2.77 – 3.27	.00	.02	-.70	-1.93 – .53	.03	-.16
Biological sex	-.89	-5.50 – 3.32	.00	-.06	1.44	-1.99 – 4.91	.01	.11	-.55	-1.75 – .56	.01	-.12

CI, confidence intervals

B, unstandardised coefficient (from bootstrapped data); ß, standardised beta coefficient; R^2, variance explained in the dependent variable (sedentary, standing or stepping time) by the independent variable (autonomous or controlled motivation to reduce sedentary behaviour).

Note: * $p < .05$; ** $p < .01$. Model ***'1'*** adjusted for activPAL wear time. Model ***'2'*** adjusted for activPAL wear time, age and biological sex. [x]significant/non-significant result for non-bootstrapped, standardised coefficient, was different from bootstrapped, unstandardised coefficient. Sedentary, standing and stepping time were calculated as percentages of activPAL wear time for use in regression analysis.

Table 5.7. Linear regressions between quality of motivation with GT3X+-assessed sedentary time, LPA and MPA (longitudinal – T1-T2)

	Sedentary				LPA				MPA			
		95% CI				**95% CI**				**95% CI**		
	B	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**	**B**	**(lower – upper)**	**R^2**	**ß**
***1* Autonomous motivation**	-1.08**	-1.81 – -.49	.13	-.37**	.63**	.21 – 1.13	.12	.35*	.46*	.02 – .96	.07	.27[x]
2 Autonomous motivation	-1.08**	-1.83 – -.50		-.36*	.63**	.17 – 1.21		.35*	.45	.03 – 1.00		.26
Age	.63	-1.19 – 2.41	.01	.09	-.38	-1.55 – .86	.01	-.09	-.21	-1.27 – .86	.00	-.05
Biological sex	-.35	-2.07 – 1.49	.00	-.04	.08	-1.33 – 1.22	.00	.02	.26	-1.15 – 1.64	.00	.06
***1* Controlled motivation**	-.11	-.70 – .44	.00	-.05	-.13	-.46 – .21	.01	-.10	.24	-.06 – .63	.04	.19
2 Controlled motivation	-.14	-.73 – .45		-.06	-.12	-.46 – .26		-.09	.25	-.04 – .63		.20
Age	.74	-1.28 – 2.67	.01	.11	-.35	-1.61 – 1.10	.01	-.08	-.35	-1.46 – .80	.01	-.09
Biological sex	-.42	-2.12 – 1.59	.00	-.05	.14	-1.21 – 1.36	.00	.03	.27	-1.09 – 1.50	.00	.06

CI, confidence intervals

B, unstandardised coefficient (from bootstrapped data); ß, standardised beta coefficient; R^2, variance explained in the dependent variable (sedentary, LPA or MPA) by the independent variable (autonomous or controlled motivation to reduce sedentary behaviour).

Note: * $p < .05$; ** $p < .01$. Model ***'1'*** adjusted for GT3X+ wear time. Model ***'2'*** adjusted for GT3X+ wear time, age and biological sex. [x]significant/non-significant result for non-bootstrapped, standardised coefficient, was different from bootstrapped, unstandardised coefficient. Sedentary time, LPA and MPA were calculated as percentages of GT3X+ wear time for use in regression analysis.

Discussion

Adopting an SDT lens (Deci & Ryan, 1985), this study aimed to examine longitudinal associations between autonomous and controlled motivation to reduce sedentary behaviour, with device-assessed sedentary time and PA in people with RA. Findings showed that autonomous motivation to reduce sedentary behaviour was associated with activPAL-assessed sedentary (negative), standing and stepping (positive) time, as well as GT3X+-assessed sedentary time (negative) and LPA (positive) in this patient group.

Autonomous motivation to reduce sedentary behaviour accounted for between 11%-19% of the variance in activPAL-assessed behaviours (sedentary time = 19%; standing time = 14%; stepping time = 11%), and between 12%-13% of the variance in GT3X+-assessed behaviours (sedentary time = 13%; LPA = 12%). Little research exists in any population, including RA, that examines the determinants ('predictors') of sedentary behaviour. This therefore makes it difficult to compare the above findings, specific to sedentariness, to previous research. The study comprising Chapter 4 of this thesis provided some insight into the associations between clinically- and patient-important RA outcomes (modelled as 'predictors') with activPAL-assessed sedentary time (modelled as an 'outcome'). From these 'predictors' (pain, fatigue, DCOOP general functional status, quality of life and subjective vitality), only hsCRP predicted higher variance in activPAL-assessed sedentary time (21%) than autonomous motivation to reduce sedentary behaviour (19%) in the current study. Additionally, only hsCRP, DCOOP general functional status and quality of life accounted for higher variance in activPAL-assessed standing time (16%, 17% and 17%, respectively) than autonomous motivation to reduce sedentary behaviour (14%) in this study. Finally, autonomous motivation to reduce sedentary behaviour predicted higher variance in activPAL-assessed stepping time, and GT3X+-assessed sedentary time and LPA, than all health-related variables measured in

Chapter 4 of this thesis. Thus, results from this thesis facilitates decisions regarding the 'most important' determinants of sedentary behaviour and PA, in order that these can be targeted as an area for future research and/or in behaviour change interventions in the RA population. Further research is required to assess whether the RA health outcomes described above are key predictors of sedentary time in RA, over and above autonomous motivation to reduce sedentary behaviour.

Research in non-RA groups have examined the links between, specifically, autonomous and controlled motivation in a PA context. For example, Koponen, Simonsen and Suominen (2017) demonstrated that autonomous motivation held a positive association with self-reported PA in people living with type 2 diabetes (R^2 = .13, for 'perceived autonomy support', 'autonomous motivation' and 'self-care competence'). Very few RA studies exist in this area. Preliminary research by Hurkmans et al. (2010) revealed that autonomous motivation was positively related to self-reported PA in this patient group, in which regulation style (autonomous and controlled motivation to engage in PA) explained 10% of the variance in PA levels. These values are similar to R^2 values reported in the current study for PA-related behaviours (activPAL-assessed stepping time [11%] and GT3X+-assessed LPA [12%]).

Importantly, regression analysis conducted in this study to examine associations between autonomous motivation to reduce sedentary behaviour with device-assessed sedentary time and PA in RA, only adjusted for device wear time, age and biological sex. It is likely that other factors contribute to engagement in these behaviours, such as body-mass index, education, socioeconomic status, disease activity and disease severity. Adjusting for such variables in future research might reduce the R^2 values revealed in this study, which corresponded to the relationship between autonomous motivation to reduce sedentary behaviour with device-assessed sedentary time and PA in people with RA.

In a recent qualitative study, Thomsen et al. (2015) called for the development of interventions targeting reductions in sedentary behaviour in RA, not solely focused on MVPA promotion. Akin to this proposition, a review has recommended that in populations with reduced mobility, reductions in sedentary time and increases in LPA should be supported, which might be more realistic than MVPA to achieve among these cohorts (Manns et al., 2012). To our knowledge, the present research is the first longitudinal study to identify modifiable determinants of sedentary behaviour among people with RA (autonomous and controlled motivation to reduce sedentary behaviour).

Results from both cross-sectional and longitudinal analysis suggested that patients who were motivated to reduce their sedentary behaviour for more autonomous reasons (e.g., because they value the benefits and/or enjoy doing so), engaged in less activPAL- and GT3X+-assessed sedentary time. These findings suggest that interventions centred on promoting more identified and intrinsic reasons for reducing sedentary behaviour among people with RA, may offer an avenue to encourage sedentary behaviour change in this patient group. Such interventions could involve similar components to those successfully delivered in previous work targeting autonomous motivation to reduce sedentary behaviour (Babic et al., 2016; Smith et al., 2017). For example, researcher-led, interactive discussion and goal-setting using novel technologies (e.g., smartphones). However, these studies targeted autonomous motivation to reduce screen-time in adolescents, making it difficult to readily generalise to people with RA. Indeed, it is likely that these patients engage in sedentary behaviour for different reasons and in different contexts, compared to adolescents. For example, in their qualitative study, Thomsen et al. (2015) revealed that RA patients engage in sedentary behaviour “when symptoms dominate”, and this might entail reading and doing crossword puzzles (mentally active sedentary behaviours), as well as watching television (passive

sedentary behaviour). Interestingly, patients also alluded to engaging in sedentary behaviour due to lack of motivation, regardless of the debilitating symptoms of RA. The authors suggested that this was indicative of how sedentary behaviour had been immersed into their daily routine for self-management purposes. Arguably, this finding also suggests that motivation may independently, or in combination with RA disease features, influence sedentary behaviour engagement among this patient group. The research of Thomsen et al. (2015) further underlines the importance of the body of work in this thesis, which has examined the associations between clinically- and patient-important health outcomes (Chapter 4) *and* quality of motivation to reduce sedentary behaviour (the current Chapter 5), with levels of sedentary time in people with RA.

An additional finding from the present longitudinal study warranting discussion, is that autonomous motivation to reduce sedentary behaviour was longitudinally positively associated with engagement in activPAL-assessed standing and stepping time, and GT3X+-assessed LPA in people with RA. These results might be due to shared variance between sedentary time and low-intensity PA, as indeed, these behaviours are highly inversely correlated. However, this premise cannot be wholly confirmed, as the behaviours of focus in this study (time in sedentary, standing, stepping and LPA behaviour) were tested in separate regression models. While this may be the case, interestingly, the association between autonomous motivation to reduce sedentary behaviour with sedentary time, measured by the gold standard activPAL, was stronger than the links held with standing, stepping and LPA. This suggests that autonomous motivation to reduce sedentary behaviour is a suitable target when specifically aiming to reduce sedentary time in RA patients, and changes in related behaviours (e.g., standing) might occur as a result.

The current study revealed that controlled motivation to reduce sedentary behaviour was not significantly associated with any objectively-assessed behaviours. These results are consistent with a systematic review in 2012 (Teixeira et al., 2012), which concluded mixed evidence for the relationship between controlled motivation with PA, with the majority of findings revealing a null association. Similarly, a recent study found no significant correlation between controlled motivation to engage in PA, with self-reported PA (as assessed with the International Physical Activity Questionnaire) (Craig et al., 2003) in schizophrenia patients (Costa et al., 2018). In the present study, examples of items pertaining to controlled motivation to reduce sedentary behaviour on the adapted BREQ-2 include, "I aim to reduce my sedentary behaviour…because other people say I should", or "…because I feel guilty when I am not doing this". Perhaps the null association between controlled motivation to reduce sedentary behaviour with sedentarity was because participants exhibiting high *or* low levels of sedentary time, did not perceive these as reasons for disengagement in sedentary behaviour. For example, a clinician may not have historically forcefully recommended reductions in sedentary time, or participants may not have experienced guilt from engagement in sedentary behaviour. This could possibly be due to lack of awareness regarding associations between sedentariness with health among people with RA, as this line of research is in its infancy. Still, based on evidence outlining the adverse role of controlled motivation for engagement in target behaviours (e.g., negative relationship with PA), minimising controlled reasons for reducing sedentary behaviour might still be important (Teixeira et al., 2012). In addition, controlled motivation has been shown to negatively affect physical and psychological well-being in individuals (Ng et al., 2012; Quested & Duda, 2011), which does not bode well for RA patients already experiencing compromised mental health (Matcham et al., 2013).

Research using an SDT perspective to examine autonomous and controlled motivation in the context of sedentary behaviour has only been conducted in non-RA populations (Babic et al., 2016; De Cocker et al., 2015; Gaston, De Jesus, Markland, & Prapavessis, 2016; Quartiroli & Maeda, 2014; Rollo et al., 2016; Smith et al., 2017). It is challenging to compare such studies with the present investigation, and this is not just attributed to limitations surrounding generalisability to RA patients. For example, Gaston et al. (2016) sought to examine the quality of motivation to engage in sedentary behaviour, and Quartiroli and Maeda (2014) used the BREQ-2 to measure quality of motivation to engage in PA, both examining associations with self-reported sedentary time. In this study, we examined motivation to reduce sedentary behaviour, which may provide more insight into determinants for interventions specifically aiming to reduce sedentarity in this patient group. Indeed, autonomous motivation to engage in sedentary behaviour would be challenging to change, as it would require efforts to prevent individuals undertaking behaviours they enjoy, or value the benefits of. In addition, sedentary behaviour change interventions specifically targeting reductions in sedentary time, rather than increasing PA, have been advocated to a greater extent (Thomsen et al., 2015). Akin to this point, it has been demonstrated in the general population that interventions aiming to increase MVPA as a vehicle to decrease sedentary time, are ineffective (Martin et al., 2015; Prince et al., 2014).

Although the present study provides important evidence alluding to the relationship between autonomous motivation to reduce sedentary behaviour with sedentary time in RA, findings should be confirmed by experimental studies. Nevertheless, initial quantitative evidence has been provided, indicating that autonomous motivation to reduce sedentary behaviour may represent a determinant of sedentary time in RA, upon which robust and informed interventions can be developed in this patient group. Prior to developing

interventions, it may be insightful to examine the extent to which autonomous motivation to reduce sedentary behaviour predicts variability in sedentariness (and potentially LPA, including standing), to the extent that it holds implications for RA outcomes.

Strengths of the present study include its longitudinal design and device-assessment of sedentary time and PA. This study also used a theoretical perspective (SDT) to address its research questions (Michie et al., 2008), which has been widely-applied in studies promoting behaviour change in different populations (e.g., PA, weight loss, smoking cessation) (Deci & Ryan, 1987, 2000, 2008a, 2008b; Ryan & Deci, 2000). Findings have provided initial evidence on autonomous motivation to reduce sedentary behaviour as a modifiable determinant of sedentary time and PA in RA. Overall, this research has added to the generally scarce evidence base regarding quality of motivation to reduce sedentary behaviour in any population, but specifically and importantly fills this gap in knowledge regarding people with RA.

Notwithstanding these interesting and important findings, there are limitations that should be addressed. First, this longitudinal study had a small sample size. Bias-corrected and accelerated bootstrapping was applied in statistical analysis in an attempt to address this limitation. The application of these approaches, however, would have still resulted in reduced power. Nevertheless, significant associations between autonomous motivation to reduce sedentary behaviour with activPAL- and GT3X+-assessed behaviours were still observed, the strength of which may have been increased with a larger sample size. Further, most participants were female and had moderate disease activity and severity, limiting generalisability to males and those with higher/lower disease activity and severity. However, it should be noted that a larger percentage of people living with RA are female (Wasserman, 2018). In addition, although device-based measures validated in RA were employed in the present investigation, the context of free-living behaviour could not be determined. Insight into the specific domains

by which these behaviours occur would be interesting, and further inform intervention development and implementation.

Finally, the present study did not incorporate all tenets of SDT that might have been relevant to sedentary time and PA in RA. An additional sub-theory of SDT, namely basic psychological needs satisfaction theory, postulates that humans have 3 basic psychological needs (‘autonomy’, ‘competence’ and ‘relatedness’) that enable them to foster intrinsic motivation (Deci & Ryan, 2000). Fulfilment of these needs leads to fostering more autonomous motivation towards a behaviour, as well as benefits in mental health (e.g., vitality and well-being) (Ryan & Deci, 2000). Basic psychological needs satisfaction theory was not applied in this study, as this research first aimed to examine the role of autonomous and controlled motivation to reduce sedentary behaviour, as a malleable determinant of sedentary time and PA in people with RA.

Conclusion

The present study provided support for the role of autonomous and controlled motivation to reduce sedentary behaviour for levels of sedentary time and PA among RA patients. Results suggest that where patients are motivated to reduce their sedentary behaviour for more autonomous reasons, they engage in less sedentary behaviour and more standing, stepping and LPA. Thus, the findings contribute to an empirical (and theoretical) bases regarding the development of RA interventions which target autonomous motivation to reduce sedentary behaviour, to encourage people living with this disease to reduce their sedentary time and increase LPA (including standing). However, future experimental studies which test the value of such SDT-based interventions are required to confirm these findings.

CHAPTER 6

EXPLORING THE ROLE OF AUTONOMOUS MOTIVATION TO REDUCE SEDENTARY BEHAVIOUR AND IMPROVE RHEUMATOID ARTHRITIS OUTCOMES: TESTING MODELS OF SEDENTARY BEHAVIOUR CHANGE

Abstract

Aim: This study tested models of sedentary behaviour change, to examine whether autonomous motivation to reduce sedentary behaviour was associated with activPAL-assessed sedentary and standing time, and in turn, RA health outcomes. **Method:** RA patients completed questionnaires to measure pain, fatigue, physical function, quality of life, psychological well-being and quality of motivation to reduce sedentary behaviour. High-sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate were measured via fasting blood samples. Disease Activity Score-28 (DAS-28) was assessed. Participants wore an activPAL and GT3X+ to measure free-living sedentary time and PA over 7 days. This protocol was repeated after 6 months. *Statistical analysis:* Hypothesised path models were; autonomous motivation to reduce sedentary behaviour →sedentary time *or* standing time →DAS-28 and hsCRP (Model 1), *or* pain, fatigue and subjective vitality (Model 2), *or* general functional status and quality of life (Model 3). **Results:** Path analysis revealed that change in autonomous motivation to reduce sedentary behaviour was significantly negatively linked to change in activPAL-assessed sedentary time (ß = -.43 [Model 1]; ß = -.44 [Models 2 and 3]), which in turn, significantly associated with hsCRP (ß = .45), fatigue (ß = .27), subjective vitality (ß = -.38), general functional status (ß = .41) and quality of life (ß = -.38). Change in autonomous motivation to reduce sedentary behaviour was significantly positively related to change in activPAL-assessed standing time (ß = .37 [Model 1]; ß = .38 [Models 2 and 3]), which in turn, significantly associated with hsCRP (ß = -.40), pain, (ß = -.27) fatigue (ß = -.30), subjective vitality (ß = .33), general functional status (ß = -.41) and quality of life (ß = .41). **Conclusion:** Findings suggest interventions targeting autonomous motivation to reduce sedentary behaviour, may predict variability in sedentary time and standing time among people with RA, to the extent that it may hold implications for several clinically- and patient-important health outcomes.

Introduction

Rheumatoid Arthritis (RA) is an autoimmune disease, characterised by chronically elevated systemic inflammation (Angelotti et al., 2017). This leads to joint pain and stiffness, and declines in physical function (Smolen et al., 2016a; Uhlig et al., 2014). Extra-articular manifestations of RA also include fatigue and depression, both highly prevalent in RA. For example, 88-98% of people living with RA report symptoms of fatigue (Hewlett et al., 2005) and 17% are diagnosed with clinical depression (Fiest et al., 2017).

Pharmacological treatment of RA has significantly improved in the last 30 years, whereby medication (e.g., disease-modifying anti-rheumatic drugs [DMARDs]) is commenced as early as possible in the disease course, with the aim of stringently controlling RA inflammatory disease activity ('treat-to-target') (Radner, Smolen, & Aletaha, 2014; Smolen et al., 2017; Versteeg et al., 2018; Weinblatt et al., 2006). Patient response to treatment is closely monitored by their Rheumatologist, using the Disease Activity Score-28 (DAS-28) (Prevoo et al., 1995; van Gestel et al., 1998). Often, RA disease activity is not optimally controlled with pharmacological treatment, and even when it is, patients may continue to report debilitating symptomology (e.g., pain, fatigue, functional disability, poor psychological well-being) (Santos et al., 2019; Taylor et al., 2016). In addition, novel therapeutic RA treatment has incurred very high healthcare costs (Chaudhari, 2008). Therefore, non-pharmacological management of RA has received increasing research attention, for example advocating increased engagement in physical activity (PA) (Santos et al., 2019).

It has been widely demonstrated that PA can improve a number of pertinent health outcomes among people with RA. Specifically, participation in moderate-to-vigorous PA (MVPA, ≥3 metabolic equivalents [METs]), has been shown to attenuate systemic inflammation, disease activity, functional disability, pain and fatigue, and enhance

psychological well-being (Cooney et al., 2011; de Jong et al., 2003; Loppenthin et al., 2015; Metsios & Kitas, 2018; Metsios et al., 2015; Plasqui, 2008; Rahnama & Mazloum, 2012; Rongen-van Dartel et al., 2015; Verhoeven et al., 2016). However, evidence suggests that people with RA typically do not engage in levels of MVPA recommended to yield such benefits (Tierney et al., 2012). It has been reported that debilitating symptomology of RA (e.g., pain, fatigue, functional disability) is a barrier to MVPA participation (Tan et al., 2019; Veldhuijzen van Zanten et al., 2015). These barriers consequently reduce the potential of MVPA as a pragmatic non-pharmacological method of improving health in this patient group. However, movement exists on a continuum, ranging from sedentary behaviour (waking behaviour expending ≤1.5 METs, whilst sitting/reclining/lying) (SBRN, 2012; Tremblay et al., 2017) through to light-intensity PA (LPA [e.g., incidental movement, lifestyle-embedded activities, 1.6-2.9 METs]), to higher-intensity MVPA. Thus, whilst MVPA and 'exercise' are most often considered necessary for health gains, RA studies should not discount the health impacts of 'non-exercise behaviours' that occur lower down the continuum, such as sedentary behaviour and LPA.

Although in their infancy, RA studies have investigated the links between sedentary behaviour and LPA with disease outcomes. Specifically, cross-sectional studies suggest that sedentary behaviour is positively associated with RA disease activity and functional disability, with the reverse associations reported for LPA (Fenton, et al., 2018c; Khoja et al., 2016; Summers et al., 2019). Additionally, LPA has been negatively linked with depressive symptoms, and positively related to subjective vitality in a recent cross-sectional study (Fenton et al., 2018c).

Cross-sectional and longitudinal data from this thesis (Chapter 4), has consolidated and extended this research. Indeed, longitudinal associations were demonstrated between

activPAL-assessed sedentary and standing time with several clinically- and patient-important RA outcomes (e.g., high-sensitive C-reactive protein [hsCRP], pain, fatigue, physical function, quality of life and subjective vitality). With further statistical examination of longitudinal data, it was concluded that these relationships were bi-directional, suggesting an opportunity to intervene at the behavioural level (sedentary and standing time) to improve pertinent RA health outcomes. Also notable, was the strong inverse correlation between activPAL-assessed sedentary time with activPAL-assessed standing time (ß = -.95). This, together with the point that these behaviours represent a large proportion of a patient's waking day (approximately 97%) (Hammam et al., 2019; Summers et al., 2019), underlines the potential of reducing sedentary behaviour and promoting LPA as a pragmatic, feasible and effective option to improve health among people with RA (Manns et al., 2012).

In order to develop effective sedentary behaviour change interventions, it is critical to identify the malleable determinants of the targeted behaviour (Chastin et al., 2015a; Chastin et al., 2016). Interventions can then aim to modify these determinants, and consequently increase the likelihood of behaviour change. In their qualitative study, Thomsen et al. (2015) suggested that enhancing motivation to reduce sedentary behaviour in RA patients might elicit sedentary behaviour change among this patient group. This proposition has been supported in the recently developed 'Systems of Sedentary behaviours' framework (SOS-framework) (Chastin et al., 2016) that highlights 'Psychology and Behaviour' (encompassing motivation) as a highly ranked research priority for establishing factors influencing sedentary behaviour 'across the life course'. Employing a theoretical basis for such research questions is important to understand the specific motivational processes underlying behaviour change. Self-determination theory (SDT) (Deci & Ryan, 1985) has provided such a basis in several behaviour change contexts (e.g., PA, weight loss, smoking cessation) (Deci & Ryan, 1987,

2000, 2008a, 2008b; Ryan & Deci, 2000) to understand the variability in the reasons *why* an individual engages in the targeted behaviour for behavioural outcomes. Thus, there is scope to investigate the role of motivation in reducing sedentary behaviour in RA, using an SDT lens.

A central tenet of SDT is the concept of 'quality of motivation', proposed to lie on a continuum from controlled motivation (lower quality) to autonomous motivation (higher quality) (Deci & Ryan, 1985, 2008a, 2008b; Ryan & Deci, 2000). Autonomous motivation is reported to be operating where behaviour is directed by identified regulation (e.g., identifying the benefits of behaviour) and/or intrinsic motivation (e.g., enjoyment of the behaviour), resulting in more optimal engagement and maintenance of the target behaviour (Deci & Ryan, 2008a, 2008b). Conversely, controlled motivation, specifically external regulation (e.g., external pressure) and/or introjected regulation (e.g., engaging in behaviour to avoid feelings of guilt), is proposed to hold negative implications for uptake of and adherence to the target behaviour (Deci & Ryan, 2008a, 2008b).

Autonomous motivation towards PA has been linked to higher levels of engagement and long-term maintenance of PA in clinical and non-clinical populations (Duda et al., 2014; Fasczewski et al., 2018; Fortier et al., 2012; Milne et al., 2008; Teixeira et al., 2012; Vancampfort et al., 2013). For example, Vancampfort et al. (2013) revealed that in patients with schizophrenia, more autonomous motivation towards PA was associated with higher levels of PA (walking and MVPA). In RA, few studies have examined the role of autonomous and controlled motivation in PA engagement among people with RA (Demmelmaier & Iversen, 2018). Cross-sectional studies by Hurkmans et al. (2010) and Yu et al. (2015a) have provided preliminary evidence in this area, revealing positive correlations between autonomous motivation towards PA with levels of self-reported PA, in this patient group.

There is a paucity of studies grounded in SDT, investigating how autonomous and controlled motivation to reduce sedentary behaviour contributes to the variability in sedentarity in any population, including RA. Current research has predominantly focused on the role of quality of motivation for reductions in screen-time among adolescents (Babic et al., 2016; Smith et al., 2017), using the Motivation to Limit Screen-time Questionnaire (Lubans et al., 2013) which is based on SDT. These studies demonstrated that enhanced autonomous motivation to reduce screen-time (e.g., "I try to limit my screen-time because I believe it is important") was related to reductions in screen-time among adolescents. Similarly, a recent online-based intervention grounded in SDT (and other theories of motivation, e.g., theory of planned behaviour), led to self-reported reductions in sedentary behaviour among adults in the workplace (De Cocker et al., 2015). However, despite using an SDT perspective, this study did not specifically target autonomous motivation to reduce sedentary behaviour as part of the intervention. Additionally, the study by De Cocker and colleagues (2015) did not examine whether changes in autonomous motivation to reduce sedentary behaviour represented the psychological mechanism by which the intervention accounted for reductions in sedentarity. Rather, this intervention was directed at modifying key constructs outlined by the theory of planned behaviour, and measured changes in self-efficacy, attitudes and intentions to reduce and interrupt sitting time.

The longitudinal study comprising Chapter 5 of this thesis provided the first insight into the relationships between autonomous motivation and controlled motivation to reduce sedentary behaviour, with levels of this behaviour in RA. These observational data indicated that increased autonomous motivation to reduce sedentary behaviour was associated with a decrease in device-assessed sedentary time, with the reverse true for device-assessed standing time in these patients. However, to provide a particularly compelling rationale for developing

and implementing interventions targeting autonomous motivation to reduce sedentary behaviour for improving health in RA, research is required which seeks to determine the degree by which variability in sedentary and standing time, attributable to autonomous motivation to reduce sedentary behaviour, may hold meaningful implications for clinically- and patient-important RA outcomes (e.g., DAS-28, pain, fatigue).

The aim of Chapter 6 of this thesis is to test models of sedentary behaviour change, which assumes autonomous motivation to reduce sedentary behaviour is linked to variability in device-assessed sedentary and standing time, and in turn, relevant RA health outcomes (autonomous motivation to reduce sedentary behaviour → activPAL-assessed sedentary time [or standing time] → RA outcomes). These models will be based on findings from Chapters 4 and 5. Thus, it is hypothesised that an increase in autonomous motivation to reduce sedentary behaviour will be linked to a decrease in activPAL-assessed sedentary time, and an increase in activPAL-assessed standing time. In turn, it is hypothesised that a decrease in activPAL-assessed sedentary time and an increase in activPAL-assessed standing time, will be associated with a decrease in DAS-28, hsCRP, pain, fatigue and DCOOP general functional status, and an increase in subjective vitality and quality of life.

Method

Chapter 3 of this thesis details the methodology for this chapter. The measures employed in the current chapter are shown in Figure 6.1[1].

[1] For the remainder of Chapter 6, questionnaires will be referred to in acronym form. Specifically, Health Assessment Questionnaire = HAQ, Dartmouth Cooperative Functional Assessment Charts = DCOOP, World Health Organisation Quality of Life = WHOQOL-BREF, Subjective Vitality Scale = SVS, and Hospital Anxiety and Depression Scale = HADS, Behavioural Regulation in Exercise Questionnaire = BREQ-2

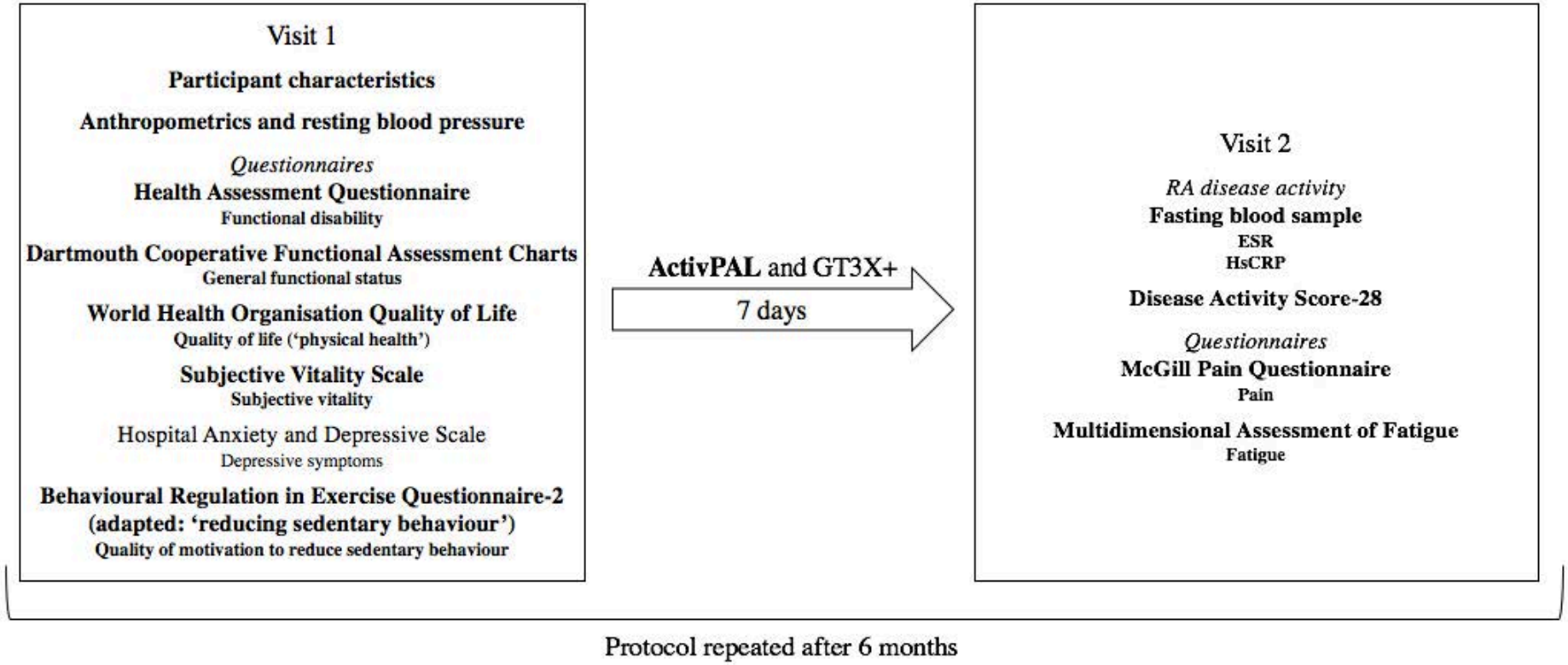

Figure 6.1 Protocol for Chapter 6 of this thesis. Measures specific to this chapter are in **bold.** ESR, erythrocyte sedimentation rate; HsCRP, high-sensitivity C-reactive protein. This study employed a longitudinal design. Participants visited the hospital for data collection at 2 time points ('Time Point 1' [T1] and 6-month follow-up 'Time Point 2' [T2]). At T1 and T2, the same protocols were employed. At T1 and T2, participants attended the hospital for 'Visit 1' and 'Visit 2', separated by 7 days.

Statistical analysis

Preliminary analysis: SPSS and AMOS software (IBM Corporation, Armonk, NY [version 24]) were used to carry out statistical analysis. Descriptive statistics at Time Point 1 (T1) and Time Point 2 (T2) were computed, in addition to calculating change scores between T1 and T2, for all measured variables (change = T2 – T1). Kolmogorov-Smirnov tests of normality and visual inspection of graphs (histograms, Q-Q plots) established that data were not entirely normally distributed, therefore non-parametric procedures were used to analyse the data. Specifically, bootstrapping (a non-parametric resampling procedure) was employed in path analysis to test all hypothesised models.

The bootstrapping process involves intensively resampling data (typically x ≥1000 samples) from the original sample data to establish 95% confidence intervals (CI), which are interpreted to determine statistical significance (Efron, 1987; Efron & Tibshirani, 1986; Efron & Tibshirani, 1994; Hopkins et al., 2009; Puth et al., 2015). Bootstrapping is advocated to deal with non-normal data in small sample sizes, it is simple to apply and can be used in an assortment of statistical tests (e.g., regression analysis, structural equation modelling) (Scharkow, 2017; Wood, 2004; Wright et al., 2011). This procedure is considered after determining whether the sample is representative of the population of interest, and is of an adequate size (Scharkow, 2017). Further, there are different means of bootstrapping data, with 'bias-corrected and accelerated bootstrapping' being one of the most commonly-employed, particularly with smaller sample sizes (≥ n = 50) (Puth et al., 2015; Scharkow, 2017). Considering our sample is n = 54, and representative of the general RA population, we considered bias-corrected and accelerated bootstrapping was appropriate to analyse data in this study. Indeed, our sample is characterised by mostly females, and participants had an average age of 58 years old. In this population, more females than males are diagnosed with RA, and

disease onset usually occurs beyond 30 years old (Wasserman, 2018). Further, participants' height, weight, BMI, body fat percentage, DAS-28, disease severity (HAQ) and disease duration is similar to descriptive data from other RA studies (Metsios et al., 2009; Sokka et al., 2008; Stavropoulos-Kalinoglou et al., 2013).

Path analysis

Specifying the models: Path analysis was employed to examine hypothesised associations between autonomous and controlled motivation to reduce sedentary behaviour with activPAL-assessed sedentary or standing time, and in turn, RA outcomes. This approach is superior to correlation and regression analysis due to the additional insight it provides regarding inter-relationships between variables. Specifically, path analysis allows; 1) examination of a proposed dependent variable (e.g., activPAL-assessed sedentary time) as an independent variable predicting additional dependent variables (e.g., pain) in the model, and 2) indirect, as well as direct, associations to be observed within the model.

Results from longitudinal regression analysis in Chapters 4 and 5 of this thesis, were used to inform construction of path models in this study. Owing to bi-directional associations observed in Chapter 4, there is a rationale to intervene at the behavioural level (e.g., reduce sedentary time and increase standing time). As such, behavioural variables were modelled as 'predictors' of RA health variables, and health variables specified as 'outcomes'. Only activPAL-assessed sedentary and standing time were included in the hypothesised models, as these behaviours held bi-directional associations (of at least medium effect size [= .3]) with assessed health variables (Chapter 4).

On this basis, 6 hypothesised models were tested to examine sequential relationships between change in autonomous and controlled motivation to reduce sedentary behaviour, with change in activPAL-assessed sedentary or standing time, and in turn, change in RA health

outcomes. Health outcomes were grouped in each model, in terms of their similarities and what made conceptual sense. Those grouped in the same models were as follows; Model 1) DAS-28 and hsCRP (RA disease activity), Model 2) pain, fatigue and subjective vitality (common symptomology), and Model 3) DCOOP general functional status and quality of life (holistic indicators of health).

Figure 6.2 illustrates the framework guiding construction of each model. Paths are specified to test the hypothesis that change in autonomous and controlled motivation to reduce sedentary behaviour will predict change in activPAL-assessed behaviour, and in turn, variability in health outcomes in RA. In addition, the path models permit examination of the indirect effects of change in autonomous and controlled motivation to reduce sedentary behaviour on RA health outcomes (via activPAL-assessed behaviours).

Despite controlled motivation to reduce sedentary behaviour not revealing longitudinal associations with free-living sedentary or standing time in these patients (Chapter 5), autonomous *and* controlled motivation to reduce sedentary behaviour were concurrently incorporated into hypothesised path models. Indeed, controlled motivation is an important facet of SDT, and can be experienced in combination with autonomous motivation towards a specific behaviour (e.g., sedentary behaviour) (Phillips & Johnson, 2018). For example, an individual may be able to experience both autonomous (e.g., because they value the benefits) and controlled (e.g., because someone tells them to) motivation to reduce sedentary behaviour at the same time. Thus, it is important to understand the independent and relative contributions of each to inform future sedentary behaviour change interventions among people with RA. This is also in alignment with previous studies exploring RA patients' quality of motivation in a PA context, using an SDT perspective (Yu et al., 2015a).

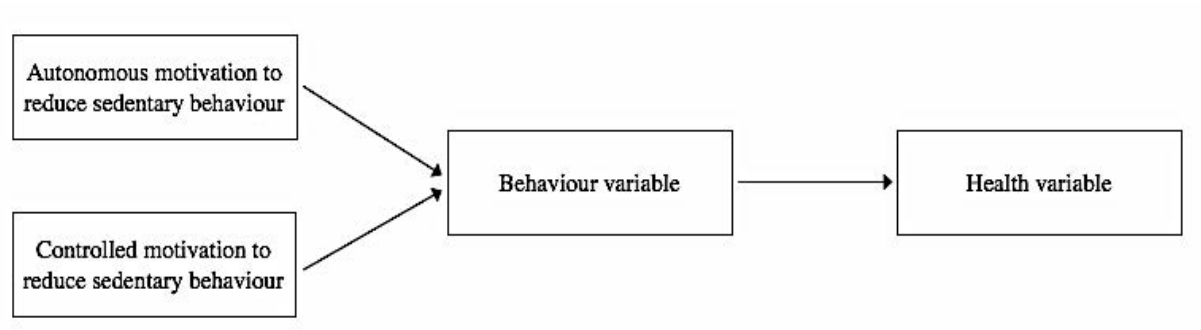

Figure 6.2 Hypothesised model of sedentary behaviour change

'Health variable', health-related correlate; 'Behaviour variable', activPAL-or GT3X-assessed behaviour

Note: ⟶ Path between variables

To ensure adequate statistical power, all variables are modelled as observed variables (rather than latent variables) to reduce the number of parameters in the model. Specifically, due to the small sample size, we were not able to test a full measurement model (specifying latent variables) for factors assessed via questionnaire (e.g., autonomous and controlled motivation to reduce sedentary behaviour) (Byrne, 2010). In addition, objectively-assessed behaviours were expressed in models as percentages of device wear time (% waking behaviour per day) to reduce the number of variables in each model, thus increasing statistical power. Each behaviour being tested (sedentary and standing time) were modelled separately due to high correlations exhibited between behaviours (ß = -.95) (van der Ploeg & Hillsdon, 2017).

Path analysis with maximum likelihood estimation was employed in conjunction with bias-corrected and accelerated bootstrapping (1000 samples) to test all hypothesised models. Statistically significant direct and indirect relationships between variables were determined by examination of bootstrapped 95% CI. Where the CI did not cross zero, a significant effect is assumed. Standardised coefficients (ß) are also reported to facilitate interpretation of the strength of each association (small = .1; medium = .3; large = .5) (Cohen, 1992) for each path.

Model fit was evaluated using fit indices appropriate for small sample sizes (Schermelleh-Engel & Moosbrugger, 2003). Specifically, the fit between the hypothesised models and the data were determined via examining the chi-square statistic (χ^2), comparative fit index (CFI), Tucker Lewis Index (TLI) and root mean square error of approximation (RMSEA; 90% confidence intervals [CI]). A non-significant χ^2 ($p > .05$), CFI and TLI values ≥ .95, and RMSEA < .06 with 90% CI (lower boundary) containing 0 indicate *excellent* model fit. A non-significant χ^2 ($p > .05$), CFI and TLI values ≥ .90, and RMSEA < .08 with 90% CI (lower boundary) < .05 suggest a *good* fit between the hypothesised model and the data. The strength and direction of path coefficients were also considered in assessing the validity of the models (Schermelleh-Engel & Moosbrugger, 2003; Schreiber et al., 2006).

Results

Information pertaining to demographics, RA disease and treatment regimen, and physical health that characterised the sample in this longitudinal study, have already been described in Chapter 3 (Table 3.2) of this thesis. Descriptive statistics relevant to this thesis chapter are reported in Table 6.1. Loss of participants in longitudinal analysis (n = 50) was mainly due to planned termination of data collection (n = 47) and lack of time (n = 3).

Table 6.1 Descriptive statistics for the total sample at T1 and T2, and change between T1 and T2 (change = T2 – T1)

	n	T1	n	T2	n	Change
Biological sex (% female)	74	71%	38	70%	X	X
Age (years)	104	57.93 ± 12.55	54	58.81 ± 12.06	54	0.50 ± 0.50
Psychosocial 'determinants'						
Autonomous motivation to reduce sedentary behaviour	104	7.26 ± 1.42	54	7.50 ± 1.51	54	-.04 ± 1.21
Controlled motivation to reduce sedentary behaviour	104	4.24 ± 1.58	54	4.22 ± 1.69	54	-.05 ± 1.72
Health 'outcomes'						
DAS-28	104	3.97 ± 1.51	54	4.00 ± 1.45	54	0.20 ± 1.27
hsCRP (mg/l)	102	6.07 ± 7.64	52	6.18 ± 8.25	52	0.90 ± 8.34
Pain	104	12.72 ± 10.94	54	13.37 ± 10.87	54	2.24 ± 11.53
Fatigue	104	24.89± 13.06	54	23.81 ± 13.21	54	-1.54 ± 8.65
HAQ functional disability	104	1.25 ± 0.81	54	1.14 ± 0.86	54	-.07 ± 0.44
DCOOP general functional status	104	17.42 ± 4.75	54	17.22 ± 4.60	54	0.28 ± 3.41
Quality of life (physical health)	104	21.17 ± 5.76	54	22.17 ± 6.22	54	0.76 ± 3.46
Subjective vitality	104	3.33 ± 1.65	54	3.40 ± 1.69	54	0.14 ± 1.24
ActivPAL						
Valid wear time (min/day)	102	913.02 ± 56.74	53	941.34 ± 60.39	53	20.49 ± 54.16
Sedentary (min/day)	102	546.05 ± 116.59	53	574.82 ± 98.81	53	37.92 ± 65.31
Standing (min/day)	102	267.51 ± 101.00	53	266.63 ± 92.72	53	-13.10 ± 59.86
Stepping (min/day)	102	99.44 ± 37.39	53	99.91 ± 40.34	53	-4.29 ± 19.83
Sedentary (%)	102	59.98 ± 12.91	53	61.39 ± 11.63	53	2.76 ± 6.82
Standing (%)	102	29.16 ± 10.47	53	28.07 ± 8.92	53	-2.06 ± 5.93
Stepping (%)	102	10.87 ± 3.96	53	10.54 ± 4.04	53	-0.70 ± 2.15

n, number of participants; T1, Time Point 1; T2, Time Point 2; DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein; HAQ, Health Assessment Questionnaire; DCOOP, Dartmouth Cooperative Functional Assessment Charts; LPA, light-intensity physical activity; MPA, moderate-intensity physical activity; X, not applicable

Note: Values are percentages (%) or mean ± standard deviation. Only change scores required for longitudinal correlation and regression analysis were computed. The HAQ and DCOOP were measured as indicators of physical function, but labelled as functional disability and general functional status, respectively. HsCRP results were unavailable for 2 participants during analysis with Enzyme-Linked Immunosorbent Assays.

Path analysis

Overall, analysis revealed all path models to demonstrate an excellent fit to the data (Table 6.2). Path coefficients (ß) and 95% CIs (lower – upper) for direct associations observed in sedentary and standing time models are presented in Figures 6.3 to 6.8. Non-standardised path coefficients (B) and 95% CIs (lower – upper) are described in the text below.

Sedentary time models

Results revealed autonomous motivation to reduce sedentary behaviour was significantly negatively associated with sedentary time in Models 1 to 3. Controlled motivation to reduce sedentary behaviour was not significantly associated with sedentary time in any model.

Model 1 (DAS-28 and hsCRP). *Direct effects:* Sedentary time was significantly positively associated with hsCRP, but was not significantly associated with DAS-28. *Indirect effects:* Autonomous motivation to reduce sedentary behaviour was indirectly negatively associated with DAS-28 (B = -.12, 95% CI = -.26 – -.00) and hsCRP (B = -.19, 95% CI = -.37 – -.03), via activPAL-assessed sedentary time.

Model 2 (pain, fatigue and subjective vitality). *Direct effects:* Sedentary time was significantly positively associated with fatigue and significantly negatively associated with subjective vitality. Sedentary time was not significantly associated with pain. *Indirect effects:* Autonomous motivation to reduce sedentary behaviour was indirectly negatively associated with pain (B = -.11, 95% CI = -.22 – -.01) and fatigue (B = -.12, 95% CI = -.28 – -.02) and indirectly positively associated with subjective vitality (B = .01, 95% CI = .03 – .32), via activPAL-assessed sedentary time.

Model 3 (DCOOP general functional status and quality of life). *Direct effects:* Sedentary time was significantly positively associated with DCOOP general functional status and significantly negatively associated with quality of life. *Indirect effects:* Autonomous motivation to reduce sedentary behaviour was indirectly negatively associated with DCOOP general functional status (B = -.18, 95% CI = -.32 – -.06) and indirectly positively associated with quality of life (B = .17, 95% CI = .04 – .30), via activPAL-assessed sedentary time.

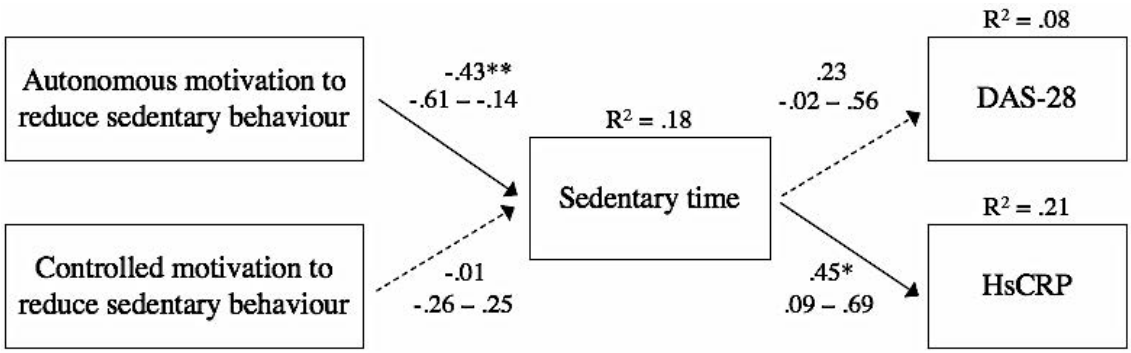

Figure 6.3 Sedentary time Model 1 (DAS-28 and hsCRP).
DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein
R^2, variance explained in the dependent variable by the independent variable
Note: * $p < .05$; ** $p < .01$. Dashed lines indicate a non-significant association.
Paths were stipulated between DAS-28 and hsCRP due to their correlation, but have not been included in this figure to facilitate interpretation.

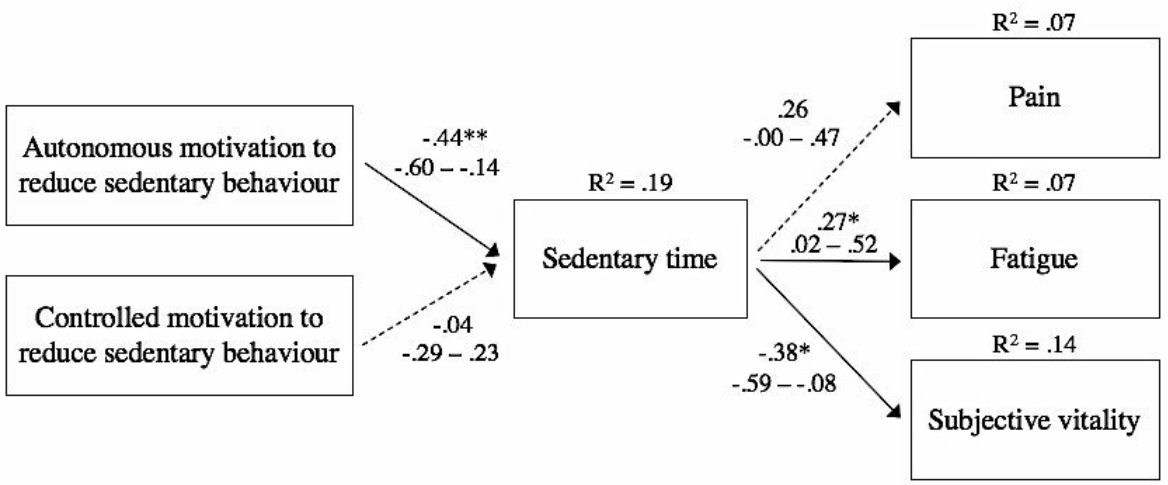

Figure 6.4 Sedentary time Model 2 (pain, fatigue and subjective vitality).

R^2, variance explained in the dependent variable by the independent variable

Note: * $p < .05$; ** $p < .01$. Dashed lines indicate a non-significant association.

Paths were stipulated between pain and fatigue, and fatigue and subjective vitality due to their correlation, but have not been included in this figure to facilitate interpretation.

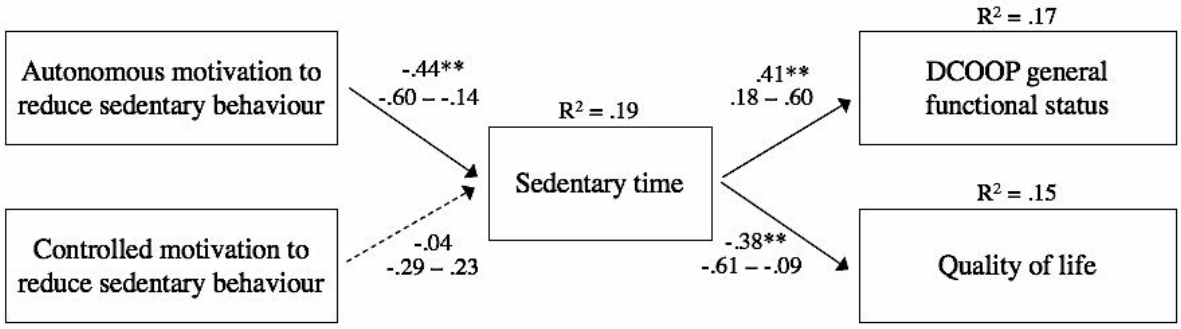

Figure 6.5 Sedentary time Model 3 (DCOOP general functional status and quality of life).

DCOOP, Dartmouth Cooperative Functional Assessment Charts

R^2, variance explained in the dependent variable by the independent variable

Note: * $p < .05$; ** $p < .01$. Dashed lines indicate a non-significant association.

Paths were stipulated between DCOOP general functional status and quality of life due to their correlation, but have not been included in this figure to facilitate interpretation.

Standing time models

Results revealed autonomous motivation to reduce sedentary behaviour was significantly positively associated with standing time in Models 1 to 3. Controlled motivation to reduce sedentary behaviour was not significantly associated with standing time in any model.

Model 1 (DAS-28 and hsCRP). *Direct effects:* Standing time was significantly negatively associated with hsCRP, but was not significantly associated with DAS-28. *Indirect effects:* Autonomous motivation to reduce sedentary behaviour was indirectly negatively associated with hsCRP (B = -.15, 95% CI = -.33 – -.00), via activPAL-assessed standing time.

Model 2 (pain, fatigue and subjective vitality). *Direct effects:* Standing time was significantly negatively associated with pain and fatigue, and significantly positively associated with subjective vitality. *Indirect effects:* Autonomous motivation to reduce sedentary behaviour was indirectly negatively associated with pain (B = -.11, 95% CI = -.21 – -.01) and fatigue (B = -.11, 95% CI = -.27 – -.01), and indirectly positively associated with subjective vitality (B = .13, 95% CI = .02 – .29), via activPAL-assessed standing time.

Model 3 (DCOOP general functional status and quality of life). *Direct effects:* Standing time was significantly negatively associated with DCOOP general functional status and significantly positively associated with quality of life. *Indirect effects:* Autonomous motivation to reduce sedentary behaviour was indirectly negatively associated with DCOOP general functional status (B = -.16, 95% CI = -.31 – -.04) and indirectly positively associated with quality of life (B = .16, 95% CI = .03 – .29), via activPAL-assessed standing time.

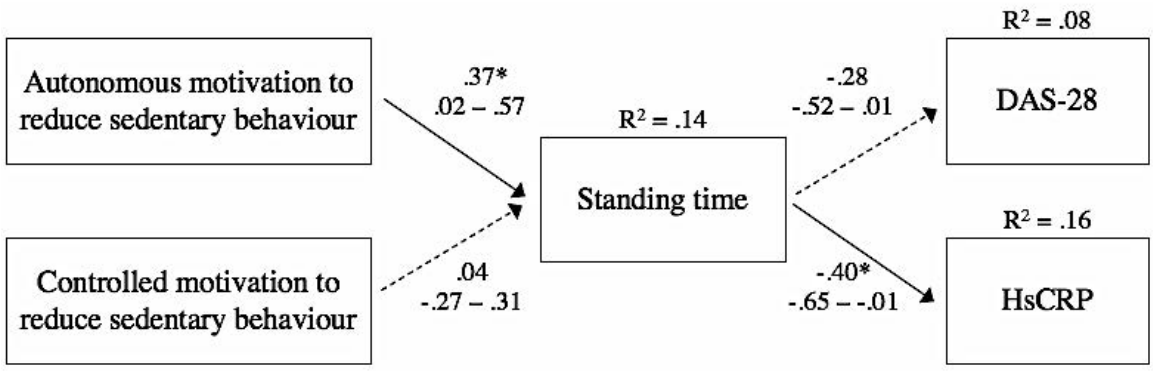

Figure 6.6 Standing time Model 1 (DAS-28 and hsCRP).

DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein

R^2, variance explained in the dependent variable by the independent variable

Note: * $p < .05$; ** $p < .01$. Dashed lines indicate a non-significant association.

Paths were stipulated between DAS-28 and hsCRP due to their correlation, but have not been included in this figure to facilitate interpretation.

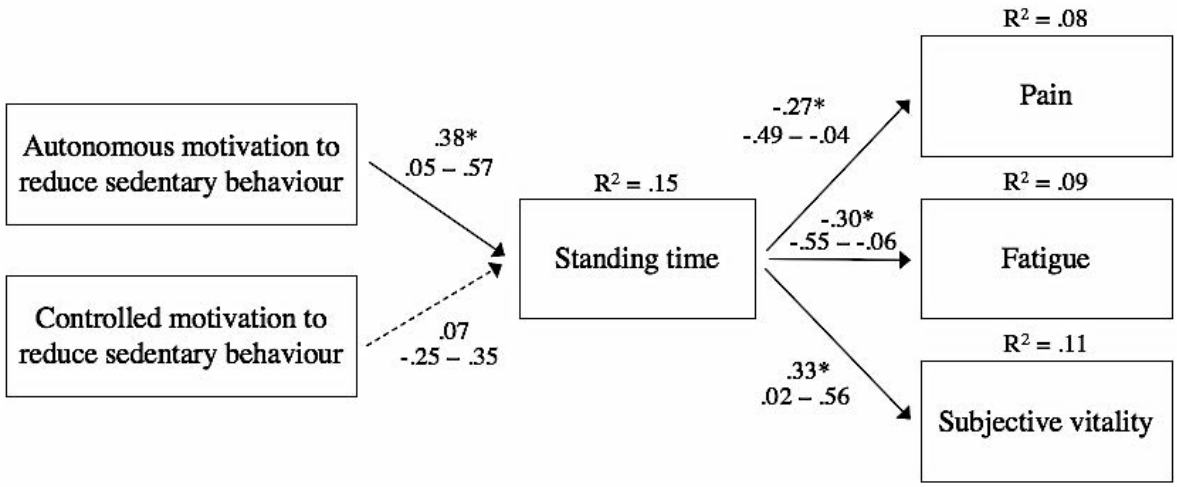

Figure 6.7 Standing time Model 2 (pain, fatigue and subjective vitality).

R^2, variance explained in the dependent variable by the independent variable

Note: * $p < .05$; ** $p < .01$. Dashed lines indicate a non-significant association.

Paths were stipulated between pain and fatigue, and fatigue and subjective vitality due to their correlation, but have not been included in this figure to facilitate interpretation.

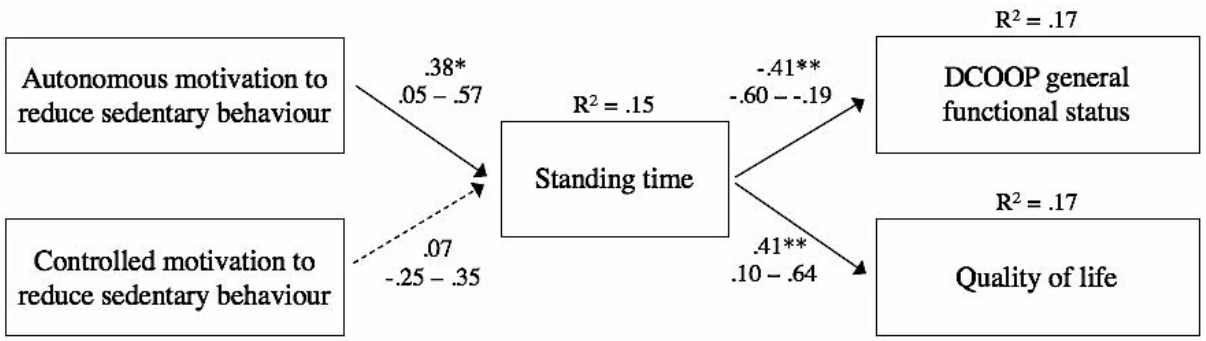

Figure 6.8 Standing time Model 3 (DCOOP general functional status and quality of life).
DCOOP, Dartmouth Cooperative Functional Assessment Charts
R^2, variance explained in the dependent variable by the independent variable
Note: * $p < .05$; ** $p < .01$. Dashed lines indicate a non-significant association.
Paths were stipulated between DCOOP general functional status and quality of life due to their correlation, but have not been included in this figure to facilitate interpretation.

Table 6.2 Model fit for hypothesised models in path analysis

Path models	χ^2	CFI	TLI	RMSEA	90% CI (low–high)	Model fit
Sedentary time models						
DAS-28, hsCRP	5.23, $p = .39$	.99	.99	.03	.00 – .20	Excellent
Pain, fatigue, subjective vitality	8.78, $p = .36$	.99	.97	.04	.00 – .17	Excellent
DCOOP general functional status, quality of life	4.98, $p = .42$	1.00	1.00	.00	.00 – .19	Excellent
Standing time models						
DAS-28, hsCRP	4.90, $p = .43$	1.00	1.01	.00	.00 – .19	Excellent
Pain, fatigue, subjective vitality	8.56, $p = .38$	.99	.98	.04	.00 – .17	Excellent
DCOOP general functional status, quality of life	5.21, $p = .39$	.99	.99	.03	.00 – .20	Excellent

DAS-28, Disease Activity Score-28; hsCRP, high-sensitivity C-reactive protein; DCOOP, Dartmouth Cooperative Functional Assessment Charts
χ^2, chi-square statistic; CFI, comparative fit index; TLI, Tucker Lewis index; RMSEA, root mean square error of approximation; CI, confidence intervals
Note: These models preceded with autonomous and controlled motivation to reduce sedentary behaviour. For χ^2, degrees of freedom were 5 for models with 2 health outcomes, and 8 for models with 3 health outcomes.

Discussion

The present study adopted an SDT lens (Deci & Ryan, 1985) to test models of sedentary behaviour change in people with RA. Specifically, path analysis revealed that change in autonomous motivation to reduce sedentary behaviour was consistently negatively associated with changes in activPAL-assessed sedentary time, or positively associated with changes in activPAL-assessed standing time, which in turn, linked to changes in clinically- and patient-important health outcomes in RA. This study's findings extended and were consistent with the findings from Chapters 4 and 5 of this thesis, and is the first to test such sequential relationships in this patient group.

Consistent with conclusions from Chapter 5, findings suggest that autonomous motivation to reduce sedentary behaviour might be a suitable modifiable target in interventions aiming to reduce sedentary time in RA. This is supported by recent qualitative research in this patient group, that suggested interventions designed to enhance motivation to reduce sedentarity, may offer an effective avenue for sedentary behaviour change (Thomsen et al., 2015). Previous sedentary behaviour change interventions have been grounded in SDT, specifically targeting reductions in screen-time in adolescents (Babic et al., 2016; Smith et al., 2017). For example, Babic et al. (2016) delivered an 'interactive seminar', 'eHealth messaging' and a 'behavioural contract' to foster autonomous motivation to limit participants' screen-time. Throughout this intervention, goal-setting was encouraged, and adolescents developed a list relating to the barriers to and benefits of reducing their screen-time, as well as citing ways by which they could overcome these barriers. Similarly, Smith et al. (2017) developed a 'researcher-led seminar' (e.g., addressing the consequences of excessive screen-time) and 'Smartphone application and website' (e.g., supporting goal-setting for behaviour change and providing motivational messages), which enhanced autonomous motivation in adolescents to

reduce their screen-time. Both interventions effectively reduced screen-time in these participants.

Informed by examples of previous research, sedentary behaviour change interventions in people with RA may entail researcher-led, interactive sessions, with an online element for goal-setting, in order to enhance autonomous motivation to reduce their sedentary behaviour. However, although these interventions have proved successful for screen-time reduction in adolescents, the efficacy of these intervention techniques cannot be generalised and applied to interventions for individuals with RA. Indeed, people living with RA are likely to differ in terms of their motives to engage in sedentary behaviour (e.g., to manage RA symptoms), and the context in which sedentary behaviour takes place. For example, Thomsen and colleagues (2015) reported that people with RA engage in sedentary behaviours such as completing crosswords and reading the newspaper, in addition to watching the television. Prior to intervention development targeting autonomous motivation to reduce sedentary behaviour for changes in sedentary in this patient group, further research should experimentally confirm these relationships. Additionally, identifying the common domains by which sedentary behaviour takes place among people with RA is important to inform intervention development, specifically to; 1) determine their "sedentary space" that could potentially be adapted (Chastin, et al., 2015a), and 2) ensure that the more 'unhealthy' sedentary behaviours are targeted (e.g., 'passive' sedentary behaviour) rather than those that may benefit patient mental health (e.g., 'mentally active' sedentary behaviour) (Hallgren et al., 2019; Hallgren et al., 2018).

In contrast to autonomous motivation, controlled motivation to reduce sedentary behaviour was not found to associate with sedentary time in these analysis. These results align with previous research in a PA context, whereby fostering more autonomous motivation holds positive associations with PA levels, whilst less internalised reasons for behaviour (controlled

motivation) have been negatively related to this behaviour, or shown no association at all (Costa et al., 2018; Teixeira et al., 2012). Interestingly, a recent study suggested that solely promoting autonomous motivation might not optimally lead to positive PA behaviour change (Phillips & Johnson, 2018). The authors suggested that there is scope to further investigate the interaction of autonomous and controlled motivation towards engagement in PA, as behaviour partly driven by the latter regulation might not always result in deleterious consequences for levels of PA. This is supported in sedentary behaviour studies, whereby higher controlled motivation to limit screen-time, was associated with less screen-time among adolescents (Lubans et al., 2013). However, this association was weak, and controlled motivation has been detrimentally linked with indicators of physical and psychological well-being in the general population (Ng et al., 2012; Quested & Duda, 2011). Therefore, considering that compromised psychological well-being is already prevalent among these patients (Fiest et al., 2017), fostering controlled motivation to reduce sedentary time in people with RA should be avoided.

This is the first study to examine the extent to which variability in sedentary time predicted by autonomous motivation to reduce sedentary behaviour, was beneficially associated with several clinically- and patient-important RA disease outcomes. Results revealed autonomous motivation to reduce sedentary behaviour accounted for 18-19% of the variance in sedentary time. In turn, sedentary time demonstrated significant positive relationships with hsCRP, fatigue and DCOOP general functional status, and negative associations with subjective vitality and quality of life. Translating the present findings to relative benefit for patients and clinicians, results demonstrate that increasing autonomous motivation to reduce sedentary behaviour by 2 on the BREQ-2 scale (e.g., responding to, “I aim to reduce my sedentary behaviour…because I enjoy doing this”, or “…because I value the benefits of doing this” from ‘2 = disagree’ to ‘4 = agree’) would equate to a reduction in

approximately 1h/day of sedentary time. In turn, this reduction in sedentary time would correspond to a 3.8mg/l decrease in hsCRP, a decrease in fatigue score by 2, an improvement in subjective vitality score by 1, enhanced DCOOP general functional status score by 3 and increased quality of life score by 1. Whilst results for DAS-28 and pain were not significant, results suggest that a decrease in sedentary time by 1h/day may result in improved DAS-28 by 0.3 and pain score by 3.

These associations are promising, when we consider that there is relative lack of information regarding the potential benefits of reducing sedentary time in RA, relative to promoting MVPA. Still, it is important to note that the hypothesised model only accounted for between 7%-21% of the variance in hsCRP (21%), fatigue (7%), subjective vitality (14%), DCOOP general functional status (17%) and quality of life (15%). Thus, adopting a more comprehensive approach towards identifying and targeting other modifiable contributors towards sedentary behaviour engagement among people with RA, at the individual, environmental and organisational level, as well as the inter-relationships between these factors, is paramount (Chastin et al., 2016). That is, whilst this is the first study to underscore the significance of autonomous motivation to reduce sedentary behaviour for levels of sedentary time and associated health outcomes among people living with RA, it is important to acknowledge that this is only one factor to consider when developing strategies to reduce sedentarity among people living with RA.

Recently, Thomsen et al. (2017) delivered a 16-week intervention aiming to reduce RA patients' sedentary time. This intervention was based on behavioural choice theory (Epstein & Roemmich, 2001) and targeted an individual's self-efficacy (Bandura, 2004) to promote 'reducing sitting time', via 'motivational interviewing'. This intervention was effective at reducing activPAL-assessed sedentary time by, on average, 1.61h/day and beneficial

improvements in health (e.g., pain measured via visual analogue scale) were observed. However, whilst demonstrating some success, the content and target of this intervention was not evidence-based. Specifically, the determinant targeted (self-efficacy) was not identified on the basis of evidence highlighting the role of self-efficacy for influencing sedentary behaviour among people with RA. Moreover, only 'general self-efficacy' was assessed, rather than 'self-efficacy to reduce sitting time' specifically. This is incongruent with the manner in which the intervention was framed (that is, with reference to reducing sitting time), limiting accurate appraisal of intervention efficacy from a theoretical perspective. Arguably, the present study provides more scope for identifying potential modifiable intervention targets, as we specifically measured autonomous motivation to reduce sedentary behaviour. Of course, experimental studies must be conducted to confirm the associations observed herein.

Interestingly, Thomsen et al. (2017) suggested sedentary time was replaced by standing time in their intervention. In the present study, activPAL-assessed sedentary and standing time exhibited a strong inverse correlation, and interpretation of these data relates to these behaviours sharing variance. That is, significant positive associations between autonomous motivation to reduce sedentary behaviour with standing time might be reflective of the relationship autonomous motivation to reduce sedentary behaviour holds with sedentary time, rather than the fact that RA patients were autonomously motivated to stand per se. These behaviours were likely to displace each other throughout the patient's day, which may be why similar links between sedentary and standing time with clinically- and patient-important RA outcomes were observed in path analysis. However, experimental models are required to examine a 'displacement association' between these behaviours and the subsequent relationships with RA health.

Still, results from the present study may suggest that encouraging people with RA to 'sit less and stand more' may lead to improvements in clinically- and patient-important health outcomes in RA. Not only may this prove beneficial to health, but this may offer a pragmatic health promotion message among this patient group. Indeed, reducing daily sedentary time by endorsing 'upright' behaviours has been advocated in a recent protocol with the Cochrane Collaboration, for interventions aiming to reduce sedentary behaviour in older adults (Chastin et al., 2017). In addition, interventions focused on 'non-exercise' behaviours have been recommended as an alternative to MVPA for people with reduced physical function (Manns et al., 2012). These findings are compelling for research seeking to establish the potential of reducing sedentary time and increasing standing time for attenuating the disease burden among people with RA.

Limitations of the present study must be acknowledged. First, similarly to path analysis undertaken in Chapter 4, 'excellent model fit' was consistently reported, suggesting that specified parameters in the hypothesised model could be trusted. It is important to note, however, that in 2 models (Model 3, sedentary time and Model 1, standing time), $\chi^2 \leq$ degrees of freedom, which may have resulted in 'excellent model fit' and consistent values for the selected indices (e.g., RMSEA = .00) (Bandalos, 2018). Second, the sample size would have reduced the statistical power of this study. Indeed, non-significant associations between sedentary and standing time with DAS-28, and sedentary time with pain, were in the expected direction, and effect sizes were in line with those observed in previous studies where sedentary time *is* significantly related to disease outcomes (Greene et al., 2006; Khoja et al., 2016). Bootstrapping was employed in path analysis in an attempt to address some concerns of reduced sample sizes, but issues related to the composition of hypothesised models remained. For example, due to the small sample size, more complex structural equation models could not

be tested. Indeed, we could not model separate BREQ-2 questionnaire items as latent variables, or include sedentary and standing time together in these analysis. However, incorporating both sedentary and standing time in the same hypothesised models may have resulted in multicollinearity, as seemingly, RA patients spend most of their waking day engaging in these behaviours.

Third, the sample in the present study was predominantly made up of female participants. Whilst this is representative of the target population, the present study is limited in its ability to generalise findings to males with RA. These participants also had moderate disease activity and severity, which again reduces the degree of generalisability to RA patients with more/less active disease. Next, the present study did not consider the 3 basic psychological needs of ‘competence’, ‘autonomy’ and ‘relatedness’ in the hypothesised model, a fundamental sub-theory of SDT (basic psychological needs satisfaction theory). Fulfilment of these basic needs has been shown to lead to more autonomous motivation towards behaviour and benefit psychological well-being (Ryan & Deci, 2000). The role of the basic needs in the context of reducing sedentary behaviour, as antecedents to autonomous motivation to reduce sedentary behaviour was not examined here. The aim of this study was to first investigate whether autonomous and controlled motivation to reduce sedentary behaviour was related to sedentary and standing time in people with RA, in turn, associating with pertinent aspects of their health. Finally, activPAL-assessment of free-living behaviour gave no scope to determine the context by which sedentary and standing time occurred. This is important knowledge for intervention design, in order to provide valuable information regarding the domain and type of these behaviours.

Notwithstanding these limitations, the present study had several strengths. Despite not capturing the context of free-living behaviour, this study employed the activPAL which is

considered the current gold standard measure of free-living sedentary time. This device has been validated against direct observation for measurement of sedentary and standing time in RA, demonstrating >98% accuracy (Chapter 2). Additionally, the analytical approach adopted allowed us to test models, which examined hypothesised associations between autonomous and controlled motivation to reduce sedentary behaviour →sedentary or standing time →clinically- and patient-important disease outcomes in RA. These results could be subsequently used to inform the development of an intervention, grounded in SDT, to reduce sedentary time in RA, which may have the potential to improve pertinent health outcomes in people with RA.

Conclusion

This is the first study to test models of sedentary behaviour change in people with RA, using an SDT lens. Specifically, present findings suggest autonomous motivation to reduce sedentary behaviour may predict variability in sedentary time among people with RA, to the extent that it may hold implications for several clinically- and patient-important health outcomes. As such, results indicate that autonomous motivation to reduce sedentary behaviour, might be a viable and malleable target in interventions aiming to reduce the burden of disease for people with RA, via sedentary behaviour change (e.g., decrease sedentary time, increase standing time). However, whilst this study provides interesting insight into these sequential relationships through observational associations, experimental studies are required to confirm these findings.

CHAPTER 7

GENERAL DISCUSSION

Overview

The Behavioural Epidemiology Framework (BEF) (Sallis et al., 2000) has guided the studies which comprise this thesis (Figure 7.1). The overarching aim was to provide new evidence regarding sedentary behaviour in RA, and begin to establish an evidence-base to inform the development of theory-based behaviour change interventions to reduce sedentary behaviour in RA.

First, addressing 'Phase 2' of the BEF, Chapter 2 validated the activPAL and GT3X+ for measurement of sedentary time and physical activity (PA) in people living with RA. These devices were subsequently employed in the longitudinal studies of Chapters 4-6 (conducted over 6 months), which addressed 'Phase 1' and 'Phase 3' of the BEF. Specifically, Chapter 4 examined longitudinal associations, including bi-directional relationships, between activPAL- and GT3X+-assessed sedentary time and PA, with clinically- and patient-important RA disease outcomes. Following this, Chapter 5 used an SDT lens (Deci & Ryan, 1985) to examine longitudinal associations between autonomous and controlled motivation to reduce sedentary behaviour, with activPAL and GT3X+-assessed sedentary time and PA in this patient group. Finally, building on knowledge generated in Chapters 4 and 5, Chapter 6 tested hypothesised models of sedentary behaviour change. This final experimental chapter was informed by Chapters 4 and 5 of this thesis, and examined longitudinal associations between autonomous and controlled motivation to reduce sedentary behaviour with activPAL-assessed sedentary time or standing time, and in turn, clinically- and patient-important RA disease outcomes. Figure 7.1 demonstrates the novel contribution each chapter of this thesis has made to the research literature in this area.

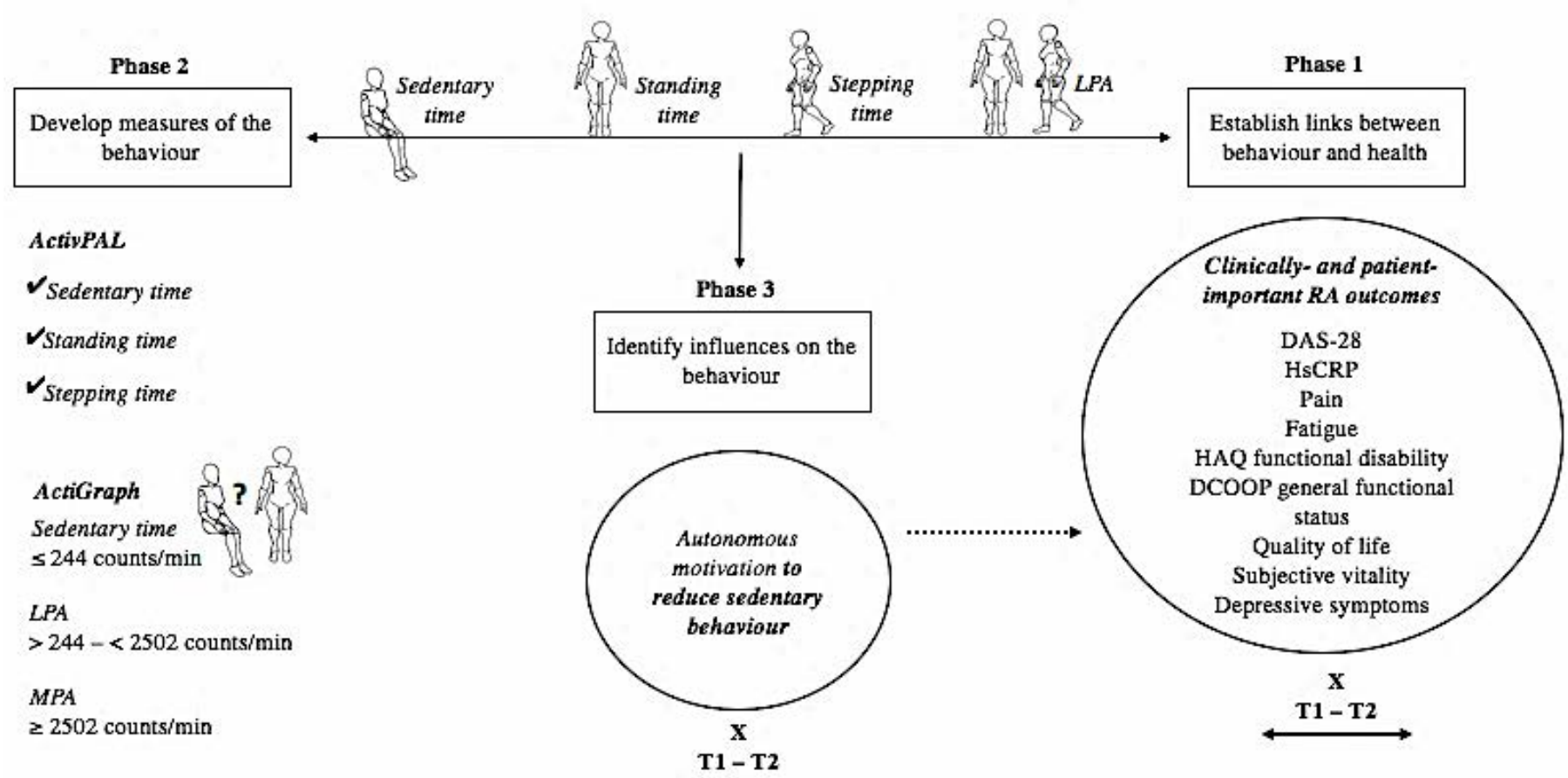

Figure 7.1 The contribution of this thesis – guided by the Behavioural Epidemiology Framework ('Phase 1' to 'Phase 3').

✔, activPAL showed good agreement vs. direct observation; **X**, cross-sectional associations present; **T1 – T2**, longitudinal associations present; ⟷ bi-directional associations present; - - - - - ▸ indirect association present via sedentary or standing time

Taken together, results demonstrated that the activPAL and GT3X+ are valid for measuring sedentary time and PA in people with RA (Chapter 2). Further, the RA-specific triaxial accelerometer cut-point developed in this study, was shown to be more accurate than a widely-used non-RA uniaxial accelerometer cut-point (<100 counts/min) (Troiano et al., 2008) at quantifying free-living sedentary time in people with RA. Findings from Chapter 4 revealed longitudinal associations between RA health features and activPAL-assessed sedentary and standing time, providing novel evidence to suggest these relationships may be reciprocal. This suggests scope to intervene at the behavioural level (e.g., reduce sedentary time, increase standing time) to reduce the burden of disease for people with RA.

Prior to intervention development, it is important that modifiable determinants of sedentary behaviour are established to form targets for such interventions. Thus, the study in Chapter 5 was grounded in SDT to explore the malleable determinants of sedentary behaviour in RA. Results demonstrated that autonomous motivation to reduce sedentary behaviour was associated with activPAL-assessed sedentary, standing and stepping time, as well as GT3X+-assessed sedentary time and light-intensity PA (LPA). This indicates that autonomous motivation to reduce sedentary behaviour might be a malleable target for future interventions targeting sedentary behaviour change in RA. Finally, Chapter 6 demonstrated that autonomous motivation to reduce sedentary behaviour predicted variability in levels of activPAL-assessed sedentary time, to the extent it holds implications for clinically- and patient-important disease outcomes in people with RA.

The following sections reiterate the main discussion points from Chapters 2, 4, 5 and 6 of this thesis, outlines their practical implications and limitations, and provides direction for conducting future research in the field of sedentary behaviour in RA.

Summary of research findings

Validation of the activPAL and ActiGraph accelerometer in rheumatoid arthritis

How does this thesis address 'Phase 2' of the Behavioural Epidemiology Framework? Chapter 2 of this thesis comprised a comprehensive validation study in order to specifically; 1a) validate the GT3X+ against indirect calorimetry to generate RA-specific triaxial (vector magnitude [VM]) accelerometer cut-points for sedentary time, light-intensity PA (LPA) and moderate-intensity PA (MPA), and 1b) validate the activPAL against direct observation for measurement of sedentary, standing and stepping time (*laboratory validation*). Then, using these data; 2) compare the validity of the new RA-specific triaxial sedentary time cut-point vs. the widely-used non-RA uniaxial sedentary time accelerometer cut-point (<100 counts/min) (Matthews et al., 2008; Troiano et al., 2008) for measurement of free-living sedentary time in RA, against the gold standard (activPAL), and 3) compare within-person estimates of free-living sedentary time, LPA and MPA, quantified using the new RA-specific vs. commonly used non-RA accelerometer cut-points (Troiano et al. 2008) (*field validation*).

Previous studies examining the levels of accelerometer-assessed sedentary time and PA in people with RA, in order to draw links between these behaviours with health, have mostly employed non-RA uniaxial cut-points calibrated in 'healthy' populations (Matthews et al., 2008; Troiano et al., 2008). However, given the different physiological requirements and associated activity profiles of the RA population (Metsios et al., 2008), these estimates of sedentary time and PA should be interpreted with caution. Indeed, there is increasing recognition of the necessity to develop and employ population-specific cut-points for accurate measurement of these behaviours, in different populations (Aguilar-Farias et al., 2014; Copeland & Esliger, 2009; Motl et al., 2009; Santos-Lozano et al., 2013). Addressing this critical need, this study was the first to calibrate the ActiGraph accelerometer against indirect

calorimetry (criterion standard) to define RA-specific triaxial (VM) accelerometer cut-points for measurement of sedentary time, LPA and MPA, in RA. The triaxial nature of accelerometry has been complimented in previous studies, highlighting its value over and above uniaxial accelerometer analysis when quantifying sedentary time and PA (Choi et al., 2012; Evenson et al., 2015). For example, such studies have suggested that when triaxial cut-points are applied, measurement error with regard to device position or rotation is removed, and non-wear can be more easily distinguished from sedentary time.

Results from this chapter also revealed that free-living sedentary time, LPA and MPA estimates significantly differed with application of RA-specific triaxial cut-points vs. non-RA uniaxial cut-points (Troiano et al., 2008) to free-living accelerometer data in this patient group (n = 100). As a result, it was concluded that the newly-developed RA-specific cut-points should be employed in future sedentary behaviour and PA research in this population, since these were developed on the basis of the specific energy requirements of activity for people with RA. Still, when recommending our RA-specific sedentary time cut-point in future work, it is important to consider the limitations of accelerometry to accurately assess behavioural *posture* (An et al., 2017; Kozey-Keadle et al., 2011) – a fundamental component of the widely-accepted definition of sedentary behaviour, stipulated by the Sedentary Behaviour Research Network (SBRN, 2012; Tremblay et al., 2017). Accelerometers classify sedentary time based on activity counts recorded below a specified cut-point (in this case, ≤244 VM counts/min). In this way, low activity counts represent low-energy expenditure, and thus low-movement behaviours. This is problematic when we consider that low-movement, non-sedentary behaviours (e.g., standing) might fall within this threshold and be inaccurately classified as sedentary. With this in mind, the activPAL posture sensor was validated against direct observation for measuring sedentary, standing and stepping time in people with RA. Findings supported previous research conducted

among other populations to confirm that the activPAL is valid for measurement of sedentary time in RA (>98% accurate), and should therefore be considered the gold standard measure of free-living sedentary time in this population (Chastin & Granat, 2010; Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016).

As such, there existed great potential to further explore the validity of the RA-specific sedentary time accelerometer cut-point using the activPAL as the criterion, to evaluate its accuracy for measuring free-living sedentary time (outside of the laboratory setting) among people with RA. Results from this free-living validation study, revealed a mean difference of 2.3h/day between sedentary time estimates generated by the RA-specific cut-point vs. the activPAL. Interpretation of Bland-Altman plots alluded to an overestimation of sedentary time where the RA-specific cut-point was employed. However, Bland-Altman plots also revealed that the RA-specific cut-point generated a smaller mean difference and narrower 95% limits of agreement relative to the non-RA cut-point, when compared to the activPAL. Overall, results suggest that whilst Receiver Operating Characteristic curve analysis generated sensitive and specific sedentary time cut-points, employing these in free-living research demonstrated that accelerometers lack agreement with the gold standard activPAL in RA, and may overestimate sedentary time. Still, findings indicate these RA-specific cut-points provide more valid estimates of sedentary time among this this patient group, relative to non-RA cut-points which have been almost exclusively employed to study sedentary behaviour in RA.

Akin to above discussion, it is conceivable that the differences in sedentary time estimates between the RA-specific cut-point vs. the activPAL resulted from some misclassification of standing time, as sedentary time. Two main points were argued to support this contention. First, in the laboratory-based validation, resulting average MET values during ‘standing’ (0.8 ± 0.2 METs) were below the threshold for defining sedentary behaviour (≤1.5

METs). Second, Bland-Altman plots illustrated a downward trend, alluding to improved agreement between sedentary time estimates derived from the accelerometer vs. the activPAL as sedentary time increased. People with RA are less likely to engage in standing time if they spend most of their waking day sedentary, thus there exists less opportunity for accelerometers to misclassify standing time. To support our interpretation of these data, Aguilar-Farias et al. (2014) revealed that their population-specific sedentary time VM cut-point (e.g., <60 count/min) was more accurate at classifying activPAL-assessed sedentary *and* standing time, compared to activPAL-assessed sedentary time.

In sum, findings revealed that the activPAL accurately assesses sedentary, standing and stepping time in people with RA. Newly-developed RA-specific triaxial accelerometer cut-points were sensitive and specific for measurement of free-living sedentary time, LPA and MPA in these patients, and were more accurate at assessing sedentary time than widely-used non-RA cut-points. It was recommended that future research in RA use the activPAL in instances where sedentary time is the outcome of interest. If this is not possible, use of our RA-specific cut-points was advocated over employment of non-RA cut-points, acknowledging the caveat that these may misclassify some standing time as sedentary.

Bi-directional associations between health with sedentary time and physical activity in rheumatoid arthritis

How does this thesis address 'Phase 1' of the Behavioural Epidemiology Framework? In the longitudinal study comprising Chapter 4, the activPAL and GT3X+ (employing newly-developed RA-specific accelerometer cut-points from Chapter 2) were used to assess free-living sedentary time and PA in people with RA, in order to specifically; 1) determine the associations between clinically- and patient-important RA outcomes, with objectively-assessed sedentary time and PA, and 2) examine whether these associations may be bi-directional.

This study overcame 2 key limitations of previous research, specifically their cross-sectional design and application of self-report to measure sedentary time and PA. Results of this study provided new evidence demonstrating longitudinal associations between several RA outcomes indicative of 'physiological' and 'psychological' health (high-sensitivity C-reactive protein [hsCRP], pain, fatigue, DCOOP general functional status, quality of life and subjective vitality), with activPAL-assessed sedentary and standing time. In addition, findings suggested the associations between some pertinent RA outcomes with activPAL-assessed sedentary and standing time were bi-directional. Some exceptions were observed, whereby significant cross-sectional or longitudinal associations were not confirmed as significant in bi-directional analysis (e.g., between hsCRP with activPAL-assessed sedentary and standing time, and Disease Activity Score-28 [DAS-28] with activPAL-assessed standing time). However, medium effect sizes were reported for these relationships, and we proposed these relationships would emerge significant with a larger sample size. Indeed, relationships between sedentary behaviour and CRP have been demonstrated in previous studies (Henson et al., 2013; Stubbs et al., 2015). This represents a very compelling finding. For example, hsCRP represents a key clinical biomarker of inflammation in RA and is linked to a number of other disease features, such as pain and physical function. This was corroborated in our findings, whereby positive correlations were exhibited between hsCRP with pain (ß = .35) and DCOOP general functional status (ß = .30). With this in mind, it might be interesting to explore the 'sedentary-inflammation' hypothesis proposed by Fenton and Kitas (2016), to examine whether exacerbation of systemic inflammation may represent a physiological mechanism through which sedentary behaviour may perpetuate disease outcomes in this patient group. Potential research directions aligned to this proposition are discussed later in this chapter.

Results from Chapter 4 provided novel and critical insight into the extent to which clinically- and patient-important disease outcomes might represent a cause *and* consequence of sedentary time (and standing time) in people with RA. With this in mind, these results point to a requirement for experimental studies that examine whether reducing sedentarity may improve RA outcomes, and confirm the value of sedentary behaviour change interventions for improving health indicators among people with RA.

Psychosocial determinants of sedentary time and physical activity in rheumatoid arthritis: a self-determination theory perspective

How does this thesis address 'Phase 3' of the Behavioural Epidemiology Framework? Grounded in SDT (Deci & Ryan, 1985), Chapter 5 of the current thesis also employed the activPAL and GT3X+ (applying RA-specific accelerometer cut-points) to examine longitudinal associations between autonomous and controlled motivation to reduce sedentary behaviour, with objectively-assessed sedentary time and PA in people with RA.

The rationale for this study was provided by evidence for the bi-directional associations between clinically- and patient-important health outcomes in RA with objectively-assessed sedentary and standing time observed in Chapter 4. Specifically, observed reciprocal relationships between DAS-28, pain, fatigue, DCOOP general functional status, quality of life and subjective vitality with sedentary time, suggested that sedentary time might represent a valuable behavioural target for non-pharmacological intervention in RA. However, prior to developing an intervention to examine the role of sedentary behaviour change for improving RA outcomes, research is required to elucidate modifiable determinants of sedentary behaviour in this patient group (Chastin et al., 2015a).

Currently, there is a lack of knowledge regarding malleable determinants of sedentary behaviour in any population. In an attempt to guide research addressing this evidence gap, the

‘Systems of Sedentary behaviours’ (SOS-framework) (Chastin et al., 2016) advocated research into ‘Psychology and Behaviour’ (encompassing motivation) as 1 of 6 top research priorities examining salient determinants of sedentary behaviour engagement across the life course. Aligned to this framework, the only qualitative study gaining insight into the experiences of sedentary behaviour among people with RA, recommended focusing on patient motivation to reduce sedentarity (Thomsen et al., 2015). With this in mind, the research questions comprising Chapter 5 of this thesis, were grounded in SDT – a psychological theory of motivation. The aim was to garner an understanding of the extent to which key tenets of SDT, applied to the context of sedentary behaviour – namely autonomous and controlled motivation to reduce sedentary behaviour – may associate with levels of sedentary time and PA in RA, and represent potential targets in sedentary behaviour change interventions.

The central notion of SDT proposes that an individual’s degree of self-determined motivation towards a behaviour (e.g., reducing sedentary behaviour), holds important implications for engagement in that behaviour (e.g., sedentary time). SDT has been used effectively as a framework for sedentary behaviour change interventions in adolescent boys, whereby enhancing autonomous motivation to reduce screen-time led to reductions in screen-time in this population (Babic et al., 2016; Smith et al., 2017). In this study, we adapted the BREQ-2 to assess autonomous and controlled motivation to reduce overall sedentary behaviour, to establish the extent that these may represent determinants of global sedentary behaviour.

Longitudinal analysis revealed change in autonomous motivation to reduce sedentary behaviour was associated with change in activPAL- and GT3X+-assessed behaviours (sedentary, standing and stepping time, and LPA). Controlled motivation to reduce sedentary behaviour was not longitudinally associated with any device-assessed behaviour (in both

Chapters 5 and 6). It is possible that people with RA, and their family, friends and healthcare professionals, might not be fully aware of the negative health risks associated with sedentary behaviour. Indeed, this is a novel area of research and there is currently limited understanding of the specific health consequences of this behaviour, particularly in this patient group. Thus, people with RA might not experience guilt associated with sedentary behaviour engagement (e.g., "I aim to reduce my sedentary behaviour…because I feel guilty if I am not doing this") and/or family/friends/healthcare professionals may not forcefully suggest that the patient should reduce their sedentarity (e.g., "I aim to reduce my sedentary behaviour…because I feel under pressure from others to do this"). Despite the null findings for this psychological construct, it has been proposed that minimising controlled motivation towards health behaviours might be important, due to; 1) the detrimental role it plays in engagement in such behaviours (e.g., PA) (Teixeira et al., 2012), and 2) the adverse associations it holds with physical and psychological well-being (Ng et al., 2012; Quested & Duda, 2011). The latter point is particularly important for people with RA, who commonly experience poor mental health (Matcham et al., 2013).

Whilst an association between autonomous motivation to reduce sedentary behaviour with sedentary time might be expected, the association with time spent standing, stepping and in LPA, could represent shared variance between these behaviours. However, owing to the small sample size and high correlation between these behaviours, we were not able to enter sedentary time into regression models with standing, stepping or LPA variables (e.g., correlations with activPAL-assessed sedentary time were ß = -.95, ß = -.55 and ß = -.64 respectively). Nevertheless, where effect sizes from separate regression models were compared, stronger associations were observed between autonomous motivation to reduce sedentary behaviour with activPAL-assessed sedentary time (ß = -.44) relative to those reported

for standing (ß = .38), stepping (ß = .33) and LPA (ß = .35). Results from Chapter 5 therefore provided original, longitudinal evidence, to suggest that autonomous motivation to reduce sedentary behaviour may represent a modifiable determinant of sedentary time in RA.

The role of autonomous motivation to reduce sedentary behaviour and improve rheumatoid arthritis outcomes: models of sedentary behaviour change

How does this thesis address 'Phase 1' and 'Phase 3' of the Behavioural Epidemiology Framework? Informed by the results of Chapters 4 and 5 of this thesis, the aim of Chapter 6 was to test models of sedentary behaviour change in RA. Specifically, this model investigated whether autonomous motivation to reduce sedentary behaviour was linked to variability in device-assessed sedentary and standing time, and in turn, clinically- and patient-important RA outcomes (autonomous motivation to reduce sedentary behaviour → activPAL-assessed sedentary time [or standing time] → RA outcomes).

Path analysis was employed to test the hypothesised relationships, and results revealed that change in autonomous motivation to reduce sedentary behaviour was consistently related to change in activPAL-assessed sedentary and standing time in this population. In turn, change in sedentary time was associated with change in several RA outcomes, including hsCRP, fatigue, subjective vitality, DCOOP general functional status and quality of life. Further, change in standing time was linked with change in all these health outcomes, with the addition of pain. Akin to results reported in Chapters 4 and 5 of this thesis, standardised path coefficients observed in path models were very similar for sedentary vs. standing time (with autonomous motivation to reduce sedentary behaviour and RA health indicators), which is likely to reflect the strong inverse correlation between these behaviours.

In this study, change in autonomous motivation contributed to 18%-19% of the variance in activPAL-assessed sedentary time, which in turn, accounted for 7-21% of the variance in

health outcomes. These findings suggest that increasing an individual's identified and/or intrinsic regulation towards reducing their sedentary behaviour (e.g., facilitating identification of the benefits of reducing their sedentary behaviour and/or their enjoyment of reducing their sedentary behaviour) might be a suitable malleable target for sedentary behaviour change interventions in these patients to improve important disease outcomes. Specifically, increasing autonomous motivation to reduce sedentary behaviour by a score of 2 on the BREQ-2 scale (e.g., responding to, "I aim to reduce my sedentary behaviour…because I value the benefits of doing this" or "…because I enjoy doing this", from 2 = disagree to 4 = agree) might result in decreased sedentary time by approximately 1h/day. In terms of inflammatory disease activity, this in turn equates to a decrease of 3.8mg/l in hsCRP. In terms of particularly relevant symptoms for the patient, this corresponds to a decrease in fatigue by a score of 2 (e.g., responding to, "Over the past week, how often have you been fatigued?", from 4 = every day to 2 = occasionally, but not most days).

In sum, this study has provided novel insight into the potential of autonomous motivation to reduce sedentary behaviour to attenuate the disease burden of RA, through changes in sedentary time in this patient group.

Practical implications

Findings from the current study are compelling, revealing that; 1) the activPAL and GT3X+ (applying RA-specific accelerometer cut-points) can be employed to accurately quantify sedentary time and PA in people with RA (with the caveat that the GT3X+ might overestimate sedentary time), 2) longitudinal associations exist between clinically- and patient-important health outcomes in RA with sedentary time, and these are largely bi-directional, and 3) autonomous motivation to reduce sedentary behaviour is longitudinally associated with sedentary time in this patient group, which in turn, are related to several clinically- and patient-

important RA outcomes. Further, most longitudinal relationships with sedentary time demonstrated in Chapters 4-6, show the reverse associations with standing time in these patients. The following sections describe the practical implications of current findings.

Levels of MVPA in the RA population are insufficient to yield benefits to health – the physically inactive status of this patient group is well known (Tierney et al., 2012). However, the population prevalence of sedentary time in RA has been documented to a much lesser extent. Given that the activPAL and GT3X+ have now been validated for measurement of sedentary time (and PA) in people with RA, these devices (preferably the activPAL) should be employed to establish levels of sedentarity among people with RA. The longitudinal studies comprising Chapters 4-6 provide some indication of levels of activPAL-assessed sedentary time in RA (9h/day), but these data were only collected in a small sample of people with RA (n = 102) and therefore cannot be generalised to RA patients beyond this particular cohort. Thus, larger studies employing the activPAL are required to determine levels of sedentariness which are typical of people living with RA.

It was also demonstrated that there is a severe lack of research examining the health-related correlates of sedentary behaviour in people with RA. Findings suggest that we must reframe research priorities imminently, to build upon this evidence base. Indeed, several clinically- and patient-important RA outcomes were related to free-living sedentary time, and analysis alluded to most of these associations being bi-directional in nature. Research efforts should be made to confirm these findings with rigorous experimental designs, which serve to elucidate whether reducing sedentary time will lead to significant improvements in RA outcomes investigated herein.

A strong inverse correlation between sedentary and standing time, and reverse associations with health and psychosocial variables, were observed throughout the longitudinal

studies of this thesis. This suggests that promoting engagement in standing behaviours may offer a way to reduce sedentary time and potentially improve deleterious RA outcomes. Establishing links between sedentary behaviour and health in RA is a critical first step in developing a rationale for interventions in this patient group, which are able to test the health effects of reducing sedentary behaviour. However, we need to target malleable determinants of sedentary behaviour in interventions, shown to associate with sedentarity – thus, if targeted, these factors may have the potential to promote behaviour change. In longitudinal analysis, results from this thesis demonstrated that change in autonomous motivation to reduce sedentary behaviour was negatively linked to change in device-assessed sedentary time in RA. These findings are the first to suggest that autonomous motivation to reduce sedentary behaviour may offer a potential avenue for interventions targeting 'too much sitting' among people with RA. As such, SDT may offer a viable conceptual framework upon which sedentary behaviour change interventions, aiming to establish the potential health benefits of reducing free-living sedentary time among people with RA, can be based.

Limitations and future directions

The studies conducted within this thesis have generated novel and important insight into the accurate measurement of sedentary time and PA in people living with RA, as well as providing the first longitudinal evidence for associations between clinically-and patient-important 'physiological' and 'psychological' health outcomes, with objectively-assessed sedentary time and PA in this patient group. Further, SDT-based psychosocial determinants of these behaviours have been hypothesised for the first time, and their potential for forming intervention targets to alleviate the disease burden of RA has been discussed.

However, prior to developing such an intervention which addresses the issue of sedentarity in RA, additional research is required to confirm the associations observed herein,

and address the limitations of the work presented in this thesis. The following sections will outline limitations regarding measurement, study design and analytical techniques employed in this thesis, and suggest areas of future research that can seek to address these limitations.

First, the activPAL and GT3X+ were shown to be valid for measurement of free-living sedentary time and PA in people with RA, however Bassett, Rowlands and Trost (2012) highlighted that several studies are required to determine the validity of an instrument for assessing these behaviours. For example, in the laboratory-based validation study comprising Chapter 2, we could not affirm the accuracy of the activPAL for measuring sit-stand transitions in RA patients. This is an essential area of future research, particularly if we may advocate the health promotion message of 'sit less, stand more' in this population. Indeed, as well as the total time engaged in sedentary behaviour, the manner by which sedentary time is accumulated has been shown to hold important implications for health in clinical and non-clinical populations (de Rezende et al., 2014; Healy et al., 2011b). In addition, the activPAL has only been validated in 1 study in 'healthy adults' for assessing the intensity of behaviour, which is currently based on step cadence, limiting its ability to measure PA (Lyden et al., 2017). Thus, the activPAL should be validated for measuring sit-stand transitions and intensity of free-living PA in people with RA. This would subsequently reduce the reliance on employing both the activPAL *and* GT3X+ in sedentary behaviour and PA research in this population.

Importantly, if future research in the RA population involves measuring habitual sedentary time only, the activPAL should be employed for this purpose, as our data supports this device as the gold standard measure of free-living sedentary time (Chastin & Granat, 2010; Edwardson et al., 2017; Kozey-Keadle et al., 2011; Sellers et al., 2016). Thus, in RA studies that wish to quantify both sedentary time *and* PA in this patient group, the GT3X+ (applying newly-developed RA-specific accelerometer cut-points developed in Chapter 2) should be

employed in combination with the activPAL, as accelerometers afford the ability to capture the intensity of free-living behaviour. Further, compliance to monitor wear was high in this study for both devices, and when they were worn in combination. The protocols employed herein, may therefore help to inform methods in future RA studies, which involve administering these devices.

The validated activPAL and GT3X+ (applying RA-specific accelerometer cut-points developed in Chapter 2) for measurement of free-living sedentary time and PA was employed in a longitudinal study (Chapters 4-6) within this thesis. Objective assessment of free-living sedentary time and PA in different populations has been recommended across the literature to generate more accurate estimates than those provided by methods offering a more subjective measure of these behaviours (e.g., self-report) (Atkin et al., 2012; Janz, 2006). With regard to count-based accelerometry, as well as employing population-specific cut-points to determine time spent in different intensities of free-living behaviour, the researcher must select non-wear criteria which has been termed the "structural foundation in the data reduction process" (Semanik et al., 2010). This involves deciding on how many minutes of consecutive '0' counts constitute the participant not wearing the device, as opposed to them being sedentary. Indeed, activity counts representing sedentary time can include '0' (e.g., ≤244 counts/min), and therefore this process is critical to the accurate exclusion of 'non-wear time' and inclusion of 'sedentary time'. In the longitudinal studies of this thesis, non-wear criteria = ≥60 min of consecutive '0' counts (with a spike tolerance of 2 min) was applied to RA patients' accelerometer data. Recent evidence suggests that ≥90 min of consecutive '0' counts may be more appropriate to apply to accelerometer data in populations with reduced physical function, who may spend longer periods of time engaged in sitting/reclining/lying behaviours (e.g., older adults) (Choi et al., 2012). However, both these criteria have been advocated by (Semanik et

al., 2010) for the RA population, and ≥60 min of consecutive ‘0’ counts have been applied in previous accelerometry studies in this patient group (Fenton et al., 2017; Fenton et al., 2018c).

Compliance was high for both devices employed in these studies, but more so for the activPAL. The activPAL has demonstrated good compliance in different populations which, in part, has been attributed to the 24h/day wear protocol typically employed (Dall et al., 2018; Edwardson et al., 2017). Despite a 24h/day protocol improving compliance relative to that of accelerometers (Edwardson et al., 2017), it also results in time-consuming and challenging extraction of sleep-time from raw data. Winkler et al. (2016) have recently developed an algorithm for identifying periods of sleep in activPAL raw data, in order for these to be subsequently removed. However, the authors acknowledged that this algorithm may not be suitable for populations with impaired mobility (e.g., people with RA), as these individuals had minimal representation in their study.

With this in mind, longitudinal studies in this thesis derived waking sedentary, standing and stepping time, by identifying sleep periods from wear time logbooks and parallel GT3X+-derived sleep periods (period of non-wear). The GT3X+ provided a relatively sound indicator of waking vs. sleep time, as participants were instructed to remove the GT3X+ when they went to bed, and replace it when they woke up. These estimates were corroborated with data from wear time logbooks and close inspection of activPAL raw data. Specifically, free-living behaviour was being classified by the activPAL as ‘sitting/lying’ at the point of GT3X+ removal, and non-sedentary behaviour (‘standing’ and ‘stepping’) resumed at the point of GT3X+ replacement. Still, despite this aiding the process of manual sleep removal from activPAL data, there are some issues with this approach. For example, the GT3X+ demonstrated lower compliance relative to that of the activPAL, which meant that data relating to device removal/replacement was unavailable for days where the aforementioned non-wear

criteria excluded GT3X+ data from subsequent analysis (e.g., valid GT3X+ data for 4 days vs. valid activPAL data for 7 days). To address this limitation, we were able to refer to wear time logbooks only, which may have presented issues concerning the accuracy of self-report. Further, even when GT3X+ data were valid, such removal/replacement times may not have represented actual sleep periods. For example, participants may have gone to bed, removed the GT3X+ and then read a book for 45 min (waking sedentary behaviour). Alternatively, participants may not have replaced the GT3X+ immediately after waking. In an attempt to address this, participants were asked to keep wearing the GT3X+ in bed until 'lights off' and replace the device at 'lights on'. Future research should focus on data reduction methods that can accurately identify sleep periods from activPAL data in people with RA.

Despite the superior validity and reliability of device-based measures of sedentary behaviour and PA relative to self-report, accelerometers and posture sensors are limited by their inability to gauge the context in which free-living behaviour occurs. Gathering contextual information regarding sedentary behaviour is a critical area for future research in people with RA, to explore the 'types' of sedentary behaviour that predominantly accumulate towards their total sedentary time. This is because some sedentary behaviours have been suggested as beneficial for psychological well-being and cognitive function (e.g., reading, social activities), or essential during day-to-day life (e.g., eating), relative to more 'passive' sedentary behaviours (e.g., watching television) in different populations (Chastin et al., 2017; Hallgren et al., 2019; Hallgren et al., 2018). Indeed, it has been reported that RA patients engage in needlework and reading the newspaper ('mentally active' sedentary behaviours), as well as watching the television ('passive' sedentary behaviours) (Thomsen et al., 2015). Thus, given that people with RA have compromised mental health (Fiest et al., 2017), it might be that some sedentary

behaviours should not be reduced in this population. This has also been noted for intervention development in older adults (Chastin et al., 2017).

Currently, no single measure exists that can assess all components of 'SITT' (Healy et al., 2011a; Tremblay et al., 2010), and would provide accurate information regarding the levels of sedentary time, patterns of accumulation and the context in which these behaviours occur. However, attempts can be made to assess as many facets of 'SITT' as possible using multiple measures, without placing too much of a burden on the participant. For example, future research in the RA population could employ self-report instruments or Ecological Momentary Assessment (real-time sampling of behaviour and experiences) in combination with the activPAL (Bann et al., 2015; Rosenberg et al., 2016; Shiffman, Stone, & Hufford, 2008), to provide estimates of sedentary, standing and stepping time, as well as indicating the context in which these behaviours took place. With this in mind, self-report measures of sedentary behaviour should be evaluated in terms of how suitable they are for people with RA, in order to increase the likelihood of accurate responses. This investigation has been conducted in patients with multiple sclerosis, whereby qualitative interviews gained insight into how patients respond to the content of currently employed sedentary behaviour questionnaires (Hensman et al., 2019).

Shifting from the *measurement* of sedentary behaviour and PA ('Phase 2' of the Behavioural Epidemiology Framework [BEF]), 'Phase 1' of the BEF requires research to determine the associations between behaviour (e.g., sedentary behaviour, assessed employing validated measures from 'Phase 2') with *health* in the target population, to rationalise the importance of the development and delivery of behaviour change interventions. Chapter 4 of this thesis has provided the first evidence for longitudinal associations between objectively-assessed sedentary time and PA with pertinent aspects of RA health, and has indicated these

associations may be bi-directional in nature. These reciprocal relationships supported the assertion that interventions to reduce sedentary time may have the scope to improve clinically- and patient-important outcomes in RA. For example, longitudinal (and bi-directional) associations were revealed between self-reported pain and fatigue, with activPAL-assessed sedentary (positive) and standing (negative) time. However, these RA health outcomes were only measured at the end of the 7-day study week – given that pain and fatigue might fluctuate day-to-day in an individual living with RA (e.g., due to a flare-up), it might be apt to assess these symptoms daily, via diaries or questionnaires, in future research. This would heighten the burden placed on the participant, but could provide more accurate assessments of these particular RA symptomology.

Findings pertaining to patients' quality of life ('physical health'), as measured by the World Health Organisation Quality of Life Questionnaire (WHOQOL-BREF) should be interpreted with caution, given its low internal reliability for this sample. This was attributed to the fact that the 'physical health' domain was extracted for analysis, reducing the number of items from the questionnaire (Tavakol & Dennick, 2011). Indeed, the WHOQOL-BREF in its entirety showed high internal reliability (α = .86).

Future studies should consolidate these findings by analysing these associations in larger, more diverse samples of people with RA. A larger sample size would allow for testing more sophisticated bi-directional models, specifically to investigate whether health variables at Time Point 1 (T1) predicts change in the behaviour variable at Time Point 2 (T2), and vice versa. In addition, despite overcoming some issues of a cross-sectional design, this longitudinal study remains observational in nature, meaning cause and effect cannot be established. Thus, the relationships emerging from these data must be tested using more rigorous experimental study designs.

Intervention studies ‘controlling’ reductions in free-living sedentary time to examine associations with health outcomes in RA should be designed. However, it might be a challenge to ‘control’ levels of sedentary time in a free-living environment to ensure that the ‘dose’ of behaviour change required to examine associations with health is achieved. Acute experimental studies allow for superior control, and could be designed to examine whether prolonged sitting/reclining/lying (e.g., 3-5h of continuous sedentary time in a laboratory) (Trinity, 2017) has a dose-response relationship with, for example, RA inflammatory disease activity. This would also serve to provide some insight into the mechanistic processes underlying sedentary time in people with RA. Indeed, on the basis of emerging evidence for the association between sedentary time and inflammation, Fenton and Kitas (2016) hypothesised a cyclical relationship between sedentary time, inflammation and pertinent aspects of RA health. Specifically, high levels of sedentary time in RA may exacerbate already elevated systemic inflammation in these patients and contribute to the progression of RA outcomes, which in turn, may lead to high levels of sedentary time (‘sedentary-inflammation hypothesis’). Thus, based on results from Chapter 4, future studies could test this hypothesis to examine the mediating role of hsCRP in relationships between sedentary time and pertinent RA outcomes (e.g., pain, fatigue, physical function).

With this in mind, future research could also examine other inflammation-driven health outcomes in RA not explored in this thesis. Indeed, the selected health variables (DAS-28, hsCRP, physical function, quality of life, subjective vitality, depressive symptoms) will not be the *only* clinically- and patient-important disease outcomes potentially affecting *and* being affected by sedentary behaviour change in RA. Specifically, sedentary time only accounted for between 7%-21% of the variance in RA outcomes in the longitudinal study. For example, future studies might seek to examine the relationship between sedentary time with cardiovascular

disease (CVD) risk, elevated in these patients due to the heightened inflammatory burden of RA (Avina-Zubieta et al., 2012). Preliminary cross-sectional research has been conducted in this area (Fenton et al., 2018a; Fenton et al., 2017), but prospective studies could offer more insight into how change in sedentary time is associated with change in CVD risk (e.g., employing the QRISK-3) over time. Additionally, acute studies examining the mediating role of inflammation in this relationship might specifically examine hsCRP, which is an indicator of CVD risk in people with RA (>3 mg/l = 'high' risk of CVD; >10 mg/l = 'very high' risk of CVD) (Graf, Scherzer, Grunfeld, & Imboden, 2009).

Underlying all longitudinal studies of this thesis, is the strong inverse correlation observed between sedentary time and standing time in people with RA (ß = -.95). This is indicative of the proposition that 'non-exercise' behaviours (sedentary behaviour and LPA) comprise most of the waking day in people with RA (Hammam et al., 2019; Summers et al., 2019). Replacing sedentary time with standing could represent an avenue through which behavioural interventions could attenuate the negative health outcomes in RA. We did not test this proposition, but this could be examined via; 1) isotemporal substitution analysis using free-living device-assessed sedentary time and PA data, and 2) acute experimental studies. For example, isotemporal substitution models have shown that replacing sedentary time (e.g., 30 min) with LPA holds positive associations with physical function in older adults (Buman et al., 2010). Isotemporal substitution analysis may offer insight into the potential of replacing sedentary time with standing in this population, but cannot confirm directly, the health consequences of sedentary behaviour change (Keadle, Conroy, Buman, Dunstan, & Matthews, 2017). This could be addressed in acute experimental studies, whereby laboratory-based studies might examine the effects of interrupting sitting with standing (and more broadly, LPA)

on different health outcomes (Crespo, Mullane, Zeigler, Buman, & Gaesser, 2016), such as inflammatory biomarkers in RA.

Further, a recent line of thinking stipulates considering *all* behaviours undertaken during a 24-h period when examining the links between specific behaviours with health. Namely, compositional analysis should be considered in future research with the RA population that takes into account the independent and interacting impact of sleep, sedentary behaviour and PA when making conclusions about their associations with disease outcomes (Chastin, Palarea-Albaladejo, Dontje, & Skelton, 2015b). Future research should also consider the effect autonomous and controlled motivation to reduce sedentary behaviour has on different interrelating behaviours during a 24-h period in people with RA. Specifically, to identify whether autonomous and controlled motivation to reduce sedentary behaviour holds significant associations with sedentary time, aside from and together with the relationships it may have with PA (e.g., LPA, and specifically standing). However, there are a severe lack of instruments specifically measuring autonomous and controlled motivation <u>to reduce sedentary behaviour</u> in any population. To our knowledge, the only instrument that has been developed in this context, grounded in SDT, is the Motivation to Limit Screen-time Questionnaire (Lubans et al., 2013). This questionnaire was developed in adolescent boys and based on items of the BREQ-2. Thus, for use in Chapters 5 and 6 of this thesis, we adapted the BREQ-2 for measurement of autonomous and controlled motivation <u>to reduce sedentary behaviour</u> in people with RA. Although this scale demonstrated high internal reliability, (α = .81 and α = .87 for autonomous and controlled motivation, respectively), we were not able to test the measurement validity of the adapted BREQ-2 for measuring quality of motivation to reduce sedentary behaviour in this patient group. This should be addressed in future research.

Studies comprising Chapters 5 and 6 did not specifically investigate links between external, introjected, identified and intrinsic regulations to reduce sedentary behaviour, with levels of sedentariness and PA in RA. Instead, autonomous and controlled motivation to reduce sedentary behaviour were calculated (autonomous motivation = identified regulation + intrinsic regulation; controlled motivation = external regulation + introjected regulation) for statistical analysis. This method is consistent with previous research (Yu et al., 2015a; Vancampfort et al., 2013) and reduced the number of variables in regression models to increase statistical power, partly addressing the limitations associated with a small sample size in this thesis. Nevertheless, examining each regulation individually could provide insight into whether one regulation was 'driving' the emerging associations to a greater extent than another. Indeed, research in a sports context has supported distinguishing between regulations in data analysis to gain a clearer and advanced understanding of the relationships between motivation with short-term and long-term behaviour (Gillison, Osborn, Standage, & Skevington, 2009; Pelletier, Fortier, Vallerand, & Briere, 2001). For example, introjected regulation has been related to short-term maintenance of exercise via promoting autonomy, and represents progression towards internalisation of behaviour (Gillison et al., 2009; Pelletier et al., 2001). As stipulated in Chapter 3, this was preliminary work which aimed to examine the presence of relationships between, broadly, quality of motivation to reduce sedentary behaviour with device-assessed sedentary time and PA in people living with RA. Based on findings from the studies in Chapters 5 and 6, future research now has a rationale for investigating the role of external, introjected, identified and intrinsic regulations in sedentary behaviour and PA engagement/disengagement in this population, to further inform sedentary behaviour change interventions.

Amotivation was not included in statistical analysis in this thesis, as it is not considered a facet of autonomous or controlled motivation. Amotivated individuals "do not act, act without intent, or lack the intention to act" (Pelletier et al., 2001), and this state could have adverse implications if directed towards healthy behaviours (e.g., reducing sedentary behaviour, engagement in PA). Although beyond the scope of this body of work, future research should examine the relationships between amotivation to reduce sedentary behaviour with levels of sedentary behaviour and PA, and in turn, clinically- and patient-important health outcomes in RA.

In addition, this thesis (Chapters 5 and 6) did not incorporate all tenets of SDT that might have been relevant to levels of sedentary time and PA in people with RA. An additional sub-theory of SDT, namely basic psychological needs satisfaction theory, postulates that humans have 3 basic psychological needs that enable them to foster intrinsic motivation. Specifically, 'autonomy', 'competence' and 'relatedness' (Deci & Ryan, 2000). Fulfilment of these needs leads to fostering more autonomous motivation towards a behaviour, as well as benefits in mental health (e.g., vitality and well-being) (Ryan & Deci, 2000). Thwarting these basic psychological needs results in more controlled motivation towards behaviour (Bartholomew, Ntoumanis, Ryan, & Thogersen-Ntoumani, 2011; Bartholomew, Ntoumanis, & Thogersen-Ntoumani, 2010). SDT suggests the social environment is central to the satisfaction of these basic needs, and holds implications for encouraging behaviour change through promoting more autonomous motivation (Deci & Ryan, 1987, 2000, 2008a, 2008b; Ryan & Deci, 2000). Specifically, the provision of autonomy support from an 'important other' (e.g., peer, parent, spouse, healthcare professional) is reported to hold positive implications for need satisfaction, quality of motivation and behavioural engagement.

Basic psychological needs satisfaction theory was not applied in this study. However, to date, research has not rigorously investigated quality of motivation for reducing sedentary behaviour as a determinant of free-living sedentary time in RA. Thus, prior to examining the basic psychological needs and their contribution to autonomous or controlled regulation, whether or not autonomous or controlled motivation to reduce sedentary behaviour is associated with free-living sedentary time in RA must first be established. For the same reason, autonomy support from an 'important other' was not examined in this study. Table 7.1 suggests ways in which autonomous motivation to reduce sedentary behaviour could be targeted, via satisfaction of the basic psychological needs, in future interventions in this patient group.

Other limitations arising from the longitudinal studies of this thesis relate to the sample. First, data from the same sample was used throughout studies in this thesis, which could have inflated the risk of Type 1 error (e.g., in regression analysis). Second, only n = 54 participants returned for 6-month follow-up (reduced to n = 53 and n = 51 based on valid activPAL and GT3X+ data, respectively). However, this was predominantly attributed to termination of data collection, and *not* due to participants wishing to no longer undertake further visits. In addition, no significant differences were found (via *t*-test and chi-square analysis) between participants included at T2, and those lost to 6-month follow-up regarding demographic, RA duration and treatment regimen, health and behaviour variables. Still, despite applying bootstrapping to overcome some of the issues of small sample sizes (Scharkow, 2017; Wood, 2004), limitations remained in relation to particular statistical analysis. For example, path analysis in Chapters 4 and 6 could not be conducted using full measurement models (structural equation modelling). For Chapter 4, this meant that bi-directional models could not explore the relationships between change in health variables and change in sedentary time in path models (and vice versa; diagonal paths in Figure 4.2) – prior regressions were required to explore these relationships

before testing for bi-directional associations in path analysis. Additionally, hypothesised models of sedentary behaviour change in Chapter 6 were not tested as full measurement models, whereby BREQ-2 questionnaire items were separate latent variables. Further, in both cases, multiple behaviours (e.g., sedentary and standing time) could not be included in the same model. However, the latter approach may have resulted in multicollinearity between these behaviours, as they comprise most of an RA patient's waking day (Fenton et al., 2017; Paul et al., 2014; van der Ploeg & Hillsdon, 2017).

Finally, generalisability of all findings from the present thesis are limited to the characteristics of the sample. RA patients were recruited from 1 hospital from a somewhat small geographical location in the UK. The sample also predominantly consisted of women and participants had an average age of 58 years old. Further, participants had moderate disease activity and severity. Yet, these descriptions are mostly representative of the RA population, where there is a higher prevalence of females and onset of disease usually occurs beyond the age of 30 (Wasserman, 2018). Furthermore, participants' height, weight, BMI, body fat percentage, disease activity (DAS-28), disease severity (HAQ) and disease duration in this thesis, closely represented descriptive data from previous studies in this patient group (Metsios et al., 2009; Sokka et al., 2008; Stavropoulos-Kalinoglou et al., 2013).

Table 7.1 Potential intervention strategies that could promote autonomous motivation by targeting the basic psychological needs of autonomy, competence and relatedness

Intervention strategy	Description	Behaviour change technique	Targets
Seminars/discussions – small group	• Researcher develops rapport with patients • Interactive and educational for the patient • Researcher provides patients with the definition of sedentary behaviour • Researcher outlines current guidelines regarding reducing sedentary behaviour* • Discuss benefits of reducing sedentary behaviour* • Discuss consequences of prolonged sedentary behaviour* • Discuss realistic ways in which patients could reduce sedentary behaviour on a daily basis (e.g., get off the bus a stop earlier than planned)* o These seminars could also take place with the patient, their family, friends and healthcare professionals to provide social support/encouragement (training might take place in order that this fosters autonomy and is not controlling)*	Provide information about the link between sedentary behaviour with health Provide general encouragement Plan social support	Autonomy Competence Relatedness
One-to-one session	• Researcher develops rapport with the patient • Interactive • Discuss the meaning of sedentary behaviour for the patient and their reasons for reducing sedentary behaviour* • Discuss barriers (and facilitators) to reduce sedentary behaviour that the patient faces on a daily basis* • Discuss specifics about the time of day whereby the patient is most/least likely to reduce sedentary behaviour* • Discuss realistic ways in which the patient could reduce sedentary behaviour on a daily basis (e.g., stand and do not sit whilst on the telephone)* • Patient-centred goal-setting • Researcher encourages incremental goal-setting to reach a 'total sedentary behaviour reduction time'* • Patient chooses how they would like to self-monitor behaviour/goals (e.g., paper checklist, smartphone app, device measuring sedentary behaviour)* • Patient schedules future contact (e.g., phone or face-to-face) with researcher to discuss progress with goals (review and adapt as necessary – patient-centred) • Patient writes behavioural contract o These sessions could also take place with the patient, their family, friends and healthcare professionals to provide social support/encouragement (training might take place in order that this fosters autonomy and is not controlling)*	Provide general encouragement Identify barriers to reducing sedentary behaviour Time management Prompt specific goal-setting Graded tasks Self-monitoring of behaviour Motivational interviewing Behavioural contract Plan social support	Autonomy Competence Relatedness

Prompting behaviour change	• Researcher encourages patients to adhere to goals they have set (e.g., smartphone app, phone call, text message) • Researcher reminds patients of the benefits of reducing sedentary behaviour* • Researcher reminds patients of the consequences of prolonged sedentary behaviour* • Researcher encourages patients to keep self-monitoring behaviour/goals with their preferred method of doing so o Prompting can also be provided by the patient's family, friends and healthcare professionals to provide social support/encouragement (training might take place in order that this fosters autonomy and is not controlling)*	Prompt practice Provide general encouragement Provide information about the link between sedentary behaviour with health Motivational interviewing Plan social support	Autonomy Competence Relatedness
One-to-one session	• Researcher provides the patient with positive support for achievement of goals • Discuss barriers overcome to achieving goals • Discuss the facilitators to achieving goals • Discuss any beneficial outcomes measured that may have resulted from achieving goals (e.g., disease activity, pain, fatigue, functional disability, quality of life, psychological well-being, CVD risk, social life) • Patient not achieving goals is encouraged by what they have achieved (e.g., focusing on sedentary time on one day compared to another – unlikely to be identical and one estimate will be lower than another – compare to self, not other patients) • Patient not achieving goals reflects on why, and strategises how this can be addressed • Discuss the meaning of sedentary behaviour and the reasons for reducing sedentary behaviour, with the patient • Discuss long-term plans for reducing sedentary behaviour – patient identifies situations that may result in reverting to previous sedentary behaviour levels, researcher helps the patient with plans to avoid or cope with these situations • Plan social support (family, friends, healthcare professionals)	Provide contingent rewards (e.g., praise, encouragement) Provide feedback Motivational interviewing Relapse prevention Plan social support	Autonomy Competence Relatedness

Note: * main areas requiring future research in order to further inform sedentary behaviour change interventions in this patient group
Behaviour change techniques have been informed by the Taxonomy of Behaviour Change Techniques (Abraham & Michie, 2008).

Conclusion

This thesis provides pertinent preliminary evidence, addressing ‘Phase 1’ to ‘Phase 3’ of the BEF, and highlights areas for future research. The accurate measurement of free-living sedentary behaviour and PA in people with RA is vital to understand dose-response relationships between sedentary behaviour and PA with RA health, identify salient determinants of such behaviours to be targeted in interventions, and subsequently evaluate the efficacy of such interventions for improving RA health. Thus, the first empirical chapter of this thesis took essential first steps to extensively validate 2 readily-employed device-based measures (activPAL and GT3X+) of sedentary time and PA in this patient group.

These devices were subsequently employed in the longitudinal studies comprising Chapters 4 to 6, which generated novel data regarding the role of sedentary behaviour and PA in RA health, and developed understanding regarding how these behaviours may be targeted through intervention. First, bi-directional associations were revealed between clinically- and patient-important RA disease outcomes with activPAL-assessed sedentary and standing time. This suggested there is scope to intervene to decrease sedentary time, in order to reduce the burden of disease for people with RA. The inverse relationships observed between standing time with these outcomes compared to sedentary time, also highlighted that replacing sedentary time with standing may offer a potential self-management strategy to improve pertinent aspects of RA health.

Building on this, SDT-based psychosocial determinants of sedentary behaviour and PA were investigated. Results demonstrated that autonomous motivation to reduce sedentary behaviour was significantly associated with activPAL-assessed sedentary and standing time in people with RA. Finally, models of sedentary behaviour change were tested, which sought to bring together a new understanding of the role of sedentary time for health in RA, and the

malleable determinants of this behaviour. Results suggested that autonomous motivation to reduce sedentary behaviour was associated with sedentary and standing time, and in turn, several clinically- and patient-important RA disease outcomes.

Together, the results of this thesis suggest that autonomous motivation to reduce sedentary behaviour may represent a modifiable determinant of sedentarity, and thus a viable intervention target in people with RA. In addition, this thesis provides the first evidence to indicate that addressing autonomous motivation to reduce sedentary behaviour in RA may encourage changes in this behaviour, to the extent that it might attenuate the burden of RA disease. However, experimental research is required to establish the value of SDT-informed interventions to reduce sedentary behaviour, and subsequently improve important health outcomes among people living with RA.

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APPENDIX 1: Information sheet and consent forms

APPENDIX 2: ActivPAL and ActiGraph GT3X+ wear time logbooks for longitudinal study

APPENDIX 3: Questionnaires for longitudinal study

APPENDIX 1

INFORMATION SHEET AND CONSENT FORMS

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Participant information sheet

Study title: Sedentary Behaviour and Physical Activity in Rheumatoid Arthritis and Osteoarthritis

IRAS ID: 198880

- Thank you for taking the time to read this information sheet. We would like to invite you to be a part of this research project. In order for you to take part we require your informed consent. After reading this information sheet, if there is any further information that you would like then please do not hesitate to contact us.

- Your participation in the study is entirely voluntary.

- Before you decide whether or not you would like to take part, it is important to understand why the research is being done and what it will involve you doing. Please read the following information carefully, and please ask us if there is anything else you would like to know.

- Parts 1 and 2 tell you what the study is about and what will be asked of you if you decide to take part.

- Part 3 gives you more detailed information about the way the study will be run.

Please take time to decide if you wish to consent to take part in the study.

Part 1

1. Why are we doing this research?

There are 2 aims to this study which are outlined below.

Aim one: The main aim of this study is to investigate the physical (e.g., pain and fatigue), psychological (e.g., wellbeing and motivation), and environmental (e.g., your perception of the local environment, local safety, and availability of green space) factors that may be associated with sedentary behaviour (i.e., the time you spend sitting or reclining) and levels of physical activity engagement amongst patients with Rheumatoid Arthritis and Osteoarthritis.

We also want to investigate how sedentary behaviour patterns and levels of physical activity engagement affect health (e.g., cardiovascular disease risk and psychological wellbeing) in patients with Rheumatoid Arthritis and Osteoarthritis.

There is currently little information available on the above relationships in Rheumatoid Arthritis and Osteoarthritis - this research will begin to help our understanding. We hope to be able to use the information obtained from this research, to help develop interventions that will enable and empower people with Rheumatoid Arthritis and Osteoarthritis to manage their symptoms through leading more physically active lifestyles.

Aim two: A secondary purpose of the study is to assess the accuracy of 2 different movement sensors (the GT3X accelerometer and the activPAL postural movement sensor) to measure physical activity and sedentary behaviour in people with Rheumatoid Arthritis. This is important to ensure that future studies using these devices in people with Rheumatoid Arthritis are assessing physical activity and sedentary behaviour accurately.

2. Why have I been chosen?

You have been approached to take part in this study because you are over 18 years old. The study will begin in September 2016 and will include up to 250 adults with Rheumatoid Arthritis and a further 250 adults with Osteoarthritis. We would like you to take part in this study for 2 'study weeks' separated by a 6-month period.

3. Do I have to take part?

No, your participation is entirely voluntary and you are free to withdraw at any stage without reason or consequences. **You have the option** to take part in **only aim 1 or aim 2,** or **both aim 1 and aim 2**.

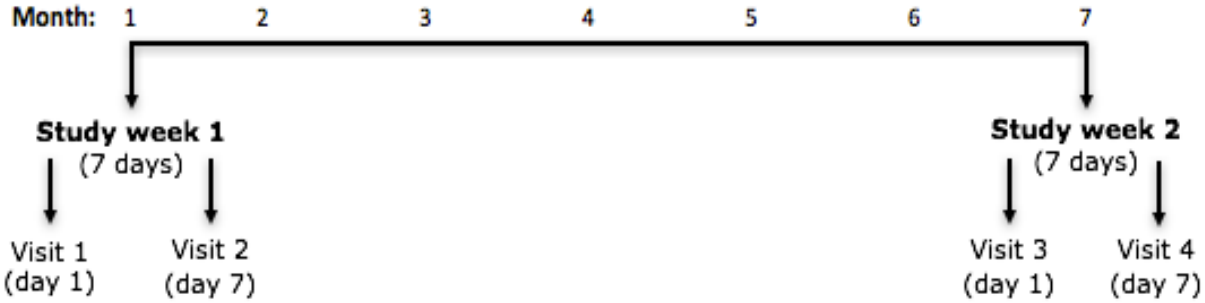
The sections below describe what you will be asked to do if you consent to take part in aim 1 and/or aim 2.

Aim 1

1. What will happen if you decide to take part?

You will be part of the study for 6-7 months. During this period, you will be asked to complete 2 study weeks. Each study week will take place over 7 days, and will occur 6 months apart. During this 6-month period, you will receive your usual medical care as required and we will ask you to continue with your normal activities of daily life – there will be no intervention (i.e., we will not ask you to change your behaviour in any way). We have chosen to use a 6-month gap between study week 1 and study week 2 as this will allow enough time for us to observe natural changes in behaviour and health which are required in order to determine if physical activity/sedentary behaviour are linked.

Each study week will start and end with a visit to the Clinical Research Unit at Russells Hall Hospital, Dudley. This means you will be asked to undertake 4 visits in total (i.e., visits 1, 2, 3 and 4). The diagram below shows a timeline of visits to the hospital.



Visits 1 and 3 (2 hours): Visits 1 and 3 will take place at the start of each study week. The same procedures will be completed during these visits.

Visits 2 and 4 (1.5 hours): Visits 2 and 4 will take place at the end of each study week. The same procedures will be completed during these visits.
You are allowed to bring a family member or friend with you to each visit. A member of the research team will carry out the study procedures.

The procedures that will be carried out during visits 1, 2, 3 and 4 are described below.

2. What will you have to do?

Screening
Before you can take part in the study, we will check your eligibility – you will be able to participate if you have a diagnosis of Rheumatoid Arthritis or Osteoarthritis, and can walk independently with the assistance of a walking aid or device if required. If eligible to take part, you will be asked to undertake the procedures outlined below.

Visits 1 and 3

The researchers, Ciara O'Brien or Sally Fenton, will carry out the following assessments:

- Resting blood pressure
  - Your blood pressure will be measured after you have rested for 5 minutes. A blood pressure cuff will be placed around your non-dominant arm and measurement taken.

- Disease Activity Score
  - Disease Activity Score-28 will be determined via counting the number of swollen and tender joints in the hands, elbows, shoulders and knees (i.e., the 28 joint count routinely used). Additional measures taken from the fasted blood sample (see below) will also help us calculate your Disease Activity Score-28.

- Fasted blood sample
  - This will be carried out using routine hospital procedures. Blood will be taken from the inside of your arm (or the back of the hand can be used). You may bring a family member or close friend with you for this procedure.

- Measurements of height, weight, and body composition
  - Body composition will be measured using the Tanita Scales (image below). After measurement of your height, you will be asked to stand on the scales and hold the scale handles for 20 seconds. This will tell us the composition of your body, in terms of the amount of muscle, fat, water and bone.

Tanita Scales

- 20-metre timed walk
  - The 20-metre timed walk test measures your speed and physical function. We will ask you to wear comfortable shoes and walk at a comfortable pace from a 'start line' to a 'finish line', 20 metres apart. The researcher will record the amount of time taken to complete the task.

- Questionnaires
  - You will be asked to complete several questionnaires that will assess the following:
    - Your perceptions of the physical environment (e.g., how close is your home to green space)
    - Your perceptions of the social environment (e.g., support from family and friends for physical activity)
    - Aspects of your physical and psychological health and wellbeing (e.g., your vitality, pain, fatigue)

At the end of visits 1 and 3, you will be invited to wear the GT3X accelerometer and activPAL postural movement sensor for a 7-day period (i.e., the 'study week'). We will ask you return these during visits 2 and 4. A member of the research team will fit you with the GT3X and activPAL, and we will provide you with written instructions on how to wear these. You will also be asked to complete a GT3X and activPAL log book and physical activity diary during the study week to help us interpret the data recorded by the GT3X and activPAL. These procedures are described in more detail below.

Study Week

Sedentary Behaviour and Physical Activity Monitors

GT3X: We will ask you to wear the GT3X accelerometer for 7 days during waking hours, and to only remove it for sleeping/bathing/water-based activities.
The GT3X is a light (27g) and small device (3.8 x 3.7 x 1.8 cm) worn on an elasticated strap on the waist on the right hip. This device can be worn either on top of or underneath your clothes.
A picture of the GT3X is shown here.

GT3X

ActivPAL: We will ask you to wear the activPAL continuously for 7 days (i.e., whilst awake and sleeping [for 24 hours a day]).
The activPAL is a light (15g) and small (3.5 x 5.3 x 0.7 cm) device that is worn on the thigh, and secured with a waterproof dressing.
A picture of the activPAL is shown here.

activPAL

Physical Activity Diary

You will be asked to complete a 3-day physical activity diary whilst wearing the GT3X and activPAL during the 7-day study week (i.e., on the Thursday, Friday and Saturday). In this diary, you will be asked to briefly report the activity being undertaken at 15-minute time intervals for each day.

Saliva Sample

On day 2 during the study week, you will be asked to provide 6 saliva samples. These samples will be collected immediately upon awakening, 30 minutes after-awakening, and then at 3, 6, 9, and 12 hours after-awakening. These samples will be collected in small test tubes that we will provide you with. Each tube will be labelled with the time of the collection, and we will ask you to set alarms on your phone to remind you to take the samples. We will ask you to

store these samples in your refrigerator and bring them with you when you return to the hospital at the end of the study week (i.e., visits 2 and 4).

Visits 2 and 4

On your second visit to Russells Hall Hospital, you will be asked to return the GT3X, activPAL, physical activity diary, and saliva samples. During this visit, the following assessments will be repeated in the same manner undertaken during visits 1 and 3:

- Fasted blood sample
- Disease Activity Score-28
- Questionnaires

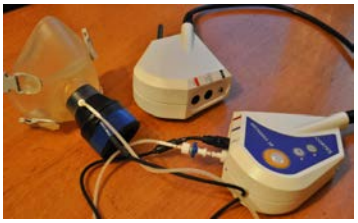
Aim 2

1. What will happen if you decide to take part?

When you consent to taking part in the main study (aim 1), we will ask you if you would like to take part in a sub-study (aim 2). If you decide to take part in aim 2, we will ask you to sign an additional consent form. All procedures relating to aim 2 of the study will be carried out during visit 2 to the hospital (i.e., at the end of the first study week). These procedures will take approximately 2 hours. This means that if you take part in both aims 1 and 2, visit 2 to the hospital will take about 3.5 hours.

2. What will you have to do?

If you consent to this part of the study, you will be asked to wear both the GT3X accelerometer and activPAL postural movement sensor whilst carrying out different activities in the laboratory in the hospital. These activities will be made up of some sedentary behaviours (e.g., doing a crossword and reading a newspaper) and some light to moderate intensity physical activities (walking on a treadmill at a slow to moderate pace). Whilst you undertake these activities, we will also ask that you wear a piece of equipment called an indirect calorimeter (shown in the images below), and we will request your permission to record the testing protocol via video camera.



The indirect calorimeter is worn using a mouth piece and a nose clip. This will enable measurement of your inspired and expired gases during the activities we ask you to undertake. If you become uncomfortable or tired at any time whilst undertaking these activities, you may stop participating.

Part 2

1. Where will I need to go to take part?

Participation in the project will take place in the Clinical Research Unit at Russells Hall Hospital, Dudley. You will be reimbursed for travel costs to the hospital.

2. What are the possible disadvantages and risks of taking part?

There are minimal risks to taking part. As with routine blood tests, you may feel a small pin prick whilst blood samples are taken, and experience dizziness or light-headedness. You may also have slight bruising in the area afterwards.

For those participants who take part in procedures related to study aim 2, you may feel tired or out of breath whilst undertaking the more moderate intensity activities.

You are able to bring a family member or friend with you whilst you participate in all parts of the study and can withdraw your consent to participate at any time.

3. What are the potential benefits of taking part?

Upon completion of the study, we will be able to provide feedback on some aspects of your general health (e.g., blood pressure and body composition). In addition, once you have worn the GT3X and activPAL for 7 days, we will be able to provide you with information relating to your physical activity and sedentary behaviour, such as the total time you spend sitting and being active each day. We will also be able to provide you with details of the results of the study once the data has been analysed and published in scientific journals.

4. What if there is a problem?

Detailed information about this is given in Part 3.

5. Will the personal data collected during the study be kept confidential?

Yes. All information collected during the study will be kept confidential. Data during study visits (i.e., physical, questionnaire and GT3X/activPAL data) will be anonymised (assigned a participant ID) and stored in locked filing cabinets and/or on password encrypted hard drives in the Clinical Research Unit at Russells Hall Hospital. This data will be accessed only by members of the research team. Biological samples will be analysed by laboratory employees. Once analysed, this data will also be anonymised and accessed only by members of the research team. Data to be used at the University of Birmingham will be anonymised and

transferred to password encrypted electronic data files for use only by members of the research team.

All data in paper form will be stored in locked filing cabinets within an archive room at Russells Hall Hospital for 10 years after study completion. Only Clinical Research Unit staff and members of the research team will have access to this archive. Electronic data will be stored in encrypted files on external hard drives belonging to the University of Birmingham and Russells Hall Hospital, and accessed only by members of the research team. This data will be destroyed 10 years after study completion. Biological samples will be stored in the laboratory at Russells Hall Hospital until disposal 10 years later.

More information regarding confidentiality may be found in Part 3.

6. Contact for further information

If you require further information, please feel free to contact the people below and ask any questions you wish.

Ciara O'Brien, MSc.
Doctoral Researcher
E-mail:
Telephone:
School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham
Edgbaston, Birmingham, B15 2TT

Dr Sally Fenton
Research Fellow
E-mail:
Telephone:
School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham
Edgbaston, Birmingham, B15 2TT

Thank you for reading so far. If you are interested to find out more, please read Part 3 before making any decision.

Part 3

1. What happens if new information about the study becomes available?

Sometimes new information arises whilst a study is still happening, and this may affect your willingness to continue to participate in the study. If this happens, your study researcher will discuss with you whether or not you want to continue in the study. If you decide to withdraw from the study, you are free to do so. If you decide to continue in the study, you may be asked to sign an updated assent/consent form containing the new information.

Also, on receiving new information, your study researcher might consider it to be in your best interests for you to withdraw from the study. Your researcher will explain the reasons if this should occur.

2. What will happen if I do not want to carry on with the study?

Your participation in the study is voluntary and you may withdraw at any time without a reason.

3. What if there is a problem?

Complaints: If you have a concern about any aspect of this study, you should contact Ciara O'Brien or Dr. Sally Fenton (contact details above). They will do their best to answer any questions you may have. If you are still unhappy and wish to make a formal complaint, you can do this using the NHS complaints procedure. Staff at Russells Hall Hospital will be able to inform you how to do this.

The Patient Advice and Liaison Service can also be contacted to answer any queries you may have. You can contact PALS by email at pals@dgh.nhs.uk, by freephone on *0800-0730510*, or you can write to: *PALS Department, Russells Hall Hospital, Dudley, West Midlands, DY1 2HQ*

Harm: If you have an accident such as a fall, whilst undertaking any of the procedures in the hospital, Dudley Group of Hospitals NHS Foundation Trust and the University of Birmingham have the indemnity for this study. The researchers carrying out the study protocol are trained with regards to the procedures used. In addition, the Clinical Research Unit is staffed with research nurses should any incident occur. You are also able to have a family member or friend accompany you to the hospital should you wish.

4. Will anyone else know I am taking part in this study?

Yes. If you have given your consent to take part in the study, we will inform your GP that you are participating. All members of the research team will know you are participating and will have access to your data. However, your data will be kept anonymous and identified by a subject number. Any questionnaires, physical information and information regarding measures of sedentary behaviour/physical activity will be identified in the same way. No

personal details will be used in any presentations or publications as required by local/regional/national regulations. The information collected during the study is confidential.

5. What will happen to the results of the research study?

Once the study is complete, the results will be published and a final report written. You may contact the researcher if you would like to get copies of any information published. You will not be identified in any reports or publications.

6. Who is organising and funding the research?

The Dudley Hospital Research Rheumatology Fund, funds the researcher Ciara O'Brien, who will be carrying out this study as part of her PhD.

7. Who has reviewed this study?

This study has been reviewed by the local Research Ethics Committee (REC) and the Health Research Authority. It will be run in accordance with all suitable guidelines aimed at ensuring proper conduct and safety of anyone taking part, including the Guidelines on Good Clinical Practice and the Declaration of Helsinki.

8. What happens now if I decide to take part?

If you would like to participate, we will arrange a time for you to visit the Clinical Research Unit at Russells Hall Hospital to consent and begin the study. We will ask if you would like to take part in aim 1, aim 2, or both aims. If you wish to take part in both aims 1 and 2 of the study, we will ask you to sign 2 separate consent forms (1 for each aim). If you have any concerns/questions regarding this research/investigation, please contact us (details in Part 2). You are able to withdraw your consent for the study at any time.

On providing consent to take part in this project, you are agreeing to the anonymised results of the study being used for scientific purposes and with the results potentially being published in a scientific journal. Once you have given your consent we will arrange a time for you to take part in the study.

The Patient Advice and Liaison Service can also be contacted to answer any queries you may have about participating in this study. You can contact PALS by email at pals@dgh.nhs.uk, by freephone on *0800-0730510*, or you can write to: *PALS Department, Russells Hall Hospital, Dudley, West Midlands, DY1 2HQ*

Thank you for taking the time to read this information sheet.

UNIVERSITY OF BIRMINGHAM

The Dudley Group NHS
NHS Foundation Trust

Participant Consent Form: Study Aim One

Study title: Sedentary Behaviour and Physical Activity in Rheumatoid Arthritis and Osteoarthritis

IRAS ID: 198880

Name of Researcher taking consent:

Dear participant, in the boxes below please initial all statements you agree with. If you do not agree and do not wish to take part in this study, please do not initial the box.

1. I confirm I have read and understood the study information sheet. ☐
2. Somebody else has explained this study to me. ☐
3. I fully understand the purpose of this study. ☐
4. I have had the opportunity to discuss the study and ask any questions. ☐
5. I am satisfied with the explanations I have been given. ☐
6. I understand that my participation in the study is my choice and I may withdraw from the study at any time without reason and without my medical care being affected. ☐
7. I am happy to take part in the study and know that I will get a copy of this signed form and information sheet to take home. ☐
8. I understand that the relevant sections of my medical notes and data collected during the study may be looked at by individuals from regulatory authorities from the NHS trust where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
9. I would like to be contacted by the research team regarding opportunities to take part in future research at Russells Hall Hospital/University of Birmingham.

   Yes ☐

   No ☐

Participant

I ……. have read the study information sheet. I understand the purpose and design of the study. I hereby give my informed consent to take part in the above project, with the knowledge that I may withdraw at any time without giving a reason, and without the standard of my medical care being affected.

Signature …….. **Date** ……..

Name (print) ……..

Person taking consent

I confirm that I have explained the nature of the study to the participant in terms that they understand, outlining both benefits and risks. I confirm that he/she has given consent freely to partake in this study.

Signature …….. **Date** ……..

Name (print) ……..

UNIVERSITY OF BIRMINGHAM

The Dudley Group NHS
NHS Foundation Trust

Participant Consent Form: Study Aim Two

Study title: Sedentary Behaviour and Physical Activity in Rheumatoid Arthritis and Osteoarthritis

IRAS ID: 198880

Name of Researcher taking consent:

Dear participant, in the boxes below please initial all statements you agree with. If you do not agree and do not wish to take part in this study, please do not initial the box.

1. I confirm I have read and understood the study information sheet. ☐
2. Somebody else has explained this study to me. ☐
3. I fully understand the purpose of this study. ☐
4. I have had the opportunity to discuss the study and ask any questions. ☐
5. I am satisfied with the explanations I have been given. ☐
6. I consent to this study being video recorded. ☐
7. I am happy to take part in the study and know that I will get a copy of this signed form and information sheet to take home. ☐
8. I understand that the relevant sections of my medical notes and data collected during the study may be looked at by individuals from regulatory authorities of from the NHS trust where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

Participant

I ……. have read the study information sheet. I understand the purpose and design of the study. I hereby give my informed consent to take part in the above project, with the knowledge that I may withdraw at any time without giving a reason, and without the standard of my medical care being affected.

Signature …….. **Date** ……..

Name (print) ……..

Person taking consent

I confirm that I have explained the nature of the study to the participant in terms that they understand, outlining both benefits and risks. I confirm that he/she has given consent freely to partake in this study.

Signature …….. **Date** ……..

Name (print) ……..

ACTIVPAL AND ACTIGRAPH GT3X+ WEAR TIME LOGBOOKS FOR LONGITUDINAL STUDY

ActivPAL monitor logbook

We ask that you wear the activPAL postural movement sensor continuously (you can sleep and bathe/shower with the activPAL on). If you do decide to take off the activPAL (e.g., if you would like to change the dressing), please use this sheet to record all of the dates and times you took your monitor off and put it on during the week.
The first line below shows an example for a person on a Monday. This person took the activPAL off at 4pm, changed the dressing, and put it on again at 4.15pm.

Date:		**Date:**		**Date:**		**Date:**		**Date:**		**Date:**		**Date:**	
Monday		**Tuesday**		**Wednesday**		**Thursday**		**Friday**		**Saturday**		**Sunday**	
Off	4:00pm	**Off**		**Off**		**Off**		**Off**		**Off**		**Off**	
On	4:15pm	**On**		**On**		**On**		**On**		**On**		**On**	
Off		**Off**		**Off**		**Off**		**Off**		**Off**		**Off**	
On		**On**		**On**		**On**		**On**		**On**		**On**	
Off		**Off**		**Off**		**Off**		**Off**		**Off**		**Off**	
On		**On**		**On**		**On**		**On**		**On**		**On**	
Off		**Off**		**Off**		**Off**		**Off**		**Off**		**Off**	

GT3X monitor logbook

Please use this sheet to record all of the dates and times you put your monitor on and took it off during the week. Please always start each day by writing the time you put the monitor on in the morning. If you take the monitor off during the day, then please write this time directly underneath your first diary entry. You should then write the time you put the monitor on again in the row directly below this.

The first line below shows an example for a person on a Monday. This person put the monitor on at 9am. They then took it off at 4pm for a shower, and put it on again at 4.15pm. Finally, they removed the monitor at 10:30pm to go to bed.

Date:		**Date:**		**Date:**		**Date:**		**Date:**		**Date:**		**Date:**	
Monday		**Tuesday**		**Wednesday**		**Thursday**		**Friday**		**Saturday**		**Sunday**	
On	9:00am	**On**		**On**		**On**		**On**		**On**		**On**	
Off	4:00pm	**Off**		**Off**		**Off**		**Off**		**Off**		**Off**	
On	4:15pm	**On**		**On**		**On**		**On**		**On**		**On**	
Off	10:30pm	**Off**		**Off**		**Off**		**Off**		**Off**		**Off**	
On		**On**		**On**		**On**		**On**		**On**		**On**	
Off		**Off**		**Off**		**Off**		**Off**		**Off**		**Off**	
On		**On**		**On**		**On**		**On**		**On**		**On**	
Off		**Off**		**Off**		**Off**		**Off**		**Off**		**Off**	

QUESTIONNAIRES FOR LONGITUDINAL STUDY

Health Assessment Questionnaire (HAQ)

Please tick the one response which best describes your usual abilities over the past 2 weeks:

Dressing and Grooming:

Are you able to:	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
Dress yourself, including tying shoelaces and doing buttons?				
Shampoo your hair?				

Rising:

Are you able to:	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
Stand up from an armless straight chair?				
Get in and out of bed?				

Eating:

Are you able to:	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
Cut your meat?				
Lift a full cup or glass to your mouth?				
Open a new carton of milk (or soap powder)?				

Walking:

Are you able to:	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
Walk outdoors on flat ground?				
Climb up five steps?				

Please tick any aids or devices that you usually use for any of these activities:

Cane (W)	
Walking frame (W)	
Built-up or special utensils (E)	

Crutches (W)	
Wheelchair (W)	
Special or built-up chair (A)	
Devices used for dressing (button hooks, zipper pull, shoe horn)	
Other (specify)	

Please tick any categories for which you usually need help from another person:

Dressing and Grooming	
Rising	
Eating	
Walking	

Please tick the one response which best describes your usual abilities over the past 2 weeks:

Hygiene:

Are you able to:	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
Wash and dry your entire body?				
Take a bath?				
Get on and off the toilet?				

Reach:

Are you able to:	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
Reach and get down a 5 lbs. object (e.g. a bag of potatoes) from just above your head?				
Bend down to pick up clothing off the floor?				

Grip:

Are you able to:	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
Open car doors?				
Open jars which have been previously opened?				
Turn taps on and off?				

Activities:

Are you able to:	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	UNABLE to do
Run errands and shop?				
Get in and out of a car?				
Do chores such as vacuuming, housework or light gardening?				

Please tick any aids or devices that you usually use for any of these activities:

Raised toilet seat (H)	
Bath seat (H)	
Bath rail (H)	
Long handled appliances for reach (R)	
Jar opener (for jars previously opened) (G)	
Other (specify)	

Please tick any categories for which you usually need help from another person:

Hygiene	
Gripping and opening things	
Reach	
Errands and housework	

Physical Activity, Reducing Sedentary Behaviour, and Breaking Up Sitting Time

Key term	Definition	Examples
Physical Activity	Any movement by your body that works your muscles, and requires energy greater than resting.	• Walking the dog • Jogging • Playing tennis • Gardening • Yoga • Swimming
Sedentary Behaviour	Behaviour that uses very little energy whilst awake ***and*** sitting or reclining.	• Sitting down whilst watching TV. • Sitting down whilst doing a crossword puzzle. • Reclining whilst reading a book.
Reducing Sedentary Behaviour	Refers to your overall attempts to spend less time sitting or lying down, ***not*** just your attempts to more frequently interrupt periods of sitting with physical activity or standing (i.e., which is called breaking up your sitting time).	• Getting off the bus at a station before the station nearest to your destination so that you have to walk further and sit for less time. • Deciding to not watch TV for an hour, but to go out for a walk instead.

Behavioural Regulation in Exercise Questionnaire-2 (BREQ-2 [adapted – quality of motivation to reduce sedentary behaviour])

Please indicate to what extent you agree or disagree with each of the following items with regard to reducing sedentary behaviour and breaking up sitting time by circling a number in the table below; bear in mind how **you GENERALLY felt** during the **past 4 weeks.**

	I aim to reduce my sedentary behaviour…				
	Strongly Disagree	**Disagree**	**Neutral**	**Agree**	**Strongly Agree**
1. Because other people say I should	1	2	3	4	5
2. Because I feel guilty when I am not doing this	1	2	3	4	5
3. Because I value the benefits of doing this	1	2	3	4	5
4. Because it is fun	1	2	3	4	5
5. But I don't see why I should	1	2	3	4	5
6. Because my friends and family say I should	1	2	3	4	5
7. Because I feel ashamed when I am not doing this	1	2	3	4	5
8. Because it is important for me to try to do this on a regular basis	1	2	3	4	5
9. But I can't see why I should bother	1	2	3	4	5
10. Because I enjoy doing this	1	2	3	4	5
11. Because others will not be pleased with me if I am not doing this	1	2	3	4	5
12. But I don't see the point in doing this	1	2	3	4	5
13. Because I felt like a failure when I have not been doing this in a while	1	2	3	4	5
14. Because I think it is important to make the effort to do this regularly	1	2	3	4	5
15. Because I find doing this pleasurable	1	2	3	4	5
16. Because I feel under pressure from others to do this	1	2	3	4	5
17. Because I get restless if I am not doing this regularly	1	2	3	4	5
18. Because I get pleasure and satisfaction from doing this	1	2	3	4	5
19. But I think doing this is a waste of time	1	2	3	4	5